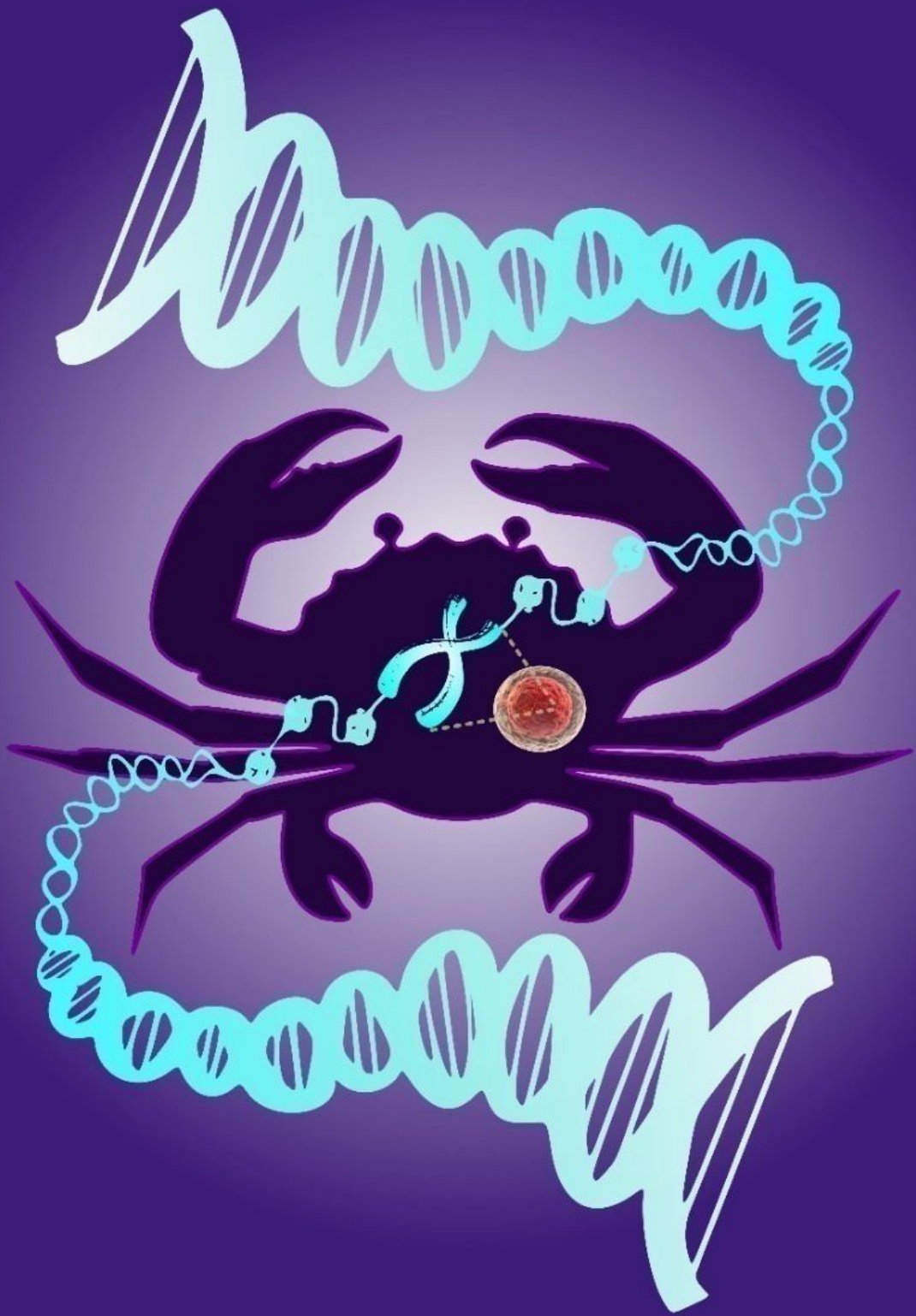
Current Oncological Abstract Service

COAS (Monthly)

December 2025, Volume 2 Issue 12



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Current Oncological Abstract Service (COAS)

Monthly

Aims of the Abstracts

The Current Oncological Abstract Service (COAS) aims to provide timely, curated abstracts from a broad spectrum of oncological literature. The objectives of the service are:

1. To deliver concise, up-to-date abstracts of recently published oncological research, covering various subfields such as medical oncology, radiation oncology, anesthesiology, surgical oncology, and hematology.
2. To assist healthcare professionals, researchers, and students in staying informed about the latest advances and trends in oncology.
3. To support clinical and research-based decision-making by providing quick access to relevant, high-impact studies.
4. To foster knowledge exchange across disciplines, promoting a broader understanding of cancer-related topics.

Scope of the Abstracts

1. COAS includes abstracts from areas such as cancer biology, genetics, epidemiology, clinical trials, and treatment modalities (e.g., chemotherapy, immunotherapy, and targeted therapies), as well as patient care practices.
2. Abstracts are sourced from global research publications, offering a comprehensive view of international advancements in oncology.
3. Priority is given to high-impact studies, systematic reviews, meta-analyses, and research with significant implications for clinical practice.
4. In addition to core oncology, abstracts may cover related fields such as molecular biology, pharmacology, palliative care, and psychological support in oncology, reflecting the interdisciplinary nature of cancer care.

Layout

The "Current Oncological Abstract Service" is designed as a targeted information resource that provides clinicians, researchers, and students in oncology with the latest research abstracts and developments in cancer-related fields. It offers a regularly updated collection of abstracts from recently published articles, journals, and reports in oncology to keep users informed about current research trends, treatments, diagnostic methods, and advancements in oncology. The service is delivered monthly via email and as a downloadable PDF available on the CNCI website.

Content Sections - The COAS includes summaries of:

- The latest and most impactful research papers.
- Updates on new treatments, drugs, and clinical trials.
- Abstracts on new diagnostic tools, biomarkers, and techniques.
- Insights into cancer prevention research and epidemiological studies.
- Information on palliative care, patient management, and supportive therapies.

Abstract Formatting Each entry in the Current Oncological Abstract Service (COAS) includes:

- The title of the article or study.
- Authors and publication details.
- A summary focused on key findings and relevance.
- Keywords for easier navigation.
- A direct link to the original source (if online access is available).

User Navigation

- An index organized by cancer types, treatment methods, and research areas to facilitate easy navigation.
- A searchable database on the web platform, allowing users to quickly locate relevant abstracts.

User Engagement

- **Feedback Mechanism**: Users can provide feedback on abstracts and suggest improvements.
- **Personalization**: Users can subscribe to specific categories or topics of interest.

Bibliographical Citation:

Title-The title of the paper is invariably given in English and non-English titles are translated into English.

Author-A maximum of ten author's names are given. In case of more than ten authors, names of first ten authors are given followed by et al.

Details-The title of the paper is followed by volume number, issue number (in parenthesis), pagination and the of publication. Late publication or late receipt of the journals (if any), language(s) and number of references cited in the publication are given in parenthesis.

Abstract-Abstracts are informative and comprehensive. New data or findings are specifically indicated.

Current Oncological Abstract Service (COAS)

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Compiler:

Dr. Sanmoy Chakraborty
Assistant **L**ibrary & **I**nformation **O**fficer

&

Mr. Ganesh Gorai
Assistant **L**ibrary & **I**nformation **O**fficer

Phone: 033 2475-9313, 033 3506-0600
Website: https://www.cnci.ac.in/
Email: cnci.library@gmail.com

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Current Oncological Abstract Service (COAS)

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Anesthesiology

25COASDEC01:

Title: An increase in skin blood flow after red blood cell transfusion is associated with an improvement in organ function in critically ill patients,

Elaine Cavalcante dos Santos, Péter Bakos, Diego Orbegozo, Hassane Njimi, Zoé Demailly, Jacques Creteur, Jean-Louis Vincent, Fabio Silvio Taccone,

Journal of Critical Care,Volume 90,2025,155204
https://doi.org/10.1016/j.jcrc.2025.155204.

Abstract: Red blood cell transfusions (RBCTs) are administered to critically ill patients to enhance tissue oxygen delivery. We investigated whether an increase in skin blood flow (SBF), a proxy for tissue perfusion, after RBCT was associated with improved organ function in non-bleeding intensive care unit (ICU) patients.This secondary analysis of a prospective cohort included 175 adult ICU patients without acute bleeding who received a RBCT. Finger SBF was measured at basal temperature (SBFBT) using skin laser Doppler before and one hour post-RBCT: patients with a ≥ 20 % increase in SBFBT were classified as SBF responders. Patients were also classified as having high (>73 PU) or low (≤73 PU) baseline SBFBT, based on the optimal pre-transfusion SBFBT threshold for predicting SBF response. Patients with a ≥ 1 point reduction in Sequential Organ Failure Assessment (SOFA) score within 24 h post-RBCT were classified as “SOFA responders”. The primary outcome was the association between SBF responder status and SOFA responder status.Of 175 patients, 103 (58.9 %) improved SOFA. There was a trend of more SBF responders in the SOFA responders than in the SOFA non-responders group (51/103 [49.5 %] vs. 26/72 [36.1 %]); p = 0.08), respectively. SBF responder status (n = 77, 44 %) independently predicted a decreased SOFA score post-RBCT (OR 2.64, 95 %CI 1.25–5.41, p = 0.01).An increase in SBFBT after RBCT was independently associated with a reduction of 1 point in SOFA score within 24 h after RBCT. These findings highlight the potential role of RBCT in improving tissue perfusion and organ function in acute illness.

Keywords: Red blood cell transfusion; Skin laser Doppler; Tissue perfusion; Critical care; Mortality; Organ dysfunction

25COASDEC02:

Title: External validation of eight different models to predict sepsis mortality in intensive care units,

Satyen Hargovan, Charlotte Simpson, Sayonne Sivalingam, Angus Carter, Ronny Gunnarsson,

Journal of Critical Care,Volume 90,2025,155174,
https://doi.org/10.1016/j.jcrc.2025.155174.

Abstract: Sepsis is a complex, heterogenous syndrome defined as life-threatening organ dysfunction due to severe infection. Existing mortality prediction models may not adequately capture the complexities of sepsis. The objectives of this study were twofold; to clarify to what extent variables belonging to eight different mortality prediction models used in intensive care units (ICU) were collected in routine medical care, and to externally validate these models.A retrospective cohort of 750 patients admitted to three ICU's with a final

diagnosis of sepsis at ICU discharge were included. Mortality prediction models were evaluated by calculating the area under receiver operating curve (AUROC) for their ability to predict 30-day mortality.The CSM-4, when used 4 h after ICU admission, predicted ICU episode-of-care mortality best with an AUROC of 0.80. It used only a few variables which are frequently retrieved in routine medical care. ANZROD 24 was the best performing model to be applied 24 h after admission with AUROC of 0.83.Time after admission may decide which prediction model is most useful. Early after ICU admission, the sepsis-specific CSM-4 mortality prediction model performed slightly better than other models. However, at 24 h after admission general models not specific for sepsis, like the ANZROD 24, performed well.
Keywords: Sepsis; Intensive care units; Mortality prediction; Area under curve; Validation study; Prognosis

25COASDEC03:

Title: Sepsis-associated liver dysfunction confounds the association between circulating PCSK9 concentration and mortality in septic patients: A single-center retrospective cohort study,

Kai-Lee Chen, Ruey-Hsing Chou, Chun-Chin Chang, Chin-Sung Kuo, Jih-Hua Wei, Ya-Wen Lu, Hsin-I Teng, Po-Hsun Huang, Shing-Jong Lin,
Journal of Critical Care,Volume 90,2025,155197,ISSN 0883-9441,
https://doi.org/10.1016/j.jcrc.2025.155197.
Abstract: Pro-protein convertase subtilisin/kexin 9 (PCSK9) is a potential therapeutic target in sepsis. However, its role as a prognostic biomarker remains unclear. This study investigated the relationship between plasma PCSK9 concentration and mortality in septic patients, focusing on the impact of sepsis-associated liver dysfunction (SALD).Patients meeting the Sepsis-3 criteria were enrolled. Plasma samples were collected within 24 h of admission. Patients were grouped into tertiles based on PCSK9 concentration and followed up for survival analysis. Further analyses were performed using Cox proportional hazard models and restricted cubic spline curves.A total 415 of patients were enrolled. Low PCSK9 group exhibited higher 28-day mortality. Among patients with liver sequential organ failure score (SOFA) ≥ 1, PCSK9 concentration displayed an inverse linear correlation with mortality, in contrast to a U-shaped pattern among those with liver SOFA = 0. Adjustment for international normalized ratio and liver SOFA diminished the significance of the association between PCSK9 concentration and mortality in the entire cohort.The association between low plasma PCSK9 concentration and mortality in sepsis may be influenced by SALD. Further investigations into the role of PCSK9 in sepsis should consider the impact of liver dysfunction on PCSK9 synthesis and prognosis.
Keywords: Sepsis; Pro-protein convertase subtilisin/kexin 9; sepsis-associated liver dysfunction

25COASDEC04:

Title: Remimazolam and propofol on preoperative and postoperative memory in general anaesthesia: A single-centre observational study,

Yuejiao Song, Zhihong Xu, Jia Wen, Biling Wu, Mengping Wei, Dan Wu, Qiaoyun Lin, Chao Liang, ShengJin Ge,

Trends in Anaesthesia and Critical Care,Volume 65,2025,101597,ISSN 2210-8440,
https://doi.org/10.1016/j.tacc.2025.101597.

Abstract: The sedative effects of remimazolam are well-established, but its impact on amnesia remains unclear. We compared the effects of remimazolam and propofol on memory before and after general anaesthesia. This study included 110 patients scheduled for elective unilateral great saphenous vein surgery under general anaesthesia. Patients were assigned to either remimazolam or propofol groups (n = 55 each) based on the attending anaesthesiologist's preference and clinical judgement. Primary outcomes included the average proportion of patients experiencing complete amnesia (inability to recall any posters) across three assessment points (10, 20, and 30 min after awakening), evaluated 24 h postoperatively. Secondary outcomes included the total number of posters recalled within 30 min after recovery and the proportion of recalled posters shown at specific time points before anaesthesia induction and after awakening. After exclusions (n = 24), 86 patients (n = 43 per group) were included. The proportion of patients experiencing amnesia within 30 min of anaesthesia recovery was significantly higher, and the total number of posters recalled within the 30-min period post-recovery was significantly lower in the remimazolam group compared with the propofol group ($P < 0.001$). Memory of the posters shown before anaesthesia induction was similar in both groups. Awakening time was significantly longer in the remimazolam group than in the propofol group ($P = 0.001$). Compared with propofol, remimazolam was associated with a more pronounced impairment of memory 30 min after anaesthesia recovery. These findings may help inform clinical selection of induction agents for general anaesthesia.

Keywords: Remimazolam; Propofol; Memory; Anaesthesia; Amnesia

25COASDEC05:

Title: Comparison of three different flow rates of oxygen with high-flow nasal cannula versus conventional nasal oxygen therapy in adult patients undergoing endoscopic retrograde cholangiopancreatography,

Arundhati Chadha, Anil Yogendra Yadav, Udit Dhingra, Gaurav Sindwani, Vinod Arora, Deepak K. Tempe,

Trends in Anaesthesia and Critical Care,Volume 65,2025,101600,
https://doi.org/10.1016/j.tacc.2025.101600.

Abstract: Endoscopic retrograde cholangiopancreatography is commonly performed under monitored anaesthesia care for diagnosis and treatment of biliary and pancreatic disorders. The procedure involves prone or semi-prone positioning, which increases the risk of oxygen desaturation during sedation. Conventional nasal oxygen therapy provides only low flow delivery and is often insufficient to maintain oxygenation. High flow nasal cannula oxygenation has emerged as a promising alternative, capable of delivering heated and humidified oxygen at higher flow rates, generating low levels of positive airway pressure, and facilitating carbon dioxide clearance. However, the most effective flow rate to prevent oxygen desaturation for high flow nasal cannula oxygenation during this procedure remains uncertain. A prospective randomized controlled trial was conducted in a tertiary care hospital between August and October 2024. A total of 102 adult patients, aged 18–70 years, with American Society of Anaesthesiologists physical status grades I to III, scheduled for

endoscopic retrograde cholangiopancreatography under sedation, were enrolled. Patients were randomized to receive either conventional nasal oxygen at 6 L per minute (n = 51) or high flow nasal cannula oxygenation (n = 51). The high flow nasal cannula group was further subdivided into three equal subgroups receiving flow rates of 30, 40, or 50 L per minute, each with a fraction of inspired oxygen fixed at 0.4. The primary outcome was the incidence of hypoxia, defined as peripheral oxygen saturation less than 92 percent lasting for at least 10 s. Secondary outcomes included severity of hypoxia, need for airway interventions, hemodynamic changes, adverse events, and patient satisfaction. The incidence of hypoxia was significantly lower in the high flow nasal cannula group (17.6 percent) compared to the conventional nasal oxygen group (35.3 percent, p = 0.042). The median lowest peripheral oxygen saturation was also higher in the high flow group (96 percent) compared to the conventional group (93 percent, p = 0.023). Among the high flow subgroups, the 50 L per minute group demonstrated the best outcomes, with the lowest incidence of hypoxia (11.8 percent) and the highest median lowest peripheral oxygen saturation (98 percent). Mild and moderate hypoxia were significantly reduced with high flow therapy, whereas severe hypoxia was rare and not different between groups. Adverse events were infrequent, with dryness of the airway slightly more common in the conventional group. Hemodynamic parameters and patient satisfaction were comparable across groups.High flow nasal cannula oxygenation is more effective than conventional nasal oxygen in preventing hypoxia during endoscopic retrograde cholangiopancreatography under sedation. A flow rate of 50 L per minute with a fraction of inspired oxygen of 0.4 provided the best balance between safety and efficacy, with superior oxygenation and minimal adverse effects. These findings support the use of high flow nasal cannula oxygenation, particularly at higher flow rates, as an adjunct to enhance patient safety in high-risk endoscopic procedures.

25COASDEC06:

Title: Comparison of continuous retrolaminar block with thoracic epidural for postoperative analgesia in upper abdominal surgery under subcostal incision: a pilot randomised clinical trial,

Poonam Kumari, Amarjeet Kumar, Chandni Sinha, Ajeet Kumar, Kunal Singh, Deepak Kumar,

Trends in Anaesthesia and Critical Care,Volume 65,2025,101608,
https://doi.org/10.1016/j.tacc.2025.101608.

Abstract: Thoracic epidural analgesia is regarded as the gold-standard analgesic method for upper abdominal surgery. The retrolaminar block is a relatively newer block used for abdominal surgeries. This study aimed to compare the postoperative analgesic efficacy of continuous retrolaminar block with thoracic epidural in patients undergoing abdominal surgery by subcostal incision.Sixty American Society of Anesthesiologists (ASAI/II) patients scheduled for abdominal surgery under subcostal incision were randomly allocated to have a continuous catheter placed for retrolaminar block (RLB group) or a catheter for thoracic epidural (TEA group) after general anaesthesia. The primary outcome of this study was 24-h postoperative morphine consumption. The secondary outcomes included intraoperative fentanyl requirement, number of patients requiring rescue analgesia, postoperative pain score (NRS), and procedure-related complications.The mean postoperative 24-h morphine

consumption was 7.32 ± 2.07 mg in the RLB group and 6.29 ± 2.29 mg in the TEA group. The difference between two groups was statistically insignificant (P = 0.06). Postoperative rescue analgesia was required in 13 patients of the RLB group and 8 patients in the TEA group. The mean total fentanyl requirement intraoperatively was 30 ± 13.99 µg in the RLB group and 20 ± 10.14 µg in the TEA group (P = 0.15). We also did not find any significant differences in postoperative pain scores between the two groups at any time points.Continuous retrolaminar block was non-inferior to thoracic epidural in providing postoperative analgesia for upper abdominal surgery via subcostal incision with a comparable duration of analgesic effect and reduction of opioid consumption.

Keywords: Epidural; Nerve block; Opioid; Postoperative pain

25COASDEC07:

Title: Impact of different tube angles on intubation outcomes with C-MACR D-blade videolaryngoscope: A prospective randomized study,

Alkim Gizem Yılmaz Selimoğlu, Ezgi Aytaç, Hatice Türe, Ferdi Menda,

Trends in Anaesthesia and Critical Care,Volume 65,2025,101594,
https://doi.org/10.1016/j.tacc.2025.101594.

Abstract: The C-MACR D-blade videolaryngoscope provides better visualization of vocal cords via the blade angle, however, stylet is required. This study compares postoperative sore throat (POST), hoarseness, intubation period and ease, subglottic damage (SGD), and hemodynamic changes to orotracheal intubation using different angled (60°-80°-90°) endotracheal tubes (ETT) with C-MACR D-blade videolaryngoscope.After Ethics Committee approval and consents taken, study was conducted in Yeditepe University Medical Faculty between June and December 2022. This prospective study involved 162 patients; who were planned to undergo general anesthesia with ASA score I-II (18–65years), randomized into three groups with closed envelope technique. In Group A ETT is bent into 90°, Group B 80° and Group C 60° using stylets. C-MACR D-blade videolaryngoscope was used. Hemodynamic data, intubation period and ease were recorded. SGD was examined with fiberoptic bronchoscope. Patients were evaluated regarding POST and hoarseness at 30 min, 4, 12, and 24 h postoperatively.Study showed intubation period was longest in Group A and shortest in Group C (p < 0.001). Group B had more POST incidence at 30 min (p = 0.040) and had the highest POST incidence in total 24 h (p = 0.040). There were no difference regarding SGD (p = 0.300) and hoarseness (30th minute p:0.610, 4th hour p:0.350, 12th hour p:0.130 and 24th hour p:0.130). In Group C intubations were easiest according to modified intubation difficulty scale (p = 0,020) however, hemodynamic response was highest (p < 0.001).We recommend using 60° angled ETTs in rapid sequence intubations. However, we do not recommend it in the population with low tolerance for hemodynamic instability.

Keywords: Postoperative sore throat; Hoarseness; Subglottic damage; C-MAC videolaryngoscope; D-blade; 60°; 80°; 90° angled endotracheal tube

25COASDEC08:

Title: Can artificial intelligence be used to support training in videolaryngoscopy – a prospective non-randomised controlled manikin study,

Moon-Moon Majumdar, Sneh Vinu Shah, Rajinder Singh Chaggar,

Trends in Anaesthesia and Critical Care,Volume 65,2025,101609,
https://doi.org/10.1016/j.tacc.2025.101609.

Abstract: There has been increasing interest in artificial intelligence (AI) to aid clinicians in airway management. larynGuide (aiEndoscopic, Switzerland) is a software that offers anatomy and navigation AI overlay on real-time videolaryngoscopy views. Our study aimed to evaluate whether larynGuide could improve tracheal intubation success and technique among clinicians, as well as to gather clinician opinion on its utility.This was a prospective, two-group, controlled, manikin study. Participants were recruited at Northwick Park Hospital from August 2024–March 2025, and allocated into two groups: videolaryngoscopy 1) with AI or 2) without AI, to perform five intubations. Primary outcomes were whether larynGuide improves first-pass success of tracheal intubation or changes the time to successful intubation.45 participants were allocated to AI overlay and 39 to no AI. There were no failed intubations or oesophageal intubations. There was one failed first-pass success (1/420, incidence of 0.24 %) in an intubation with AI overlay. Time to passage of the bougie, and of the tracheal tube through the glottic opening were faster without AI (Kruskal-Wallis ANOVA $p = 0.00017$, $p = 0.00005$ respectively). There was no significant difference in supervisor-assessed intubation technique score ($p = 0.30$), or participants' perception of improvement in their own technique ($p = 0.52$) between AI and non-AI groups. The majority of participants (83.1 %) felt that the AI was extremely, very or somewhat useful.

Although intubations with AI overlay took longer, there was no significant difference in supervisor-assessed technique or self-assessed improvement. Participants saw value in the overlay, especially for training. While AI shows potential in enhancing videolaryngoscopy training and use, further research is required to determine its safety, effectiveness, and optimal integration into practice.

Keywords: Airway management; Artificial intelligence; Intubation; Training; Videolaryngoscopy

25COASDEC09:

Title: Comparison of face mask ventilation before and after the administration of neuromuscular blocking drugs: An observational study,

Smriti Agrawal, Arun Kumar Handigodu Duggappa, Suvajit Podder, Deepali Shetty, Shweta Sinha, Savan Kumar Nagesh, Arun Parthasarthy, Hemamalini Sridharan,

Trends in Anaesthesia and Critical Care,Volume 65,2025,101596,ISSN 2210-8440,
https://doi.org/10.1016/j.tacc.2025.101596.

Abstract: Face mask ventilation (FMV) is essential during general anaesthesia and airway management. While neuromuscular blockade (NMB) is routinely used to facilitate intubation, its impact on the quality of FMV in patients with non-difficult airways remains uncertain.To evaluate the effect of NMB on FMV by comparing ventilation parameters before and after neuromuscular blockade.In this prospective observational study, 55 adult patients (ASA I–III, BMI <30 kg/m2) who underwent elective surgery under general anaesthesia were enrolled. Following induction with fentanyl and propofol, FMV was initiated. The mean exhaled tidal volume (VTe), mean peak inspiratory pressure (PIP), and modified Han score were recorded over 1 min. Vecuronium (0.1 mg/kg) was administered, and the same parameters were reassessed after complete neuromuscular blockade (train-of-four count zero) was achieved.

Difficult FMV was defined by inadequate tidal volume, an absent chest rise, no end-tidal CO2, or SpO2 <90 %.After NMB, the tidal volume significantly increased (300.44 ± 64.54 mL to 331.89 ± 66.98 mL; $p < 0.001$), and minute ventilation improved (4.21 ± 0.90 L/min to 4.65 ± 0.94 L/min; $p < 0.001$). The PIP decreased significantly (17.67 ± 3.29 to 16.11 ± 3.09 cm H2O; $p < 0.001$), indicating improved respiratory mechanics. The proportion of patients with modified Han grade 1 increased from 54.5 % to 70.9 % after muscle relaxant treatment, although this difference was not statistically significant ($p = 0.565$).Neuromuscular blockade improves FMV by increasing ventilation parameters and reducing inspiratory pressures. These findings support the use of NMB as a facilitator of effective FMV in patients with non-difficult airways.

Keywords: Face mask ventilation; Neuromuscular blockade; Airway management; General anaesthesia; Ventilation efficiency; Peak inspiratory pressure

25COASDEC10:

Title: Temperature profiles in adult intensive care unit patients treated for infection in a tertiary intensive care unit: A single-centre prospective observational cohort study,

Bianca B. Crichton, Allie Eathorne, Julieann Coombes, Chloe Edwards, Patricia M. Falleni, Kevin B. Laupland, Diane M. Mackle, Manoj Saxena, Jackson Smeed-Tauroa, Kyle C. White, Paul J. Young,

Critical Care and Resuscitation,Volume 27, Issue 4,2025,100121,ISSN 1441-2772,
https://doi.org/10.1016/j.ccrj.2025.100121.

Abstract: The objective of this study was to evaluate temperature profiles in patients treated for infections in the intensive care unit (ICU) to establish the number of patients who might be eligible for a clinical trial of therapeutic warming.A prospective observational study was conducted in a Wellington ICU over a 3-month period in 2024 including consecutive adult unplanned admissions and excluding those with brain injury or seizures.We screened 200 eligible patients. Our primary outcome was the proportion of all unplanned ICU admission episodes where patients were treated for infection within 14 days in the ICU. Patients treated for an infection were divided into four groups (≥38.3 °C, ≥37.5–38.2 °C, 36–37.4 °C, and <36 °C) using their most recent temperature prior to the first antimicrobial in the ICU (or at admission for patients already on antimicrobials). A key physiological/process measure was the fever deficit, defined as the number of degree-hours <38.3 °C within 24, 48, and 72 h.A total of 43.3% of unplanned ICU admissions resulted in treatment of infection within 14 days. A total of nine of 123 patients had a body temperature ≥38.3 °C (7.3%) when first treated for infection in the ICU, while 94 of 123 patients (76.4%) had a body temperature <37.5 °C. Fever deficits over 24-, 48-, and 72-h periods increased by decreasing body temperature group with a high proportion of hours spent with a body temperature <38.3 °C in all groups. A large number of patients treated for infection in the ICU may be able to be included in a trial evaluating induced hyperthermia.

Keywords: Intensive care; Sepsis; Therapeutic hyperthermia; Temperature; Fever deficit

25COASDEC11:

Title: Sepsis in the absence of fever: Determining the criteria for and feasibility of future therapeutic temperature management trials,

Kyle C. White, Kevin B. Laupland, Manoj Saxena, Bianca Crichton, James McCullough, Prashanti Marella,
Critical Care and Resuscitation,Volume 27, Issue 4,2025,100135,
https://doi.org/10.1016/j.ccrj.2025.100135.

Abstract: The purpose of this study is to examine the occurrence, characteristics, and outcomes of intensive care unit (ICU) patients with sepsis and the absence of fever. Multicentre, retrospective cohort study. Twelve ICUs in Queensland, Australia. Adults (≥18 years) admitted to the ICU with sepsis between 1 January 2015 and 31 December 2021 were eligible for inclusion. Patients admitted with seizures, traumatic brain injury, postcardiac arrest, end-of-life care, and elective surgery were excluded, as were readmissions. The primary outcome was fever deficit (defined as degree-hours under 38.3°C) during the first 72 h of ICU admission, and all-cause 30-day mortality was the key secondary outcome.
Of 89,117 admissions, 15,612 were included. Admission temperatures were ≥38.3°C in 1026 (6.6%), 37.5–38.2°C in 2096 (13.4%), 36–37.4°C in 9216 (59.0%), and <36°C in 3274 (21.0%). Temperatures changed rapidly over the first 12 h and, by 24 h, approached reasonably stable levels. For the admission temperature groups of ≥38.3°C, 37.5–38.2°C, 36–37.4°C, and <36°C, fever deficits were a median of 47 (interquartile range (IQR), 24 to 72), 53 (IQR, 29 to 83), 69 (IQR, 40 to 100), and 85 (IQR, 52 to 123) degree-hours, respectively, and 147 (14%), 248 (12%), 1,104 (12%), and 549 (17%) died by day 30. After controlling for confounders, a high fever deficit, defined as a fever deficit above the median, during the first 24 h of ICU admission, was not associated with all-cause 30-day mortality (OR 1.02, 95% CI, 0.93–1.13; p = 0.7). Fever deficits were large, particularly when the initial body temperature was not febrile. Only 1 in 15 ICU patients with sepsis had an initial body temperature ≥38.3°C. Approximately 2000 adults a year with sepsis and an initial body temperature <37.5°C would potentially be eligible for a trial of therapeutic hyperthermia in our 12 ICUs.

Keywords: Critical illness; Intensive care unit; Sepsis; Fever

25COASDEC12:

Title: Building the future of ICU care: Is our digital foundation strong enough? A multicentre survey of Australian and New Zealand intensive care units,

Kristen S. Gibbons, Renate Le Marsney, Andrew Goodwin, Rayna Reddy, Patricia Gilholm, David Pilcher, Ben Gelbart,
Critical Care and Resuscitation,Volume 27, Issue 4,2025,100133,
https://doi.org/10.1016/j.ccrj.2025.100133.

Abstract: The objective of this study was to assess data-related resources, infrastructure, and capabilities in Australia and New Zealand (ANZ) intensive care units (ICUs). Electronic multicentre survey was conducted. ANZ ICUs between June and October 2024. All ANZ ICUs contributing to the Australian and New Zealand Intensive Care Society Adult Patient Database and/or Australian and New Zealand Paediatric Intensive Care Registry were included in this study. There are none to declare. The main outcome measures included types of medical records, digital data capture and research availability, digital enhancement plans, staffing, and research collaboration. Of 209 ICUs, 112 (54%) responded; 13 paediatric, 21 mixed, and 78 adult ICUs, with responses from all ANZ jurisdictions. Overall, 59% used

paper records (5 paediatric and 61 mixed/adult), 28% digitised (7 paediatric and 24 mixed/adult), and 59% electronic health records (EHRs; 10 paediatric and 56 mixed/adult), with most EHRs introduced within the last decade (76%). In units with an EHR, 59% collected data secondly or minutely in the EHR and >75% collected EHR data on patient demographics, clinical notes, laboratory results, medications, fluids, bedside monitors, and respiratory support devices. Data Managers were employed within 45% of ICUs, with 96% able to extract data for audit and 92% for research. Respondents reported frustrations with delayed EHR implementation and limited data extraction mechanisms. Substantial variability exists across ANZ ICUs in digital health adoption, data capture, and data management resources. Quantifying differences in digital information, improving data extraction, and building collaborative networks are key steps for supporting research and innovation across units.

Keywords: Intensive care; Digital health; Electronic health record; Health informatics

25COASDEC13:

Title: Assessment of outcomes in postaneurysmal subarachnoid bleed patients admitted to the intensive care unit utilizing the subarachnoid haemorrhage international trialist clinicoradiological prediction model for dichotomised functional outcome and mortality,

David Mogg, James Walsham,
Critical Care and Resuscitation,Volume 27, Issue 4,2025,100126,ISSN 1441-2772,
https://doi.org/10.1016/j.ccrj.2025.100126.

Abstract: The objective of this study was to assess the Subarachnoid Haemorrhage International Trialist (SAHIT) prediction model in a tertiary adult intensive care unit (ICU) cohort when assessing patient outcomes against predicted outcomes, firstly by assessing the discrimination and validation of the model in the Princess Alexandra Hospital (PA) intensive care cohort and secondly comparing the predicted outcomes using the SAHIT model to the actual cohort outcomes using a Monte Carlo simulation.Six logistic regression models designed by the SAHIT Collaboration Group were applied to the PA cohort considering early predictive factors such as clinical grade and treatment modality to predict the risk of both mortality and unfavourable outcome at 6 months according to the Glasgow Outcome Score. The six SAHIT logistic regression models were applied to a retrospectively collected cohort of aneurysmal subarachnoid patients who were admitted to the ICU, generating individual risk scores for mortality and poor functional outcome. Area under the curve (AUC) and calibration slope/intercept and Brier score were used to assess the strength of the model in interpreting the current data set. A Monte Carlo analysis was used to compare the actual mortality outcomes to the predicted outcomes to determine if the cohort performance was better or worse than predicted by the mortality model.Overall, the PA cohort actual mortality was higher than the predicted mortality rate based on the risk scores generated by the SAHIT models, demonstrated by Monte Carlo simulation using the SAHIT model risk scores. The core, neuroimaging, and full models for functional outcome produced AUCs of 0.719 (95% confidence interval [CI]: 0.55–0.84), 0.709 (95% CI: 0.55–0.83), and 0.738 (95% CI: 0.58–0.85). Regarding mortality, the respective AUCs were 0.684 (95% CI: 0.57–0.78), 0.678 (95% CI: 0.56–0.77), and 0.749 (95% CI: 0.64–0.84). Regarding calibration, there was modest calibration in general, with higher degrees of calibration in the fully functional

outcome model. The cohort outcomes for mortality occurred at a rate higher than the risk predictions suggested using the logistic regression created by the SAHITs. Applying the externally trained model provided adequate discrimination and modest calibration, yet underestimated risk when applied to the intensive care cohort, reflected in the probability density function analysis. Using the SAHIT models in this cohort may result in underestimation of mortality for the individual patient, and the accuracy of the model is not sufficient for individual patient prediction. These results challenge the appropriateness of using admission-based models for dynamic ICU populations and highlight the urgent need for critical care–specific prognostic tools.

Keywords: Subarachnoid; Intensive care; Aneurysmal; Prediction; Model

25COASDEC14:

Title: κ-Opioid receptor activation suppresses triple-negative breast cancer progression by inducing urea cycle dysfunction and mitochondrial damage in vitro and in mice,

Yumiao Shi, Yiying Tao, Zhiying Pan, Xiaoqiang Wang, Chaojin Zhang, Shujing Zhou, Daxiang Wen, Guojun Qian, Weifeng Yu, Jie Tian,

British Journal of Anaesthesia,Volume 135, Issue 6,2025,Pages 1803-1815,ISSN 0007-0912, https://doi.org/10.1016/j.bja.2025.07.093.

Abstract: Triple-negative breast cancer (TNBC) is an aggressive malignancy with limited therapeutic options. Opioids are commonly used for perioperative and chronic pain management in patients with cancer. Notably, the κ-opioid receptor (KOR) has shown antitumour potential, but its therapeutic impact in TNBC is unknown.We analysed KOR expression in TNBC patient cohorts and tissue microarrays. The effects of the KOR agonist U69593 were assessed on key malignant phenotypes in vitro, including apoptosis and mitochondrial integrity. We then validated its impact on tumour growth and metastasis using subcutaneous and haematogenous mouse models.KOR expression was downregulated in TNBC tissue (n=60, P=0.0004), and higher KOR levels were associated with more favourable patient prognosis (n=45 low vs 15 high, P=0.03). The KOR agonist U69593 suppressed TNBC progression both in vitro, by inhibiting cell proliferation, migration, and invasion while inducing apoptosis, and in vivo, by suppressing tumour growth and metastasis. U69593 induced severe mitochondrial damage, evidenced by loss of mitochondrial membrane potential and depleted intracellular adenosine triphosphate. Metabolomic profiling revealed that this was linked to disruption of the urea cycle, leading to the accumulation of toxic ammonia. Restoring urea cycle function by overexpression of the key enzyme ornithine transcarbamylase rescued TNBC cells from U69593-induced apoptosis and abrogated its antitumour effects.These findings demonstrate that the KOR agonist U69593 restrains TNBC progression by disrupting urea cycle function and compromising mitochondrial integrity, highlighting the potential of dual-action therapeutics that combine effective analgesia with direct antitumour activity.

Keywords: ammonia; κ-opioid receptor; mitochondrial damage; triple-negative breast cancer; urea cycle

25COASDEC15:

Title: The MyPath Pain Pathway: Developing a Digital Patient-Centred Care Pathway for Cancer Pain,

Morena Shkodra, Amaia Urrizola, Marie Fallon, Per Sjøgren, Marieke van den Beuken-van Everdingen, Katarina Hagen, Lore Decoster, Daniela Mosoiu, Marianne Jensen Hjermstad, Tonje Lundeby, Stein Kaasa, Augusto Caraceni,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 592-601,ISSN 0885-3924,
https://doi.org/10.1016/j.jpainsymman.2025.08.012.

Abstract: Cancer pain affects up to 45% of patients, with more than 30% experiencing moderate to severe pain. Despite established guidelines, over 40% of patients receive inadequate pain management, severely impacting their quality of life. While effective pain assessment is essential, a standardized approach is lacking in both research and clinical practice.MyPath, a European Union-funded project, aims to implement a patient-centered care (PCC) approach across nine European cancer centers by systematically assessing and managing common symptoms and psychosocial issues to improve PCC for cancer patients. The aim of the present article is to describe the development of the clinical content for the MyPath Pain Care Pathway (PCP), based on patient reported outcomes (PROs) and clinical assessment, designed to offer standardized multidimensional pain management.Between September 2022 and August 2024, an international, multidisciplinary steering group developed a systematic method for assessing and diagnosing cancer pain using evidence-based guidelines.The MyPath PCP pain assessment includes five key components: pain etiology, location, intensity, flares, and treatment (including relief and dose-limiting side effects), in line with the ICD-11 classification. Data will be gathered through digitalized PROs and clinical consultation in the MyPath's digital solution, which will suggest individualized pain management strategies. The first version of the tool will be implemented in 2025, with further adaptations based on feedback from patients, caregivers, and healthcare professionals.The MyPath PCP represents a digital standardized pain assessment approach to improve the quality of pain management for cancer patients across clinical settings.

Keywords: CANCER pain; patient-centered care; care pathways; personalized care; palliative care

25COASDEC16:

Title: Impact of Prognostic Notifications on Inpatient Advance Care Planning: A Cluster Randomized Trial,

Jessica E. Ma, Kayla W. Kilpatrick, Clemontina A. Davenport, Jonathan Walter, Yvonne Acker, Noppon Setji,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 602-612,
https://doi.org/10.1016/j.jpainsymman.2025.08.013.

Abstract: A poor prognosis is an important trigger for advance care planning (ACP) conversations, but clinicians often overestimate prognosis. To determine whether ACP note documentation increases by notifying inpatient physicians that a patient is at high risk of mortality. A pragmatic cluster randomized trial at an academic medical center from September 2021 to December 2022 randomized attending physicians on the inpatient

medicine team. An email and page notification was sent to physicians randomized to intervention group for admitted patients at high risk of 30-day and 6-month death based on a machine learning model. The notification recommended to have and document an ACP conversation in the electronic health record (EHR). The primary outcome was documentation of an ACP conversation during hospital admission by the randomized physician. The secondary outcome was ACP note documented by any clinician during the hospital admission. Healthcare utilization outcomes included length of stay and discharge to hospice. Seventy randomized physicians (35 in each group) cared for 314 unique patients (138 control and 176 intervention) at high risk of mortality. Patients of physicians randomized to the intervention group were more likely to have a documented ACP conversation by the randomized physician compared to the control group (34.7% vs. 19.6%; OR 2.04; 95% CI 1.16–3.59). There was no significant change in ACP documentation by any clinician (52.8% intervention vs. 42.8% control group, OR 1.31; 95% CI 0.81–2.13) Machine learning mortality model notifications can motivate physicians to document ACP conversations during a hospitalization.

Keywords: Advance care planning; inpatient medicine; machine learning

25COASDEC17:

Title: Centering Community Voices: Evaluating Stakeholder Engagement in Pediatric Palliative Care Research,

Camille R. Murray, Elizabeth Reisinger Walker, Maura Savage, Khaliah Johnson,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 664-671.e3,
https://doi.org/10.1016/j.jpainsymman.2025.08.041.

Abstract: Black and Native American children in the United States experience disparities in serious illness care and outcomes which are compounded by systemic inequities. These disparities necessitate research approaches that center the voices of racially minoritized families, combat systems of oppression, and promote culturally humble care. Community-based participatory research (CBPR) emphasizes engaging affected communities throughout the research process.In this evaluation, we assessed the engagement of a stakeholder advisory board (SAB) convened to guide a study about racism in pediatric serious illness care.We used a mixed method combined process and outcome evaluation to explore SAB members' perceptions of meaningful participation in meetings and agency in influencing the project's direction. Themes from observation data, Zoom chat logs, and post-meeting surveys were synthesized using triangulation.Three themes emerged: consistent and active engagement, building connection through empathy and humor, and shared purpose and personal commitment. These findings suggest that members' relationships with each other and sense of purpose fueled sustained engagement. Real-time response to improvement suggestions by SAB members fostered trust with the research team and promoted members' understanding of their capacity within the project.The SAB facilitated meaningful contributions toward the larger project from members and provided an emotionally supportive environment where participants could process shared experiences of racism in healthcare. The findings demonstrate the alignment between CBPR and values of palliative care and the value of iterative evaluation in community-engaged pediatric serious illness health equity research.

Keywords: Pediatric; palliative care; racism; community-based participatory research (CBPR); evaluation

25COASDEC18:

Title: Describing the Uniquely Vulnerable Patients Served by an Outpatient Non-Oncologic Palliative Clinic,

Megan Pogue, William Leach, Elizabeth Franko, Grace Joseph, David Rigas, Gillian Love,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 691-697,
https://doi.org/10.1016/j.jpainsymman.2025.09.010.

Abstract: Outpatient nononcologic palliative care is a growing field with an evolving identity. The objective of this study was to assess patient demographics and clinical utilization of an outpatient nononcologic palliative care clinic.We collected and analyzed data from the first two years of an urban, nononcologic palliative care clinic within a quaternary academic center.The diagnoses with highest clinic utilization were heart failure (46.2%) and end-stage lung disease (16.6%). The medical complexity of these patients was high, with geriatric patients comprising 55% of the clinic population and 95.3% of patients meeting criteria for polypharmacy. Insurance data demonstrated a socially vulnerable population served with 65.6% of patients on a Medicare product, 36.7% on a Medicaid product, and 4.7% uninsured. 21.3% of new clinic visits were for medical cannabis certification. Patients elected for telehealth visits more often than age matched patients in the general primary care setting and were less likely to no-show to telehealth visits. Primary diagnosis impacted frequency of follow up, with patients with end stage lung disease returning more regularly than patients with heart failure.Nononcologic palliative care serves a uniquely medical vulnerable population and can be supported through utilization of clinical infrastructure that is already in place, establishing multidisciplinary collaborations, and utilizing telehealth.

Keywords: Palliative care; heart failure; end stage lung disease; ambulatory care

25COASDEC19:

Title: Goal-Concordant Care in People With Amyotrophic Lateral Sclerosis Receiving Palliative Care,

Michael J. Bonares, Jennifer Shapiro, Vishniha Vijayanathan, Agessandro Abrahao, Lorne Zinman, Christine Lau,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 679-690,
https://doi.org/10.1016/j.jpainsymman.2025.08.046.

Abstract: Although it is known where people with amyotrophic lateral sclerosis (ALS) are dying, less is known about whether they are dying where they want to.To determine the rate of dying in a preferred place and factors associated with doing so in people with ALS receiving clinic-based specialist palliative care.Retrospective cohort study of people with ALS receiving clinic-based specialist palliative care in Toronto, Canada between July 2022 and February 2024. Association between preferred and actual place of death was determined using a $\chi 2$ test. Factors associated with dying in a preferred place were determined using a multivariable binary logistic regression analysis.In 367 individuals, at time of consultation, median age was 67 years; 60.8% had a Palliative Performance Scale score between 50% and 60%, and 43.3% had noninvasive ventilation. Mortality rate up to February 2024 was 41.7%.

About 85.4% stated a preference to die at home, 8.7% in hospital, and 5.9% in a hospice facility, whereas 54.9% died at home, 34% in hospital, and 11.1% in a hospice facility. Of those with known preferred and actual place of death, 70.1% died in a preferred place ($\chi 2$ = 36.2; P < 0.001). Dying in a preferred place was associated with increasing age (odds ratio [OR] = 1.1; 95% confidence interval [CI] = 1.0–1.1) and having noninvasive ventilation (OR = 2.5; 95% CI = 1.0–6.2).Younger age and not having noninvasive ventilation at the time of consultation may suggest a higher risk of goal-discordant end-of-life care and the need to engage in early future planning when these factors are identified.

Keywords: Amyotrophic lateral sclerosis; goals of care; palliative care; end-of-life care; outpatient clinics; retrospective studies

25COASDEC20:

Title: Adolescents' and Young Adults' Perspectives on Decision-Making and the Emotional Experience of Having Advanced Cancer,

Nelda Itzep, Jessica Moore, Colleen Gallagher, Michael Roth, Peyton Martin, Mike Hernandez, Karen M. Moody,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 569-581,
https://doi.org/10.1016/j.jpainsymman.2025.07.036.

Abstract: Adolescents and young adults (AYAs) with advanced cancer represent a unique and vulnerable population. Little is known about the optimal approach to support their medical decision-making needs.The objective of this cross-sectional survey study was to elucidate the perspectives of AYAs with advanced cancer regarding their emotional experience of having cancer and their decision-making needs.Between April 2020 and December 2023, AYAs with advanced cancer were surveyed using the Herth Hope Index (HHI), the Peace, Equanimity, and Acceptance of Cancer Experience scale (PEACE), The Human Connection scale (THC), and the Child and Adolescent Participation in Decision Making Questionnaire (CAPDMQ). Descriptive analyses, t-tests, and Wilcoxon rank-sum tests were used to assess associations between demographic and clinic variables with patient responses.Fifty-seven AYAs participated. The median age was 22 years (range: 15–29); 51% were female. Majority of participants were White (68%), non-Hispanic (61%), single (96%), and Christian (67%). The most common diagnosis was sarcoma (39%). Most participants reported acceptance and peace with their illness, yet many struggled with changes in physical appearance, the unfairness of getting cancer, and angry feelings related to their illness. Participants also reported high levels of therapeutic alliance with their doctors. These AYAs reported remaining hopeful and future oriented despite their prognosis. They also reported a strong belief that AYAs should be involved in decision-making.Most AYAs accepted their illness and found peace, yet many still felt the burden of disease and fear about the future. Despite this, they felt hopeful and remained future oriented. AYAs value being involved in decision-making; further work is needed to develop clinical guidelines to facilitate shared decision-making for this population.

Keywords: Adolescents; young adults; advanced cancer; decision-making; hope; peace

25COASDEC21:

Title: Research Burden in Pediatric Cancer: A Mixed Methods Study From the PediQUEST Response Trial,

Erika Tsuchiyose, Deborah Feifer, Alexandra F. Merz, Madeline Avery, Ijeoma J. Eche-Ugwu, Opeyemi Awofeso,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 649-663,
https://doi.org/10.1016/j.jpainsymman.2025.08.032.

Abstract: Research burden in pediatric advanced cancer is understudied. To analyze study burden among parents and children participating in the PediQUEST Response Trial, and explore associated factors, including belonging to historically marginalized (HM) backgrounds or facing economic hardship (EH). Mixed-methods secondary analysis of data collected for an RCT. Children ≥2 years old with advanced cancer and a parent were enrolled for 18-weeks across five US pediatric cancer centers. Trough thematic analysis, we examined all parents and child (≥8yo) interviews to identify burden sources. We created a six-level "degree of burden" variable that integrated qualitative data (burden sources, levels 0–3) and quantitative data (dropout status, levels 4–5). Social disparity was grouped as: neither HM nor EH, either HM or EH, and both. We used ordinal logistic regression to explore burden-disparity associations. Among 154 randomized dyads, 149 had HM/EH data; 102 families completed interviews (102 parents, 44 children). Two burden themes were identified: study-related and daily life stressors. Most parents (62.4%) and children (48.8%) had burden levels 0-3; high levels (4–5) affected about 20% of families. Social disparity levels were 47.7% HM-/EH-, 30.9% HM+ or EH+, and 21.5% HM+/EH+. Parent burden increased with social disparity (HM+ or EH+ vs. HM-/EH-: cumulative OR 2.3, 95%CI 1.1, 5.1; HM+/EH+ vs. HM-/EH- OR 4.9, 95% CI 1.9, 12.2); no associations found for child's burden. Study burden was mostly low to moderate but higher in families endorsing social disparities. Enhanced support strategies may promote diversity in pediatric advanced cancer research. Clinicaltrials.gov NCT03408314.

Keywords: palliative medicine; Cancer; health inequities; empirical and qualitative research; pediatrics

25COASDEC22:

Title: Perceived Gaps Between Wishes and Practice in End-of-Life Sedation for Psycho-Existential Suffering,

Sayaka Maeda, Tatsuya Morita, Kengo Imai, Hiroyuki Otani, Akemi Shirado Naito, Satoru Tsuneto,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 582-591.e2,
https://doi.org/10.1016/j.jpainsymman.2025.08.011.

Abstract: Continuous deep sedation (CDS) for psycho-existential suffering is controversial and often regarded as a last-resort option at the end of life. The frequency with which patients desire CDS for this reason remains unclear.This study aimed to explore the prevalence of patients with cancer under palliative care in Japan who expressed a desire for CDS to alleviate psycho-existential suffering. It also sought to understand their condition at the time of expressing this desire, underlying suffering, and alternative interventions. This nationwide questionnaire survey involved all certified hospices and palliative care units (PCUs) across

Japan. Participants answered a questionnaire regarding the administration of and expressed desire for CDS to relieve psycho-existential suffering, along with patients' status when such a desire was expressed.Data from 306 facilities were analyzed. Approximately 0.2% of deceased patients received CDS solely for psycho-existential suffering, while 2% expressed a desire for it during the two-year study period. While only one-quarter of PCUs reported administering CDS for this purpose, three-quarters reported patients expressing a desire for it, with variation in the proportion across facilities. Patients' desire for CDS was frequently associated with existential suffering and often associated with the wish for an early death. A significant gap existed between patients' desire for CDS due to psycho-existential suffering and its actual implementation. Palliative care providers face the critical challenge of understanding patients' complex needs, providing appropriate care and support, and guiding ethical decisions for patients, families, and medical teams.

Keywords: Ethics; end-of-life; wish for an early death; desire to hasten death; euthanasia; continuous deep sedation until death

25COASDEC23:

Title: Quality Matters: Effect of High-Quality Early Palliative Care in Advanced Cancer,

EunKyo Kang, Su-Jin Koh, Jung Hun Kang, Yu Jung Kim, Seyoung Seo, Jung Hoon Kim, Jaekyung Cheon,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 638-648,
https://doi.org/10.1016/j.jpainsymman.2025.08.031.

Abstract: Early palliative care (EPC) is an integral treatment for advanced cancer patients, improving quality of life and symptom management, but the impact of its quality on outcomes is less understood.

This study aimed to quantify the quality of EPC and analyze its longitudinal association with depression levels, quality of life (QoL), patient survival, and self-management strategies in patients with advanced cancer. This secondary analysis included 144 advanced cancer patients from a randomized controlled trial in South Korea. Participants were stratified into high-quality (N = 76) and low-quality (N = 68) EPC groups based on Quality Care Questionnaire–Palliative Care scores. Outcomes including QoL (McGill Quality of Life Questionnaire, EORTC QLQ-C15-PAL), depression (PHQ-9), and self-management strategies (SMASH Assessment Tool Short Form) were assessed at baseline, 12, 18, and 24 weeks. Two-year overall survival was analyzed using Kaplan–Meier curves and log-rank tests, while repeated measures used generalized estimating equations and linear mixed-effects models. The high-quality EPC group demonstrated a significantly lower prevalence of depression at 24 weeks (14.7% vs. 39.1%, P = 0.036) and a higher 2-year survival rate (P = 0.006) compared to the low-quality group. Significant improvements were observed in existential and social burden (MQOL) and self-management preparation and implementation strategies (SAT-SF) at 18 and 24 weeks in the high-quality EPC group. Overall QoL measured by EORTC QLQ-C15-PAL showed minimal group differences. The quality of EPC services significantly impacts depression, patient survival, aspects of QoL, and self-management capabilities. These findings emphasize the importance of high-quality EPC beyond mere provision.

Keywords: Palliative care; quality; depression; survival; quality of life; self-management

25COASDEC24:

Title: Outcomes of Palliative Care in Extracorporeal Life Support: A Systematic Review,

Whitney A. Kiker, Anna L. Condella, Astrid Grouls, Daniel Brodie, Leanne Delaney, Eddy Fan, Teresa Jewell,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 613-626,
https://doi.org/10.1016/j.jpainsymman.2025.08.016.

Abstract: Use of palliative care in extracorporeal life support (ECLS) has increased, but its impact on patient- and family-centered outcomes remains unclear. To examine the relationship between specialty palliative care and patient- and family-centered outcomes for patients receiving ECLS. We conducted a systematic review of PubMed, EMBASE (Elsevier), CINAHL Complete (EBSCOhost), Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials (Wiley) through August 26, 2024. Two investigators independently screened titles and abstracts, followed by full-text review for inclusion. Data were extracted for prespecified critical and important outcomes, and evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. Nine observational studies were included, incorporating data from 21,417 patients receiving ECLS, with 4368 seen by specialty palliative care. For all outcomes, certainty of evidence was very low. Two studies included a critical outcome: one found no difference in “average pain” and one reported more goals-of-care notes, comparing those seen by palliative care to those not seen. Five studies reported longer ECLS duration among those with palliative care consultation compared to those without. Three studies performed statistical comparisons of survival for patients with and without palliative care consultation and found no significant differences in hospital mortality. Few studies have investigated patient- and family-centered outcomes related to specialty palliative care for patients receiving ECLS. Specialty palliative care does not appear to correlate with mortality, supporting the concept that palliative care can support goals-of-care conversations and end-of-life decision making without negatively affecting patient survival. However, limitations of the existing data preclude meaningful conclusions about the relationship between specialty palliative care and other patient- and family-centered outcomes. Additional research is needed to clarify the optimal role of specialty palliative care in this population.

Keywords: Palliative care; extracorporeal life support; clinical outcomes

25COASDEC25:

Title: Guided Mindfulness of Death to Reduce Fear of Death in Cancer Patients: Randomized Controlled Study,

Tan Seng Beng, Leow Yong Wen, Ng Siew Yoong, Noor Elyna binti Mohd Abdul Latif,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 547-556.e2,
https://doi.org/10.1016/j.jpainsymman.2025.08.002.

Abstract: This study aimed to assess the effectiveness of guided mindfulness of death in reducing fear of death in cancer patients. A parallel-group, nonblinded randomized controlled study was conducted at the University of Malaya Medical Centre, Malaysia, involving 52

cancer patients with moderate to severe fear of death. Participants were randomly assigned to either a mindfulness of death intervention group or a control group. The intervention consisted of four guided mindfulness exercises focusing on death awareness. Primary outcomes were measured using a numerical rating scale for fear of death (NRS) and the Death and Dying Distress Scale (DADDS), with secondary outcomes measured using the Suffering Pictogram. The intervention group experienced a significant reduction in fear of death scores, overall suffering score, and total suffering score, compared to the control group. Feedback from participants indicated that while most found the exercises beneficial, some reported discomfort or conflict with their religious beliefs, particularly in exercises involving body decomposition and near-death visualizations. Mindfulness of death exercises effectively reduce fear of death, distress, and suffering in cancer patients. However, the intervention may not be suitable for all due to cultural and religious factors, underscoring the need for tailored approaches in clinical settings.

Keywords: Palliative care; mindfulness; fear of death; suffering; cancer

25COASDEC26:

Title: Global Consensus-Based Essential and Expanded Packages for Palliative Care and Pain Relief for Adults and Children: A Delphi Study,

Tania Pastrana, Liliana De Lima, Veronica Dussel, Xiaoxiao Jiang Kwete, Julia Downing, Marie Fallon,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 627-637.e3,
https://doi.org/10.1016/j.jpainsymman.2025.08.027.

Abstract: In 2018, the Lancet Commission on Global Access to Palliative Care and Pain Relief introduced the concept of serious health-related suffering (SHS) to quantify the need for palliative care and proposed an essential package of palliative care and pain relief (PCPR) to address it. However, this package did not account for complex and specialized needs, and its global implementation has been limited. We conducted a multistage, modified Delphi study to update and expand the initial Essential Package for children and adults Two international panels -adult and pediatric- representing diverse geographical regions and income levels participated in two Delphi rounds. External validation was conducted by global experts in palliative care. Retention rates for the Delphi rounds were 79.5% for adults and 64.0% for children. Consensus was achieved on the updated Essential Packages for both adults and children, with minor modifications. Expanded Packages were developed, including additional medications, equipment, and human resources to address broader needs. The study also revealed persistent inequities in medicine availability, particularly in low- and middle-income countries, and limited awareness of the Lancet Commission's Essential Package among health professionals. These globally validated Essential and Expanded Packages for adults and children offer a practical adaptable framework to guide national health strategies, strengthen palliative care services, and reduce SHS. Their adoption can meaningfully contribute to achieving Universal Health Coverage.

Keywords: Palliative care; global health; essential health packages; Serious health-related suffering (SHS); Delphi method

25COASDEC27:

Title: Pediatric Home-Based Palliative Care and Hospice: Characterizing and Comparing the Populations,

Ben Reader, Sibelle Aurelie Yemele Kitio, Steven M. Smith,

Journal of Pain and Symptom Management,Volume 70, Issue 6,2025,Pages 672-678,ISSN 0885-3924,
https://doi.org/10.1016/j.jpainsymman.2025.09.002.

Abstract: Home-based palliative care (HBPC) and hospice programs offer support for children with complex life-shortening conditions. However, there is little comparison of the characteristics and care trajectories of children and young adults enrolled in HBPC versus hospice, particularly across different age groups.To compare the characteristics of children and young adults who received HBPC and/or hospice and identify differences and similarities between these populations.A retrospective cohort study of children birth-21 years of age who received HBPC and/or hospice in their home between 1/2019-12/2022 at a single site. Data were manually extracted from the electronic health record. Statistical analyses included descriptive statistics, chi-square or Fisher's exacts tests for categorical variables, and Mann-Whitney U tests for non-normally distributed continuous variables. Subgroup analyses excluded children <1 year of age due to differences unique to population including utilization of perinatal palliative care or palliative care in the neonatal intensive care unit.Of 113 participants, hospice recipients were younger (median 2 vs. 7 years; P = 0.033), more likely to have an oncologic diagnosis, and had a higher mortality during the study period (69.6% vs. 22.1%; P < 0.001). HBPC participants had more hospital admissions, longer inpatient stays, and more outpatient visits. Subgroup analyses of children ≥1 year revealed diagnosis and code status differences, with hospice participants more likely to have 'allow natural death' orders and experience a code status change.Among children and young adults, significant differences exist between those receiving HBPC and those receiving hospice care, particularly in age, diagnosis, and healthcare utilization.

Keywords: Pediatric palliative care; pediatric hospice; home-based care

25COASDEC28:

Title: Baseline Amplitude Ratios of Median Nerve Somatosensory Evoked Potentials: Clinical Implications During Carotid Endarterectomy,

Swantje de Abreu Malchow, Parisa Moll-Khosrawi, Kristen K. Thomsen, Hans O. Pinnschmidt, Bernd Saugel, Christian Zöllner, Leonie Schulte-Uentrop,

Journal of Cardiothoracic and Vascular Anesthesia,Volume 39, Issue 12,2025,Pages 3484-3494,
https://doi.org/10.1053/j.jvca.2025.08.011.

Abstract: To (1) examine associations between the ipsi-to-contralateral median nerve somatosensory evoked potential (mSSEP) baseline amplitude ratio (=IAR) and clinical symptoms, cerebral infarction, or ischemic injury in the ipsilateral middle cerebral artery territory in patients undergoing carotid endarterectomy (CEA); and (2) evaluate the IAR as a predictor of clamp-induced ischemia.A retrospective cohort study.Single-center study, Department of Anesthesiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.Patients after CEA with mSSEP monitoring between 2015 and 2019.A total of 221

patients were categorized into subgroups (S/I groups): asymptomatic or symptomatic patients without infarction and/or injury (-S/-I and +S/-I, respectively), symptomatic patients with old infarction (+S/+Io), and symptomatic patients with (sub-)acute infarction and/or injury (+S/+Ia). Predictors of clamp-induced ischemia were evaluated in 228 patients.The effects of S/I groups, sex, age, and stenosis degrees on the IAR were tested in uni- and multivariable models. A statistically significant effect was found for "S/I groups." The mean IAR differed statistically significantly between the four subgroups (pF < 0.001); -S/-I, +S/-I, and +S/+Io had significantly higher mean IARs than the reference +S/+Ia. The association between predictor variables and a significant amplitude decline during carotid cross-clamping was examined using univariable and multivariable logistic regression models. A total of 16 of 228 patients (7%) experienced a significant amplitude decline. Solely contralateral carotid artery occlusion showed an indicated effect (odds ratio 4.21, 95% confidence interval 0.76-23.38, p = 0.1).In CEA patients, a decreased IAR reflects the acuity of an infarction or injury but does not predict clamp-induced ischemia. Contralateral carotid artery occlusion showed a trend toward predicting clamp-induced ischemia.

Keywords: Carotid artery stenosis; carotid surgery; symptomatic; intraoperative neuromonitoring; predictor; intraoperative ischemia

25COASDEC29:

Title: Development and Validation of an Online Nomogram Calculator to Predict Postoperative Pneumonia in Elderly Patients with Esophageal Cancer after Transthoracic Esophagectomy,

Jingjing Liu, Yanfeng Wang, Yanping Wang, Weidong Mi, Qiang Fu,

Journal of Cardiothoracic and Vascular Anesthesia,Volume 39, Issue 12,2025,Pages 3465-3474,

https://doi.org/10.1053/j.jvca.2025.07.033

Abstract: Postoperative pneumonia after esophagectomy is common, which may seriously burden elderly patients and aggravate their postoperative conditions. We sought to create an online nomogram calculator to predict postoperative pneumonia in elderly patients with esophageal cancer after transthoracic esophagectomy. Multivariable prediction models. The Chinese People's Liberation Army (PLA) General Hospital. Elderly patients (N = 607) underwent transthoracic esophagectomy between January 2012 and December 2019. Confirm the occurrence of postoperative pneumonia. Univariable and multivariable logistic regression analyses were used to identify independent risk factors for postoperative pneumonia. A nomogram calculator was constructed according to the independent risk factors in the training cohort and then tested in the validation cohort. Multivariable logistic analysis showed that preoperative leukocyte count (p = 0.018), partial pressure of carbon dioxide (pCO2) (p = 0.024), tumor location (p = 0.038), and operative duration (p < 0.001) were independent risk factors for postoperative pneumonia. We then developed a nomogram calculator using these four factors. The C-statistics of this nomogram in the training, validation, and entire cohorts were 0.680, 0.655, and 0.669, respectively. Risk analysis and decision curve analysis revealed that the nomogram provided good diagnostic power and net benefit. We developed an online nomogram calculator that can predict the risk of postoperative pneumonia in elderly patients with esophageal cancer after transthoracic esophagectomy simply and conveniently.

Keywords: postoperative pneumonia; elderly patients; esophageal cancer; nomogram; esophagectomy

25COASDEC30:

Title: Real-world Experience of Angiotensin II and Renin Usage in Patients With Distributive Shock:A Single-center Descriptive Study,

Andreja Möller Petrun, Mario Gorenjak, Franc Svenšek, Nives Matković Lonzarić, Alenka Strdin Košir,

Journal of Cardiothoracic and Vascular Anesthesia,Volume 39, Issue 12,2025,Pages 3359-3367,
https://doi.org/10.1053/j.jvca.2025.08.044.

Abstract: To evaluate real-life use of angiotensin II, a novel vasopressor, and renin, which can be used as a marker of endogenous angiotensin II deficiency and disease severity. A retrospective observational single-center cohort study. Four intensive care units in one university hospital. Adult patients with distributive shock, no limitations of active care, and with ongoing use of vasoconstrictors (norepinephrine base ≥0.3 mcg/kg/min plus vasopressin), who were admitted between August 2022 and August 2023. Septic shock (38/42, 90.5%) and post-cardiopulmonary bypass vasoplegia (4/42, 9.5%) were the causes of distributive shock. After the initiation of angiotensin II, a decrease in the norepinephrine base dose at 4, 24, and 48 hours (0.40 ± 0.25 mcg/kg/min, 0.21 ± 0.11 mcg/kg/min, and 0.13 ± 0.06 mcg/kg/min, respectively), and a decrease in vasopressin dose were observed. Renin concentration decreased after initiation of angiotensin II from 376.90 ± 168.50 mU/L to 188.24 ± 167.47 mU/L ($p < 0.01$). Control renin was lower in survivors to hospital discharge compared with nonsurvivors (78.06 ± 121.14 mU/L in survivors, v 259.07 ± 163.4 mU/L in nonsurvivors, $p < 0.01$). Angiotensin II can be used to decrease the doses of non-angiotensin II vasopressors, and renin concentration may potentially aid in the prognostication of patients with distributive shock.

Keywords: intensive care medicine; distributive shock; vasopressor; angiotensin II; renin; norepinephrine; vasopressin

25COASDEC31:

Title: Predicting post-cardiac surgery vasopressor use in a large, multicenter national cardiac surgical database,

Enya Martic, Mohammad Asghari-Jafarabadi, Jenni Williams-Spence, Julian A. Smith, Christopher M. Reid, Lavinia Tran, David Pilcher, Tim G. Coulson,

Journal of Cardiothoracic and Vascular Anesthesia,Volume 39, Issue 12,2025,Pages 3350-3358,
https://doi.org/10.1053/j.jvca.2025.09.005.

Abstract: To develop a model to predict post-cardiac surgery vasopressor administration and describe hospital variation in practice. Retrospective analysis.Multi-institutional. All patients who underwent cardiac surgery with cardiopulmonary bypass between 2012 and 2021. The study cohort was divided into a development set (80%) and a validation set (20%). Univariate logistic regression was used to identify variables associated with postoperative vasopressor administration. The least absolute shrinkage and selection operator was used to develop

parsimonious models with variables known preoperatively only (preoperative model), as well as preoperative and immediate postoperative variables (postoperative model). Model discrimination and calibration were performed on both the development and validation sets. The study included 106,348 patients across 33 hospitals. The incidence of postoperative vasopressor administration was 29.3% (n = 31,157). Significant interhospital variability in the rate of the outcome was observed, ranging from 1.20% to 69.4% (median, 22.3%). Fixed effects models with patient and surgical variables were developed for postoperative vasopressor administration, with an area under the receiver operating curve of 0.56 and 0.60 preoperatively and postoperatively, respectively. Accounting for the hospital of admission through mixed effects multilevel modeling improved the area under the receiver operating curve to 0.75 and 0.76 preoperatively and postoperatively, respectively. Post-cardiac surgery vasopressor administration can only be predicted with poor to fair accuracy based on patient and surgical variables alone. Significant institutional variation in the rate of vasopressor administration exists, seemingly unrelated to measured patient and surgical factors, and predictive ability improves substantially when this is considered.

Keywords: vasopressor; cardiac surgery; risk prediction

25COASDEC32:

Title: Effects of Preoperative Oral Carbohydrates on Insulin Resistance and Postoperative Recovery in Diabetic Patients Undergoing Coronary Artery Bypass Grafting: A Preliminary Prospective, Single-Blinded, Randomized Controlled Trial,

Shicheng Zhang, Lixian He, Yiping Yu, Xin Yuan, Tao Yang, Fuxia Yan, Fei Xu, Yan Zhang, Shiwei Pan,

Journal of Cardiothoracic and Vascular Anesthesia,Volume 39, Issue 12,2025,Pages 3338-3349,

https://doi.org/10.1053/j.jvca.2025.07.036.

Abstract: Previous studies have demonstrated that preoperative oral carbohydrates (CHO) can alleviate postoperative insulin resistance (IR) and enhance recovery in non-diabetic patients undergoing cardiac surgery. However, the potential benefits in diabetic patients remain unclear. This study aimed to investigate the effects of preoperative CHO on IR and postoperative recovery in diabetic patients undergoing off-pump coronary artery bypass grafting (OPCAB). A prospective, single-center, single-blind, randomized controlled trial. The study was conducted in the Adult Cardiac Surgery Ward 6 of a large-volume cardiovascular center. A total of 62 consecutive diabetic patients scheduled for isolated OPCAB were prospectively enrolled between July 8, 2022, and April 28, 2023. Participants were randomized in a 1:1 ratio to the CHO group or the control (CTRL) group using computer-generated random numbers. Patients in the CHO group received 335 mL of a carbohydrate drink containing 50 g of carbohydrates 8 to 12 hours before surgery, while those in the CTRL group followed routine fasting protocols. The primary endpoint was postoperative IR, assessed by the homeostasis model assessment. Secondary endpoints included postoperative inflammatory markers and stress responses (e.g., serum cortisol levels), while exploratory endpoints focused on in-hospital clinical outcomes. Baseline characteristics were comparable between groups. CHO administration significantly reduced postoperative inflammatory markers but did not significantly improve IR. Stress response

was attenuated in the CHO group, though the difference was not statistically significant. Postoperative drainage was higher in the CHO group, but no differences were observed in other clinical outcomes. Preoperative CHO may attenuate inflammatory and stress responses without increasing perioperative risk in diabetic patients undergoing OPCAB, although its effect IR remains uncertain.

Keywords: preoperative carbohydrates; diabetes mellitus; off-pump coronary artery bypass grafting; insulin resistance; recovery

25COASDEC33:

Title: Changes in Respiratory Variation of Velocity-Time Integral and Peak Velocity of Left Ventricular Outflow Tract after Tidal Volume Challenge Predict Fluid Responsiveness in Elderly Patients with Low Tidal Volume Ventilation: A Prospective Observational Study,

Jing-jie Wan, Jin Xie, Ke Peng, Jun Chen, Yu-kun Zhang, Fu-hai Ji,

Journal of Cardiothoracic and Vascular Anesthesia,Volume 39, Issue 12,2025,Pages 3379-3386,

https://doi.org/10.1053/j.jvca.2025.08.028.

Abstract: We hypothesized that changes in respiratory variation of velocity-time integral (ΔVTI) and peak velocity (ΔVpeak) of left ventricular outflow tract after tidal volume challenge (TVC) better predict fluid responsiveness in elderly patients with low tidal volume ventilation. A prospective observational study. A tertiary teaching hospital. Ninety-six critically ill elderly patients without arrhythmias under mechanical ventilation were enrolled in this study. TVC was performed by increasing the tidal volume from 6 to 8 mL/kg of predicted body weight. Passive leg raising was performed to identify fluid responders (increase in stroke volume >10%). Pulse pressure variation (PPV), ΔVTI, and ΔVpeak were measured before and 1 minute after TVC. Receiver operating characteristic curves and gray zones were used to assess the ability of changes in PPV (ΔPPVTVC), ΔVTI (ΔVTITVC), and ΔVpeak (ΔVpeakTVC) after TVC to predict fluid responsiveness. The mean age was 75 years, and 75% were male. Forty-five (46.9%) patients were the responders. The area under the receiver operating characteristic curves for ΔPPVTVC to predict fluid responsiveness was 0.89 (95% confidence interval 0.82-0.95, $p < 0.001$), including 43.8% of patients in the gray zone. ΔVTITVC and ΔVpeakTVC predicted fluid responsiveness with AUCs of 0.96 (95% CI 0.90-0.99, $p < 0.001$) and 0.94 (95% CI 0.87-0.98, $p < 0.001$), including 11.5% and 19.8% of patients in the gray zones, respectively. In elderly patients with low tidal volume ventilation, ΔVTITVC and ΔVpeakTVC predicted fluid responsiveness accurately and better than ΔPPVTVC.

Keywords: elderly patients; fluid responsiveness; peak velocity; tidal volume challenge; velocity-time integral

25COASDEC34:

Title: Combined Fascia Iliaca Compartment-Sciatic Nerve Blocks Reduce Early Cardiovascular Events in Chronic Limb-Threatening Ischemia: A Propensity Score–Matched Retrospective Study,

Manman Liu, Wanxia Xiong, Jie Liu, Biling Wu, Youwen Chen, Yuejiao Song, Xiaoru Lin, Ming Ding, Chao Liang,
Journal of Cardiothoracic and Vascular Anesthesia,Volume 39, Issue 12,2025,Pages 3475-3483,
https://doi.org/10.1053/j.jvca.2025.08.009.
Abstract: To compare postoperative outcomes between combined fascia iliaca compartment–sciatic nerve blockade (FICB-SNB) and monitored anesthesia care (MAC) in patients with chronic limb-threatening ischemia (CLTI) undergoing lower-extremity revascularization (LER).Retrospective matched cohort study (1:1 propensity score matching).Single-center analysis of CLTI patients undergoing LER.216 matched pairs (total n = 432) selected from 505 eligible patients.FICB-SNB (n = 216) versus MAC (n= 216). Primary outcomes: Compared to MAC, FICB-SNB did not significantly reduce in-hospital major adverse cardiovascular events (MACE) (odds ratio [OR], 0.49; 95% confidence interval [CI], 0.18-1.32; p = 0.15) or 1-year MACE (p > 0.05). Secondary outcomes: FICB-SNB demonstrated superior postoperative analgesia, reducing rest pain by 67% (OR, 0.33; 95% CI, 0.23-0.48; p < 0.001). No differences were observed in myocardial injury after noncardiac surgery, complications, or amputation rates (p > 0.05 for all). FICB-SNB improves analgesia but does not significantly reduce short- or long-term MACE. The trend toward lower in-hospital MACE suggests transient intraoperative cardiovascular stabilization not sustained at 1 year. A prospective randomized trial with standardized protocols to control confounders and validate clinical trends is warranted.
Keywords: chronic limb-threatening ischemia; fascia iliac compartment block; lower extremity revascularization surgery; major adverse cardiovascular events; sciatic nerve block

Cancer Research

25COASDEC01

Title: Piperlongumine Induces Apoptosis and Autophagy via the MAPK/NK-κB Pathway in Human Breast Cancer Cells

Yun-Seo Jang, Su-Ji Jeon, Sang-Woo Lee et.al.

Anticancer Research December 2025, 45 (12) 5423-5434;
https://doi.org/10.21873/anticanres.17878

Abstract: Piperlongumine, a major alkaloid compound found in long pepper (Piper longum L.), is used to treat tumors, malaria, bronchitis, and asthma. This study aimed to investigate the anticancer effects of piperlongumine on SK-BR-3 and T47D human breast cancer cell lines, focusing on its potential to induce apoptosis and autophagy.Materials and Methods: Cell viability was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay to determine whether piperlongumine reduced breast cancer cell survival. Apoptosis was evaluated through 4′,6-diamidino-2-phenylindole staining for morphological changes and flow cytometry was conducted for quantitative analysis. Acridine orange staining was performed to examine autophagy induction. Western blotting was used to analyze the expression of proteins associated with apoptosis, the mitogen-activated protein kinase (MAPK)/NF-κB pathway, and autophagy.Results: We observed an increase in the apoptosis-related proteins Bax and cleaved poly (ADP-ribose) polymerase, while apoptosis was associated with decreased Bcl-2. Among the MAPK-related proteins, the expression of phosphorylated extracellular signal-regulated kinase (p-ERK) decreased, whereas that of phosphorylated c-Jun N-terminal kinase (p-JNK) and phosphorylated p38 (p-p38) increased. The autophagy-related protein phosphorylated mammalian target of rapamycin (p-mTOR) was decreased, whereas Beclin 1 and LC3-II expression levels increased, indicating autophagy induction.Conclusion: In SK-BR-3 and T47D breast cancer cell lines, piperlongumine induces apoptosis via the MAPK/NF-κB pathway and promotes autophagy. These findings suggests that piperlongumine may serve as a potential therapeutic agent against human breast cancer cells.

Keywords: Piperlongumine, breast cancer, apoptosis, autophagy, MAPK/NF-κB pathway

25COASDEC02

Title: Renal Function With Enfortumab Vedotin in Metastatic Urothelial Carcinoma: A Multicenter Retrospective Study in Japan

Yuki Kobari, Junpei Iizuka, Hanae Kondo et.al.

Anticancer Research December 2025, 45 (12) 5645-5654;
https://doi.org/10.21873/anticanres.17898

Abstract: Patients with metastatic urothelial carcinoma (mUC) often experience impaired renal function because of tumor invasion, nephroureterectomy, and chemotherapy. Enfortumab vedotin (EV) has been approved in Japan as a third-line treatment for advanced UC. This study aimed to assess renal function changes in patients with mUC receiving EV therapy.Patients and Methods: We retrospectively analyzed renal function changes and clinical outcomes in 63 patients with mUC who received EV following platinum-based chemotherapy and immune checkpoint inhibitors. Data were collected from five Institutions in Japan from September 2021 to September 2024.Results: The median baseline estimated

glomerular filtration rate (eGFR) was 44.1 ml/min/1.73 m2. Chronic kidney disease stage remained unchanged in 54% of patients, upstaging in 17%, and downstaging in 29%. The median change rate in eGFR was 2.6%. The median overall survival was 12.0 months in the eGFR ≥45 ml/min/1.73 m2 group and 15.4 months in the eGFR <45 ml/min/1.73 m2 group. The objective response rate was 45% in the eGFR ≥45 ml/min/1.73 m2 group and 34% in the eGFR <45 ml/min/1.73 m2 group. Adverse events (AEs) of any grade occurred in 84% of patients with eGFR ≥45 and 69% of those with eGFR <45, with grade ≥3 AEs reported in 7% and 13% patients, respectively.Conclusion: EV did not significantly impair renal function in patients with mUC. Comparable efficacy and safety were observed regardless of baseline eGFR, supporting the feasibility of EV in patients with impaired renal function.
Keywords: Enfortumab vedotin, chronic kidney disease, urothelial carcinoma, renal function

25COASDEC03

Title: Growth Suppression and Selective Disruption of F-Actin by α-Santalol in Human Melanoma Cells

Ritesh Chandrasekaran, Michael L. Lu, Chandradhar Dwivedi Et.Al.
Anticancer Research December 2025, 45 (12) 5399-5407;
https://doi.org/10.21873/anticanres.17876
Abstract: α-Santalol, a major component of sandalwood oil, has been shown to have chemopreventive and antitumor effects in different pre-clinical cancer models. The present study was undertaken to determine the in vitro efficacy of α-santalol on SK-MEL2 human melanoma cells and an immortalized human keratinocyte cell line (HaCaT).Materials and Methods: In this study, we employed 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, Trypan blue, wound-healing, and annexin V apoptosis assays, as well as confocal microscopy for imaging F-actin rhodamine phalloidin/4′,6-diamidino-2-phenylindole-stained cells to investigate the cytotoxicity, cell viability, migratory potential and apoptotic cell death, respectively, of cells treated with different concentrations of α-santalol or dimethyl sulfoxide for different time periods.Results: Results showed that α-santalol treatment significantly reduced SK-MEL2 cell viability and wound-healing ability, while only affecting HaCaT cells at higher concentrations. α-Santalol treatment also disrupted cytoskeletal structure and F-actin in SK-MEL2 cells, whereas HaCaT cells were more resistant to this effect.Conclusion: The selective growth-inhibitory and anti-migratory effects of α-santalol on humanmelanoma cells warrants future studies to systemically explore the mechanistic details involved.
Keywords: α-Santalol, melanoma, apoptosis, F-actin, fluorescence microscopy

25COASDEC04

Title: Leucine-rich Repeat-containing 15 as a Potential Marker and Therapeutic Target in Cervical Cancer

Thi Hai Ly Dao, Keiichiro Nakamura, Kazuhiro OKAMOTO et.al.
Anticancer Research December 2025, 45 (12) 5409-5421;
https://doi.org/10.21873/anticanres.17877
Abstract: Leucine-rich repeat-containing 15 (LRRC15) is a recently identified cancer-associated fibroblast (CAF) marker found in various types of cancer. However, its functional role and clinical significance in cervical cancer (CC) remain unclear.Materials and Methods:

We analyzed LRRC15 expression in 20 normal cervical (NC) tissue samples and 87 CC tissue samples using RT-qPCR. Correlations between LRRC15 expression and clinicopathological parameters and prognosis in CC patients were evaluated. The biological functions of LRRC15 and its effects were investigated in CC cell lines with and without human papillomavirus (HPV) infection.Results: LRRC15 expression was significantly associated with lympho-vascular space (LVS) involvement in patients with CC ($p<0.001$). Patients with high LRRC15 expression had significantly poorer progression-free survival outcomes than those with low LRRC15 expression ($p=0.014$). LRRC15 knockdown suppressed WNT and focal adhesion kinase (FAK) signaling, leading to increased Caspase3/7 expression and, consequently, enhanced apoptosis in CC cells, regardless of HPV infection.Conclusion: LRRC15 expression is a marker of poorer prognosis in patients with CC, suggesting that LRRC15 represents a potential therapeutic strategy for CC.

Keywords: Cancer-associated fibroblasts, cervical cancer, leucine-rich repeat-containing 15human papilloma, virus, potential therapeutic strategy

25COASDEC05

Title: Cytoreductive Surgery With or Without Intraperitoneal Chemotherapy for Peritoneal Spread from Appendiceal Neoplasms and Cancers

Jung Wook Suh, Hwan Namgung, Jae Won Jo et.al.

Anticancer Research December 2025, 45 (12) 5753-5763;
https://doi.org/10.21873/anticanres.17908

Abstract: Cytoreductive surgery (CRS) and intraperitoneal chemotherapy are standard treatments for the peritoneal spreading from appendiceal tumours. We aimed to assess and compare outcomes after CRS, with or without intraperitoneal chemotherapy, in patients with peritoneal spreading from appendiceal neoplasms and malignancies.Patients and Methods: In this retrospective study, we analysed prospectively collected data from patients with appendiceal tumours and peritoneal metastases who were treated with CRS and intraperitoneal chemotherapy. Survival analysis was performed to evaluate overall survival, completeness of cytoreduction (CCR) 0-1, subgroup outcomes, and survival-influencing factors.Results: We analysed data on 47 patients, including 10 (21.3%) with appendiceal neoplasms and 37 (78.7%) with appendiceal cancer. By the last follow-up visit, 23 patients had survived. The 5-year survival rate was significantly higher in the appendiceal neoplasm group (50%) than in the appendiceal cancer group (21.6%). Patients with CCR grades 2-3 had a 6.7-fold higher risk of mortality than those with CCR grades 1-2. Additionally, appendiceal cancer was associated with an 8-fold higher risk of mortality than low-grade appendiceal neoplasms. Postoperative chemotherapy was associated with 74.6% risk reduction, highlighting its potential benefits.Conclusion: Peritoneal metastases from appendiceal tumours, particularly pseudomyxoma peritonei arising from low-grade appendiceal mucinous neoplasms, show acceptable oncologic outcomes with aggressive treatment approaches, such as CRS combined with intraperitoneal chemotherapy. Therefore, CRS should be performed in cases where complete cytoreduction is achievable.

Keywords: Appendiceal cancer, appendiceal neoplasm, cytoreductive surgery, intraperitoneal chemotherapy, peritoneal spread

25COASDEC06

Title: Prognostic Factors in Non-small Cell Lung Cancer Patients Treated With Immune Checkpoint Inhibitors

Yutaka Takahara, Ryudai Abe, Sumito Nagae et.al.

Anticancer Research December 2025, 45 (12) 5633-5644;
https://doi.org/10.21873/anticanres.17897

Abstract: Immune checkpoint inhibitors (ICIs) have emerged as a first-line treatment for advanced non-small cell lung cancer (NSCLC), offering the potential for long-term survival. However, predictors of sustained clinical benefit in patients without driver gene mutations remain poorly defined. This study aimed to identify clinical and therapeutic factors associated with long-term survival in NSCLC patients treated with ICIs.Patients and Methods: We retrospectively analyzed 97 NSCLC patients treated with ICIs. Patients who survived for >3 years were classified as the long-term survival group, and those who did not were categorized as the non-long-term survival group. Clinical characteristics and treatment-related factors were compared between these two groups.Results: Of the 97 patients, 22 (22.7%) were classified into the long-term survival group. This group included a higher proportion of younger patients, patients who responded to initial ICI therapy, and patients who discontinued treatment due to immune-related adverse events (irAEs). Multivariate analysis identified younger age and low neutrophil-to-lymphocyte ratio (NLR) as independent predictors of long-term survival. Adenocarcinoma histology and switching administration of ICIs (i.e., changing from a PD-1 to a PD-L1 inhibitor or vice versa) showed clinically suggestive, though marginally significant, associations with prolonged survival.Conclusion: Younger age and low NLR were associated with long-term survival in NSCLC patients treated with ICIs. Adenocarcinoma and switching administration may have potential clinical relevance. These findings highlight the importance of patient selection and strategic management of ICI therapy. Nevertheless, confirmation in larger prospective cohorts is warranted.

Keywords: ICI rechallengeimmune checkpoint inhibitorimmune-related adverse events (irAEs)non-small cell lung cancerprognosis.

25COASDEC07

Title: The single nucleotide polymorphism rs155787 on the autophagy gene of SQSTM1 is associated with silicosis susceptibility: A multi-stage study

Lijing Jiang, Fan Wang, Mingwei Huai et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111744

Abstract: To investigate the association between single nucleotide polymorphisms (SNPs) in autophagy-related genes (ATGs) and susceptibility to silicosis.Methods: Used silicosis genome-wide association study (GWAS) data and multiple publicly available databases to identify autophagy-associated positive expression quantitative trait locus (eQTL)-SNPs. Candidate positive SNPs were subsequently validated for their association with silicosis susceptibility in an independent population. Additionally, quantitative real-time polymerase chain reaction (qRT-PCR) was employed to explore the expression of target genes. Finally, gene enrichment analysis was performed to preliminary explore the biological functions and potential pathways associated with the identified susceptibility genes.Results: A total of 15

SNPs in 10 ATGs were finally obtained after screening. Validation phase results indicated a significant association between the mutant G allele of rs155787 on the Sequestosome 1 (SQSTM1) and an increased risk of silicosis (additive model: odds ratio (OR)= 1.55, 95 % confidence interval (95 % CI): 1.05–2.28, P = 0.027). Combining GWAS and validation phase data, the mutant G allele was correlated with heightened silicosis susceptibility (additive model: OR=1.70, 95 % CI: 1.22–2.36, P = 0.002). The eQTL results indicated that significantly higher SQSTM1 expression in AG and GG genotypes than in AA genotypes (P < 0.05). Bioinformatics analysis revealed that SQSTM1 may bind to a range of autophagy proteins and immunoproteins to activate the biological process of macroautophagy, which influences the development of silicosis.Conclusion: The rs155787 locus on the SQSTM1 may be associated with silicosis susceptibility, and the mutant G allele may serve as a potential risk factor. Furthermore, the A>G variation at this locus was observed to upregulate SQSTM1 gene expression. Additional large-scale studies are necessary to further validate our findings.

25COASDEC08

Title: HRD1 promotes chronic alcoholic liver disease by mediating ACSL3 ubiquitination and degradation

Lu Meng, Yan Hu, Xuzi Zhao et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111753

Abstract: Alcohol-associated liver disease (ALD), one of the most frequent chronic liver diseases globally, is characterized by steatosis. HMG-CoA reductase-degrading protein 1 (HRD1) participates in the endoplasmic reticulum-associated protein degradation pathway through the recognition, translocation, and ubiquitination of substrate proteins. HRD1 is implicated in endoplasmic reticulum stress, oxidative stress and cell metabolism; however, the function of HRD1 in ALD remains unclear.Aims: We aimed to explore the contribution and underlying molecular mechanism of HRD1 in alcoholic liver disease. Methods: Mice were administered adeno-associated virus 9 encoding HRD1- or ACSL3-specific shRNA via intravenous injection, followed by feeding with a Lieber–DeCarli liquid diet containing 5 % ethanol. HepG2 cells were transfected with either HRD1 siRNA or HRD1 overexpression plasmids prior to ethanol exposure.Results: Hepatic HRD1 expression was significantly increased under alcohol conditions. Hepatocyte-specific HRD1 knockdown markedly attenuated alcohol-induced hepatic injury, inflammation, oxidative stress and lipid metabolism disorders in vivo. Additionally, similar results were shown in vitro. Mechanistically, acyl-CoA synthetase long chain family member 3 (ACSL3), a key regulator known to ameliorate hepatic steatosis, was identified as a novel substrate of HRD1. HRD1 facilitates the ubiquitination and degradation of ACSL3. Interestingly, HRD1 knockdown significantly suppressed fatty acid synthesis and promoted fatty acid oxidation, which was reversed by ACSL3 silencing both in vivo and in vitro.Conclusion: In summary, HRD1 functions as a key mediator of ALD by ubiquitinating ACSL3, thereby promoting lipid dyshomeostasis, and aggravating ALD. Our findings reveal novel mechanistic insights into HRD1 and identify ACSL3 as a new downstream target of HRD1 to facilitate ALD treatment.

25COASDEC09

Title: Prenatal exposure profiles to Benzophenones and their impacts on thyroid hormones

Khelfi Abderrezak, Alsayed Ahmad Dana, Azzouz Mohamed

Toxicology Letters, Volume 414, December 2025,
https://doi.org/10.1016/j.toxlet.2025.111746

Abstract: Purpose: Prenatal exposure to Benzophenones and their potential health impacts remain insufficiently studied, particularly among vulnerable populations such as pregnant women. The lack of research is concerning given the suspected risks these endocrine-disrupting chemicals (EDCs) may pose to neonatal health, especially in relation to thyroid hormone regulation. This study seeks to address this research gap by measuring prenatal exposure profiles to Benzophenones in women living in Algiers. Specifically, it aims to explore the associations between Benzophenone levels in umbilical cord blood and disruptions in thyroid hormone levels at the time of delivery. Additionally, the study investigates the possible link between women's exposure to specific sources and the resulting endogenous levels of Benzophenones.Methods: This was a descriptive study carried out on 154 paired mother-newborns after gathering necessary information using a questionnaire. Umbilical cord blood was collected and TSH and thyroid hormones (FT3 and FT4) were measured by electrochemiluminescence while Benzophenones (BP-1, BP-2, and BP-3) were detected by LC-MS/MS.Results: BP-1, BP-2, and BP-3 were detected in 29.87 %, 0 %, and 48.05 % of analyzed samples. Mean concentrations were 0.330 and 0.787 µg/g for BP-1 and BP-3, respectively. Significant negative association was found between levels of FT3 and concentrations of BP-3 in cord blood (β= -0.237), as well as a negative association between levels of FT4 and prenatal concentrations of BP-1 (β= -1.028). Notably, prenatal exposure to Benzophenones did not exhibit significant alterations on birth outcomes. A significant association linked lower levels of BP-1 with the tendency to read ingredient labels on cosmetic products by pregnant women (P = 0.024). Conclusion: In this Algerian population of parturient women, high exposure profiles to BP-1 and BP-3 through placental blood were associated with altered levels of thyroid hormones (FT4 and FT3, respectively). It appears these two compounds exert a diminishing effect on thyroid function. Such changes may involve adverse effects on maternal health and child development, especially on the nervous system.

25COASDEC10

Title: Urinary metal mixtures and cataract: Findings from a U.S. population-based study and network pharmacology analysis

Runzi Yang, Jing Li, Rui Liu et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111751

Abstract: To analyze the effects of various urinary metals on cataract using National Health and Nutrition Examination Survey data.Methods: Multivariate logistic regression was used to analyze the relationship between nine urinary metals and cataract. Weighted quantile sum (WQS) was used to analyze the positive and negative effects of various metals on cataract. The global and independent effects were analyzed using Bayesian kernel machine regression (BKMR). Network pharmacological analysis was used to explore the mechanism of metals

on cataract.Results: A total of 2207 participants were participated in the study. After excluding the influence of covariates, it was found that the concentrations of Ba, Sb, and Tl were significantly correlated with the prevalence of cataract. WQS showed that Cd, Pb, and Ba had the strongest negative effects on cataracts, while Tu and Co had the strongest positive effects. BKMR showed that the overall effect of nine urinary metals had no significant relationship with cataract, there was a significant positive correlation between Co and cataract, and a significant negative correlation between Pb and cataract under certain conditions. Co and cataract interact through various pathways, including Interleukin-4 and Interleukin-13 signaling. AKT1 may be the key protein in the correlation.Conclusion: Urinary metal concentrations may be associated with the risk of ocular outcomes. While our findings suggest potential links between Co and cataract, these results should be interpreted with caution due to the cross-sectional nature of the data. Further longitudinal studies are needed to confirm these associations and to explore possible threshold levels for clinical or public health monitoring.

25COASDEC11

Title: Epigenetic effects of cadmium and lead in asthma: Cadmium-specific associations with ADRB2 methylation and miRNA-146a expression in Egyptian Adults

Heba Mohamed Aboubakr, Shimaa Ahmed Alsaeed, Rabab Abdulmoez Amin Eltokhy et.al.

Toxicology Letters, Volume 414, December 2025

https://doi.org/10.1016/j.toxlet.2025.111754

Abstract: Asthma is a prevalent health condition with significant global impact. Heavy metals, especially lead and cadmium, have been markedly linked to asthma etiology, however, studying their epigenetic mechanisms remains limited. to study the association between exposure to lead and cadmium, the methylation of the ADRB2 gene, and the expression of miRNA-146a in adult asthma patients.Methods: A case-control study included 35 adult asthma patients and 35 sex and age-matched healthy controls. Blood lead, cadmium, ADRB2 5′-UTR methylation and miRNA-146a expression levels were measured for all participants.Results: Blood cadmium and ADRB2 5′-UTR methylation levels showed significantly higher values, blood lead levels showed higher, but nonsignificant, values, miRNA-146a expression levels showed significantly lower values in asthma patients, compared to controls. Blood cadmium positively correlated with ADRB2 5′-UTR methylation and negatively correlated with miRNA-146a expression. Regression analysis found that blood cadmium, ADRB2 5′-UTR methylation, and miRNA-146a expression levels were associated with asthma occurrence, showing significant odds ratios (95 % CI). Significant novel cutoff values for differentiating between healthy and asthmatic patients were set by ROC curve analysis.Conclusion: Blood cadmium is significantly linked to asthma, with increased ADRB2 5′-UTR methylation, and reduced miRNA-146a expression. The significant odds ratios and the novel cut off values demonstrate potential clinical applicability, offering promising epigenetic biomarkers for asthma prediction and diagnosis in Egyptian adults. Measures to minimize heavy metals' environmental exposure are recommended.

25COASDEC12

Title: Investigating the application of 3D skin models in micronucleus assay and comet

assay

Tianyin Lin, Huan Luo, Jingqiu Sun et.al.

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Abstract: Conventional two-dimensional (2D) cell culture models for genotoxicity testing often yield false-positive results due to their limited metabolic capacity and lack of tissue architecture. Three-dimensional (3D) reconstructed human skin models offer a more physiologically relevant alternative for evaluating genotoxicity. In this study, the reproducibility, dose–response, and predictive performance of the micronucleus test (MNT) and comet assay were systematically assessed using 3D skin models EpiSkin-MNT and T-Skin. A panel of reference chemicals, including both genotoxic and non-genotoxic agents, was tested. Cytotoxicity was measured using ATP and adenylate kinase (AK) assays; genotoxicity endpoints included micronucleus frequency and comet assay parameters such as tail intensity and tail moment. Both assays exhibited clear dose-dependent increases in genotoxic markers for positive controls, while negative controls showed no significant response. Use of the DNA repair inhibitor aphidicolin in the comet assay enhanced the sensitivity of DNA damage detection. The integration of 3D skin models with MNT and comet assays provides a robust, reproducible, and physiologically relevant platform for genotoxicity assessment, supporting the transition from animal-based methods and aligning with regulatory trends.

25COASDEC13

Title: A chemoproteomic strategy for identifying protein covalent binding targets of clozapine: An approach for advancing clozapine toxicity research

Steven Lockhart, Yasser Tabana, Seyed Amirhossein Tabatabaei Dakhili

Toxicology Letters, Volume 414, December 2025
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Abstract: Schizophrenia affects a significant proportion of individuals, wherein a subset of patients is described as treatment-resistant. Clozapine (CLOZ) is an atypical antipsychotic, which is reserved for these patients and is superior in its anti-suicidal activity. However, it carries numerous serious warnings and is well-known for its risk of drug-induced agranulocytosis. The mechanism of toxicity is unclear and could be due to CLOZ's protein covalent binding and off-target effects through its reactive metabolites produced from neutrophil myeloperoxidase (MPO) activity. We hypothesize that identifying and analyzing the protein-CLOZ adducts will contribute to our understanding of toxicity pathways. We have developed a novel clickable CLOZ (Click-CLOZ) derivative and have designed click chemistry protocols for protein identification. The HL-60 (human promyelocytic leukemia) cell line and isolated human neutrophils express MPO significantly and were used to identify the protein covalent targets of Click-CLOZ. In HL-60 cells, LC/MS analysis revealed many Click-CLOZ-bound proteins (compared to the vehicle control). Some captured proteins were known for their roles in DNA replication, immune responses and oxidative stress, such as cathepsin G, MPO, ribophorin I and P1-MCM3. In neutrophils, Click-CLOZ-bound proteins included MPO, S100, and DEFA1B, which are also associated with neutrophil-mediated oxidative stress and immune responses. In conclusion, the application of click chemistry proteomics has facilitated a novel approach to identify multiple CLOZ-bound protein targets

that will be used to advance our understanding of the toxicity of CLOZ.

25COASDEC14

Title: Environmental relevant concentrations of TBBPA cause complex toxicological mechanisms

Yuxing Liao, Yilin Wang, Hao Dong et.al.

Toxicology Letters, Volume 414, December 2025,
https://doi.org/10.1016/j.toxlet.2025.111767

Abstract: Tetrabromobisphenol A (TBBPA) is a widely used brominated flame retardant recognized for its environmental persistence, bioaccumulation and toxicological potential, raising concerns about its hazardous effects on both ecological systems and human health. Our research investigated the hepatotoxicity of TBBPA at environmentally relevant concentrations (1–100 nM) using transformed human liver epithelial-2 (THLE-2) cells. Results demonstrated that TBBPA exposure induced cell alterations in cell density, nuclear irregularities and fibrosis-like extensions. Transcriptomic analysis revealed significant perturbations in pathways related to metabolism, cellular stress responses, inflammatory responses, cell proliferation, substance transport and degradation. Further investigations revealed the most obvious gene expression profile changes at 1 nM TBBPA exposure, however, higher concentrations (10 nM and 100 nM) of TBBPA appeared to cause more severe hepatotoxicity. RT-qPCR and molecular docking experiments confirmed the changed gene expression and TBBPA-Protein binding. These findings elucidate complex mechanisms of TBBPA-induced effects in hepatocytes, highlighting the environmental health risks of TBBPA.

25COASDEC15

Title: Recommendations for the calculation of inhalation exposure to cosmetic spray products: A comprehensive review

W. Steiling, H. Assaf Vandecasteele, F. Boisleve et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111771

Abstract: Consumer products such as cosmetic spray products must be safe. Strict rules to ensure this for cosmetic spray products are established by the EU Cosmetic Products Regulation, as well as by scientific advisory panels. In this article several default values are proposed from the literature to improve the consistency and accuracy of inhalation exposure assessments performed for cosmetic spray products. The use of these default values is given for the most relevant spray product types currently on the EU market. The use of well-known exposure calculation models (e.g. one-box and two-box models) are discussed for their applicability to estimate consumer inhalation exposure to certain spray product types. The availability of measured data from experimental studies is limited due to the complication caused by parameters such as technical product information relating to droplet/particle sizing of the airborne product. In some cases, there is reliance on conservative, worst-case input values (e.g., spray time and the amount released from the product container) for exposure assessment of individual product uses. Where the authors have identified data gaps for certain parameters for specific product types during the literature review, recommendations are provided for additional consolidated default values to promote the safety assessment.

25COASDEC16

Title: Chronicle of mixture effects: Sensitivity differences in multiple toxicity endpoints of transgenic C. elegans and assessment of combined toxicity interactions

Peng Huang,Shu-Shen Liu, Jiake Li et.al.

Toxicology Letters, Volume 414, December 2025
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Abstract: The pesticide, as the typical emerging contaminants, has brought significant benefits to agricultural production due to its widespread use. However, the excessive residue of pesticides in environmental media poses potential risks to both the environment and human health. Therefore, this study focused on three typical pesticide residues (aldicarb (ALD), methamidophos (MET) and triazophos (TAP)) that were commonly detected in fruits and vegetables, using the DAF-16 transgenic strain of Caenorhabditis elegans (C. elegans) as a model organism. Three binary and one ternary mixture systems were designed using the direct equipartition ray design and the uniform design ray method, resulting in a total of 20 mixture rays. These were used for multi-endpoint toxicity tests on C. elegans. The results indicated that all mixture rays exhibited higher sensitivity at the endpoints of lifespan and reproduction inhibition compared to the mortality endpoint. Furthermore, the sensitivity to lifespan and reproduction inhibition varied across the different mixture rays. The mixture toxicity interaction assessment results indicated that with increasing toxicity effects, a concentration ratio-dependent phenomenon was observed in the toxicity interactions. Furthermore, when the effect level exceeded 30 %, opposite toxicity interaction outcomes (i.e., the shift from antagonism to synergism or vice versa) emerged across different toxicological endpoints. These findings pose significant challenges for the assessment of mixture combined toxicity.

25COASDEC17

Title: Hematological effects of chronic heavy metal exposure in children from marginalized occupational communities in Mexico

Karen B. Méndez-Rodríguez, Francisco J. Pérez-Vázquez, Evelyn Van Brussel et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111776

Abstract: Children engaged in precarious labor activities may experience exposure to environmental contaminants, including heavy metals, particularly in marginalized communities. Limited evidence exists regarding the potential hematological implications of such exposures in pediatric populations. A cross-sectional study was conducted among 50 children (<18 years) from three communities in San Luis Potosí, Mexico, engaged in informal recycling (Zone B), artisanal brickmaking (Zone C), or artisanal stone-carving (Zone A). Urinary concentrations of 15 metals were determined by ICP–MS, and hematological parameters were assessed using an automated analyzer. Associations were examined using nonparametric statistics, age-adjusted correlations, Bayesian Kendall's Tau analysis, and post hoc power evaluation. Distinct urinary metal profiles and hematological parameters were observed across the study zones. Zone B showed higher concentrations of Cr, Co, Ni, Al, and Sn, whereas As was elevated in Zone C. Hematological differences included higher WBC, lymphocyte, granulocyte counts, and MPV in Zone C. Age-adjusted correlations identified associations of As with WBC, lymphocyte, and granulocyte counts; Co

with platelet indices; and negative correlations of Ni, Al, and Sn with several hematological variables. Bayesian analysis confirmed robust associations for Co with WBC, Al with granulocytes, and Sn with MPV. This study provides exploratory evidence of associations between urinary metal concentrations and hematological parameters in children engaged in precarious labor activities. While preliminary, the findings underscore the importance of child-focused public health strategies and support the need for larger, longitudinal studies to validate these associations and clarify their implications.

25COASDEC18

Title: Exposure to the trichloroethylene metabolite S-(1,2-dichlorovinyl)-L-cysteine under hypoxic conditions (%O2 =2 %) alters differential gene expression and mitigates decreased invasion capacity, compared to normoxic conditions (%O2 ≥ 21 %) in HTR-8/SVneo cells

Franny H. Stein, Nora H. Le, Elana R. Elkin

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111773

Abstract: Trichloroethylene (TCE) is a volatile organic compound used as an industrial solvent until the recent EPA phaseout. Despite regulatory restrictions, legacy TCE pollution persists in soil and groundwater and poses a risk to human health. This chemical exerts its toxic effects through its metabolites including the glutathione conjugation metabolite S-(1,2-dichlorovinyl)-L-cysteine (DCVC). Although a known nephrotoxicant, limited research has explored its effects on placental development – despite a reported epidemiological association between maternal exposure and elevated risk of restricted fetal growth. The placenta plays a critical role in the first trimester, functioning under hypoxic conditions to support fetal growth. Extravillous trophoblasts (EVTs), essential for placental development, are sensitive to environmental stressors. In this study, effects of human-relevant DCVC concentrations on cytotoxicity, differential gene expression, and invasion capacity were evaluated and compared under normoxic and hypoxic conditions using the placental EVT cell line HTR-8/SVneo. Differential gene expression between normoxic and hypoxic controls was also evaluated to characterize the simulated hypoxic experimental conditions. DCVC exposure induced significant cytotoxicity at concentrations as low as 10 μM under both normoxic and hypoxic conditions. DCVC also caused differential gene expression under both conditions, with a more robust response under normoxia. Similar biological pathways were altered under both conditions, including those involved in oxidative balance, cell migration, and apoptotic signaling. Invasion capacity significantly decreased with 10 and 20 μM DCVC under normoxia but was partially rescued under hypoxia, indicating a possible protective effect. Overall, HTR-8/SVneo cell responses to DCVC were similar under both oxygen conditions, with some evidence of hypoxia offering mild protection. This study builds on previous literature and offers new evaluation of exposure under different simulated oxygen conditions mimicking those experienced during the first trimester of pregnancy.

25COASDEC19

Title: Chlormequat chloride inhibited thyroid hormone in the pregnant rats by regulating sodium/iodide symporter

Celigeer, Wei Tian, Zongzhen Wu et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111772
Abstract: Chlormequat chloride can increase agricultural production by making the stem of the crops shorter and stronger, so it has become one of the most popular growth regulators in the world and humans are widely exposed to it. However, besides its regulatory effects on the growth of the plants, our previous studies have demonstrated that chlormequat chloride can also affect maternal and embryonic homeostasis in the rats. To better understand the regulatory effect of chlormequat during pregnancy, in this study, pregnant rats were orally exposed to chlormequat chloride at 0, 0.05, 0.5 and 5 mg/kg.bw from gestation day (GD) 0–20, we found that levels of maternal thyroid hormones (THs) were inhibited on GD11 and the brain weight of the pups was affected on postnatal day (PD) 10. To understand the mechanisms of the decreases in THs, we found that the sodium/iodide symporter (NIS), which is responsible for the uptake of iodide by thyrocytes in the biosynthesis of THs, was inhibited in pregnant rats by chlormequat chloride dose-dependently. Furthermore, the thyrotropin (TSH) induced cAMP dependent protein kinase A (PKA) signaling pathway, which is the up-stream regulating pathway of NIS, was also inhibited by chlormequat chloride in the pregnant rats. However, the TSH-PKA-NIS pathway was not affected by chlormequat chloride in the non-pregnant female rats. To summarize, chlormequat chloride caused down-regulation of NIS and thus inhibited synthesis of maternal THs during embryonic development, and leads to altered postnatal brain weight.

25COASDEC20

Title: Long-term supplementation of taurine induces hepatic steatosis and disrupts bile acid homeostasis in male mice

Tong Shi, Shu-Yun Zhang
Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111778
Abstract: Taurine, a sulfur-containing amino acid, is widely used in energy drinks and nutraceuticals. However, the long-term effects of taurine supplementation on liver metabolism remain incompletely understood. Here, male C57BL/6 mice were administered 3 % taurine in drinking water for 32 weeks. Taurine treatment reduced body weight and abdominal fat, suggesting potential anti-obesity effects. However, hepatic lipid accumulation and steatosis were evident in taurine-treated mice. Serum levels of alanine aminotransferase, alkaline phosphatase, cholesterol, non-esterified fatty acids (NEFA), total bile acids, and hepatic triglycerides were markedly elevated. Taurine significantly upregulated hepatic expression of the fatty acid transporter Cd36, thereby enhancing hepatic fatty acid uptake and promoting lipid deposition, while increasing lipolytic enzymes Atgl and Hsl expression in white adipose tissue, contributing to increased circulating NEFA and subsequent hepatic lipid accumulation. Moreover, taurine disrupted the negative feedback regulation of bile acid biosynthesis in the enterohepatic circulation, increased bile acid synthesis and uptake, altered bile acid transport, and elevated both conjugated and unconjugated bile acid species. Histological and molecular analyses further revealed taurine-induced hepatic inflammation, characterized by perivascular immune cell infiltration and upregulation of pro-inflammatory cytokines and mediators. Importantly, taurine-induced metabolic alterations in lipid and bile acid homeostasis were evident as early as 5 weeks, preceding the onset of histological

steatosis. Collectively, these findings demonstrate that prolonged taurine supplementation promotes hepatic steatosis and inflammation, accompanied by dysregulation of bile acid homeostasis. The study highlights the potential metabolic risks associated with chronic taurine intake and underscores the need for caution when considering taurine-based health supplements.

25COASDEC21

Title: Transgenerational toxicity of tralomethrin in zebrafish: Parental exposure induces developmental defects in offspring

Yueping Huang, Wenmin Feng, Jinli Zhang et.al.

Toxicology Letters, Volume 414, December 2025

https://doi.org/10.1016/j.toxlet.2025.111777

Abstract: Tralomethrin (TRA), a widely used type II pyrethroid insecticide, belongs to a class of pesticides frequently detected in aquatic environments, raising concerns about its potential chronic and transgenerational toxicity. This study aimed to evaluate the long-term effects of environmentally relevant concentrations of TRA (0.05, 0.5, and 5 μg/L) on adult zebrafish and their offspring. Adult zebrafish were exposed to TRA for 150 days, during which phenotypic observations, histological assessments, biochemical assays, transcriptomic profiling, and developmental evaluations of F1 progeny were conducted. Following TRA exposure, male zebrafish exhibited increased body weight, and a significant decline in spawning rate was observed. Histological and biochemical analyses revealed gill and ovarian abnormalities, accompanied by oxidative stress and apoptosis in ovarian tissues. Transcriptomic analysis of TRA-exposed ovaries revealed gene enrichment in glutathione metabolism and signaling pathways including Hedgehog and Wnt, reflecting oxidative stress and developmental disruption. In the F1 generation, TRA exposure led to decreased survival and hatching rates, along with developmental abnormalities including pericardial edema, spinal curvature, and impaired swim bladder inflation. Gene expression analyses of swim bladder marker genes and regulatory pathways further corroborated TRA-induced disruption in organogenesis. Overall, these findings demonstrate that chronic TRA exposure can induce multi-level toxic effects in zebrafish, including reproductive impairment and transgenerational developmental defects. This study highlights the urgent need to assess the ecological risks of pyrethroid pesticides and to incorporate long-term and transgenerational endpoints into environmental risk assessment.

25COASDEC22

Title: Co-exposure to low levels of DEHP, procymidone, Cd2 + , Pb2+, and 1-nitropyrene may damage mouse ovary and uterus via Hippo pathway and circPVT1

Yushan Li, Hui Nie, Shiyun He et.al.

Toxicology Letters, Volume 414, December 2025

https://doi.org/10.1016/j.toxlet.2025.111770

Abstract: High doses of Di-(2-ethylhexyl) phthalate (DEHP), procymidone (PCM), Cd2+, Pb2+, and 1-nitropyrene (1-NP) induce reproductive toxicity in female experimental animals. However, evidence regarding female reproductive toxicity at low levels of combined exposure (co-exposure) to these substances is lacking. In this study, these environmental chemicals, which met or minimally exceeded the relevant standards, were administered

simultaneously to 4-week-old female mice. After 21 days of exposure, the mice were kept feeding for 1 week and then sacrificed. Subsequently, their blood, ovaries, and uteri were taken. Co-exposure to concentrations ≥ 1/3 of the maximum allowable concentration (MAC) for each of these chemicals, as per relevant standards, was revealed to impair ovarian and uterine development in mice. This exposure activated the Hippo pathway, resulting in a decrease in ERα and circPVT1, and an elevation of miR-149. Co-exposure to these compounds in levels marginally lower than the MACs of each chemical also elevated cleaved CASPASE-3 levels. These changes showed a dose–response relationship. Joint exposure to these substances at values ≥ 1/3 of each average concentration in the blood could elicit similar biological effects in the ovaries and uteri cultured in vitro. Therefore, this study hypothesized that co-exposure to low levels of these environmental chemicals results in ovarian and uterine impairment in mice and that this damage may be linked to the activation of the Hippo pathway, downregulation of ERα and circPVT1, and upregulation of miR-149.

25COASDEC23

Title: Microbiological toxicology of the new antibiotic aditoprim on human intestinal microbiota

Junhao Wang, Chunbei Liu, Fangtong Gu et.al.

Toxicology Letters, Volume 414, December 2025

https://doi.org/10.1016/j.toxlet.2025.111780

Abstract: Aditoprim (ADP) is a novel dihydrofolate reductase inhibitor. It has potent antibacterial activity, low toxicity, and no mutagenicity. These characteristics position it as a promising candidate for further research in clinical veterinary medicine and its effect on humans. Therefore, this research aimed to investigate the impact of ADP on human microbiota. ADP (0, 1, 16, and 128 mg/L) was added to chemostats containing human intestinal flora. Microflora communities, short-chain fatty acids (SCFAs), and the rate of antibiotic resistance were monitored at different time points before and after the administration of ADP. Salmonella Typhimurium inoculation was used to assess the gut microbiota's colonization barrier over a period of three days. The results indicate long-term exposure to higher levels of ADP (16 and 128 mg/L) disrupted the colonization barrier of intestinal flora and increased the proportion of resistant bacteria. 16S rRNA sequencing data indicate that high levels of ADP caused significant changes in gut microbiota, especially Bacteroides fragilis and Bacteroides uniformis. This study assessed the microbiological safety of ADP in vitro for the first time by simulating the human gut microbiota environment. The findings showed that 1 mg/L was the no observable adverse effect concentration, and the microbiological acceptable daily intake was determined to be 91.67 μg/kg.BW/day.

25COASDEC24

Title: Comparison of the serum levels of proteins involved in microtubule stabilization in patients with alcohol or heroin use disorder

Huseyin Kayadibi, İhsan Cetin, Mehmet Emrah Karadere et.al.

Toxicology Letters, Volume 414, December 2025

https://doi.org/10.1016/j.toxlet.2025.111782

Abstract: In patients with alcohol or heroin use disorder, we aimed to examine the effects of alcohol or heroin use and treatment on the serum levels of microtubule stabilization

proteins.Method: A total of 64 patients with 32 alcohol and 32 heroin use disorder, and age-gender matched healthy volunteers were included in this study. Fasting blood samples were taken from patients before and after three weeks of treatment, and from healthy volunteers on the first working day after first interview.Results: Compared to healthy controls, there were statistically significant decreases for serum levels of microtubule associated protein-2, tau protein, phospho tau protein, glial fibrillary acidic protein, glial cell line derived neurotrophic factor and progranulin, while there was a statistically significant increase for serum levels of Nogo-A in patients with alcohol use disorder ($P < 0.001$, $P < 0.001$, $P < 0.001$, $P < 0.001$, $P < 0.001$, $P = 0.002$ and $P < 0.001$, respectively). In patients with heroin use disorder compared to healthy controls, there was a statistically significant increase only for serum level of Nogo-A ($P < 0.001$). Only post-treatment serum progranulin level of patients with alcohol use disorder was statistically significantly higher than pre-treatment levels ($P = 0.040$).Conclusion: It was considered that these proteins may be a potential biomarker in terms of reflecting molecular level of damage caused by alcohol or heroin use, as well as distinguishing patients with and without alcohol or heroin use disorder. Further studies with long term treatments may be performed to investigate the optimum therapy period, since three weeks of treatment may not be enough to repair this damage.

25COASDEC25

Title: DBDPE inhibits myogenic differentiation of C2C12 cells through inhibiting mitochondrial function and PI3K/AKT/mTOR signaling pathway

Xinfang Tan, Jinglan Li, Yang Peng et.al.

Toxicology Letters, Volume 414, December 2025

https://doi.org/10.1016/j.toxlet.2025.111783

Abstract: In recent years, decabromodiphenyl ethane (DBDPE), a type of brominated flame retardant, has gained popularity in industry as an alternative to decabromodiphenyl ether (BDEs). However, DBDPE exposure poses environmental pollution and primarily impacts muscle contraction and the reproductive endocrine system. The cellular implications and underlying mechanisms of DBDPE's effects on muscle remain poorly understood. In the present study, we investigated the effect of DBDPE on myoblast differentiation, apoptosis, as well as the potential mechanisms involved. The results demonstrated that exposure to DBDPE disrupted the differentiation of myotubes, inhibited cell proliferation, and increased levels of reactive oxygen species (ROS), ultimately leading to cell death. In addition, the RNAseq analysis revealed that DBDPE mainly affected the biological processes in mitochondria related to oxidative phosphorylation, ATP synthesis coupled electron transport, etc. Then we demonstrated that DBDPE inhibited mitochondrial membrane potential and ATP production, implying DBDPE resulted in mitochondrial dysfunction in C2C12 cells. Mechanistically, we showed that PI3K/AKT/mTOR signaling pathway was inhibited by DBDPE in C2C12 cells. And the apoptosis rate was significantly increased by DBDPE as demonstrated by increased active caspase-3 and TUNEL signal. Taken together, these findings suggest that low-dose exposure to DBDPE hampers myogenic differentiation and mitochondrial function, and increased cellular apoptosis through PI3K/AKT/mTOR signaling pathway, providing important insights for understanding its environmental toxic effects and conducting risk assessments.

25COASDEC26

Title: Comprehensive estrogenicity assessment of 4-methylbenzophenone via in vivo, in vitro, and in silico approaches within an integrated testing strategy framework

Darlene Mae D. Ortiz, Ngoc Minh-Hong Hoang, Handule Lee et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111784

Abstract: 4-Methylbenzophenone (4-MBP) is extensively used as a photoinitiator in ultraviolet-cured printing inks and food packaging. This study comprehensively evaluated its estrogenic activity using an Integrated Testing Strategy (ITS) incorporating in vivo, in vitro, and in silico methodologies. Repeated oral administration of 4-MBP at 300 mg/kg (lowest observed effect concentration, LOEC) in ovariectomized rats significantly increased relative uterine weight (0.11 ± 0.01 % vs. 0.05 ± 0.00 % in controls) and serum estradiol levels elevated serum estradiol levels (4-fold over vehicle control). Histological analysis confirmed estrogenic alterations, including epithelial thickening, glandular degeneration, and stromal inflammation. Although estrogen receptor α (ERα) expression remained unchanged, aromatase (CYP19) was significantly upregulated in uterine tissue, suggesting that enhanced estrogen biosynthesis plays a key role in the effects elicited by 4-MBP. In vitro assays showed that 4-MBP activated ER transcription in HeLa9903 cells with a maximum relative proliferative capacity (RPCmax) of about 200 % compared with 1 nM 17β-estradiol, and significantly induced MCF-7 cell proliferation at 10^{-5} M, coinciding with peak CYP19 mRNA expression. CYP19 expression was also increased at the mRNA and protein levels, and evidence of post-transcriptional regulation was observed at higher concentrations (10 μM). In silico molecular docking and dynamic simulations corroborated these findings demonstrating strong binding affinities of 4-MBP to ERα (docking score as low as −8.7 kcal/mol) and ERβ. Our results indicate that 4-MBP exerts estrogenic effects by elevating estrogen synthesis and inducing direct ER transcriptional activation. These findings highlight the utility of ITS for evaluating endocrine-disrupting chemicals and emphasize the need for regulatory consideration of 4-MBP and structurally related compounds in consumer products.

25COASDEC27

Title: Metabolic activation, hepatic protein covalent binding, and cytotoxicity of arctigenin

Yuqin Chen, Zixia Hu, Guode Zhao et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111785

Abstract: Arctigenin (ATG) is an important component isolated from the fruit of the medicinal plant Arctium lappa L., with anti-inflammatory, antiviral and anti-tumor properties. Although ATG has been reported to induce hepatotoxicity in beagle dogs and SD rats, and the underlying mechanisms remained unclear. The aim of this study was to investigate the metabolic activation of ATG and to define the potential correlation between the metabolic activation of ATG and its hepatotoxicity. A quinone methide intermediate was identified in vitro and in vivo, and CYP3A dominated the metabolic activation. ATG was found to show significant cytotoxicity at 50 μM in cultured mouse primary hepatocytes. The ATG-derived quinone methide metabolite assaulted cysteine residue of hepatic protein to form protein

covalent binding. The observed protein modification was most likely associated with the cytotoxicity of ATG observed.

25COASDEC28

Title: 1-NP hijacks endocrine-metabolic checkpoints and disrupts testicular steroidogenesis by suppressing the cAMP-PKA-CREB-HMGCR axis

Xin-xin Zhu, Wei-wei Zhang, Ming-yue Hao et.al.

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111781

Abstract: 1-Nitropyrene (1-NP), a representative reproductive toxicant enriched in nitro-PAHs, is a known reproductive toxicant. Although our previous studies demonstrated that 1-NP impairs testosterone synthesis, its effects on other critical processes in testosterone biosynthesis, particularly cholesterol metabolism, remain unknown. Using in vivo and in vitro models, we investigated 1-NP's effects on cholesterol homeostasis and steroidogenesis. Mice were exposed to 1-NP (0, 1.25, 5 mg/kg), a mouse Leydig tumor cell line (MLTC-1) were treated with 0.1, 1 μM 1-NP along with hCG stimulation. IBMX was used for intervention experiment. Key assays included ELISA, qPCR, Western blot, filipin staining, and cholesterol/testosterone quantification. This study demonstrates that 1-NP exposure significantly depletes intracellular free cholesterol without altering total cholesterol, leading to testosterone reduction. Mechanistically, 1-NP decreases cAMP levels, impairing PKA nuclear translocation and CREB Ser133 phosphorylation, thereby downregulating the cholesterol synthesis rate-limiting enzyme HMGCR at both transcriptional and translational levels. Critically, phosphodiesterase inhibitor IBMX rescues cAMP levels, reverses HMGCR suppression, and restores free cholesterol pools and testosterone synthesis, establishing that 1-NP induces endocrine disruption via a novel cholesterol metabolic pathway. While limitations exist, this work redefines 1-NP toxicity as "metabolic sabotage" of specialized endocrine pathways, providing a framework for signal-pathway-targeted interventions against pollution-associated endocrine disruption.

25COASDEC29

Title: Impact of microplastics and nanoplastics on human health: Mechanistic insights and exposure pathways

Mohd Fazal Ur Rehman, Mohammad Muaz Khan, Mohammad Mansoob Khan

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111769

Abstract: Microplastics (MPs) and nanoplastics (NPs) have emerged as critical environmental contaminants with potential adverse effects on human health. This review examines the various ways MPs and NPs can be spread in the environment and their potential impact on humans. They can be introduced into the environment through multiple sources, like synthetic textiles, cosmetics, packaging, and industrial processes. These particles enter the human body through ingestion, inhalation, and skin contact, and they deposit in various tissues, including the lungs, kidneys, and gastrointestinal tract. Additionally, they can cross embryonic layers and reach the placenta. They can cause inflammation, oxidative stress, metabolic disorders, genotoxicity, and immunotoxic effects upon interaction, as confirmed by in-vivo and in-vitro studies. Furthermore, long-term exposure to MPs and NPs causes various

complications to the human body, including metabolic disorders or even the development of cancers. Despite the presence of much evidence, a significant gap remains in fully understanding the mechanism of toxicity posed by MPs and NPs exposure and its long-term health outcomes. There is an urgent need for extensive investigations and improvement in standardized methods to evaluate the human health impact of MPs and NPs. This review explores current evidence on exposure pathways, bioaccumulation mechanisms, and health outcomes and identifies critical knowledge gaps.

25COASDEC30

Title: Neurovascular toxicity of dichlorvos: Crosstalk between endothelial dysfunction and neurodegeneration

Igbayilola Yusuff Dimeji, Ngabea Murtala, Adekola Saheed Ayodeji

Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111775

Abstract: O,O-Dimethyl O-(2,2-dichlorovinyl) phosphate (DDVP), commonly referred to as dichlorvos, is one of the most widely used organophosphorus insecticides for agricultural and domestic pest control, especially in low- and middle-income countries, due to its low cost and effectiveness. While acute neurotoxicity through the irreversible inhibition of AChE and subsequent cholinergic overstimulation is well documented, there is growing evidence that DDVP exerts broader chronic effects, particularly those involving the neurovascular system. Specifically, endothelial dysfunction and disruption of the bloodsingle bondbrain barrier have been shown to be early events that link vascular injury to neurodegeneration. These databases included PubMed, Scopus, Web of Science, ScienceDirect, EMBASE, and the Toxicology Data Network. The terms used in the search included "dichlorvos," "DDVP," "organophosphate pesticide," "neurotoxicity," "endothelial dysfunction," "bloodsingle bondbrain barrier," "neurodegeneration," "oxidative stress," and "crosstalk." The inclusion criterion was peer-reviewed studies published in English between 2000 and 2025, which involved in vivo and in vitro experimental studies that reported DDVP-induced neurovascular toxicity. Studies not related to DDVP, publications in languages other than English, and non-peer-reviewed sources were excluded. Studies suggest that DDVP impairs endothelial integrity through disrupting the homeostasis of oxidative stress, nitric oxide, and inflammatory signalling. This type of endothelial insult impairs selectivity in BBB permeability, enabling the infiltration of circulating toxins and cytokines into the central nervous system, thus promoting neuronal apoptosis, mitochondrial dysfunction, and neuroinflammation. These findings suggest that the neurotoxicity of DDVP extends beyond synaptic cholinergic mechanisms but includes neurovascular-crosstalk-driven degeneration. This review synthesizes current mechanistic insights into DDVP-induced neurovascular toxicity and recognizes the neurovascular unit as a critical target in organophosphate poisoning. Elucidation of the interplay between endothelial dysfunction and neuronal injury opens new avenues for risk assessment, preventive strategies, and therapeutic interventions for pesticide-related neurodegenerative disorders.

25COASDEC31

Title: Reproductive effects of dibutyl phthalate (DBP) toxicity in the testes of mammalian and avian species

Musa Zakariah, Reneilwe.A. Molele, Mohammed A.A. Mahdy et.al.
Toxicology Letters, Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111779

Abstract: Dibutyl phthalate (DBP), a widely used phthalic acid esters (PAEs), is a well-studied endocrine-disrupting chemical. It is one of the most and studied endocrine disruptors associated with reproductive disorders and infertility. Despite its prevalence, its exact mechanisms of action remain poorly understood. This review provides an overview of DBP's reproductive toxicity and explores its mechanisms in mammalian and avian species. Exposure to DBP during sexual differentiation disrupts the proliferation and maturation of Sertoli and Leydig cells, potentially leading to cryptorchidism, hypospadias, a shortened anogenital distance, and abnormal penile development in mammalian species. Additionally, it can cause atrophy of the seminiferous tubules and apoptosis of spermatogenic cells in both mammalian and avian species. Its effects are multifaceted, operating at hormonal levels by altering the release of hypothalamic, pituitary, and peripheral hormones, and at intracellular level by disrupting signalling cascades, nuclear and membrane receptors, altered steroidogenic gene expression, DNA disruption, and alteration of vimentin cytoskeleton proteins. It is important to note that the severity of reproductive toxicity varies between species at identical DBP concentrations, likely due to differences in metabolism. Nonetheless, existing data consistently implicate DBP in reproductive malformations that can lead to male infertility across species. This review highlights the need for further research into low-dose effects and species-specific responses to better understand and mitigate DBP's impact on reproductive health.

25COASDEC32

Title: Molecular mechanisms by which benzo[ghi]perylene promotes cell proliferation and DNA damage via downregulation of the chimeric RNA TVP23C-CDRT4/miR-24–3p axis

Sili Chen, Liqin Xiong, Xinlan Wu et.al.
Toxicology Letters,Volume 414, December 2025
https://doi.org/10.1016/j.toxlet.2025.111755

Abstract: We investigated the toxicity of benzo[ghi]perylene (BghiP), a prevalent polycyclic aromatic hydrocarbon (PAH). Transcriptome analysis of control and BghiP-exposed human bronchial epithelial cells (BEAS-2B) led to the identification of a novel chimeric RNA (chRNA), TVP23C-CDRT4, whose expression is significantly downregulated by BghiP in vitro and in vivo. Funcionally, overexpression of TVP23C-CDRT4 inhibited BghiP-induced cell proliferation and DNA damage, whereas its knockdown exacerbated these detrimental effects. Mechanistically, TVP23C-CDRT4 acts as a molecular decoy for miR-24–3p. Thus, BghiP-induced suppression of TVP23C-CDRT4 unveils a novel mechanism of PAH toxicity, highlighting its anti-proliferative and genome-protective roles relevant to the early stages of carcinogenesis.

25COASDEC33

Title: Leucine inhibits degradation of outer mitochondrial membrane proteins to adapt mitochondrial respiration

Qiaochu Li, Konstantin Weiss, Fuateima Niwa et.al.

Nature Cell Biology volume 27, November 11, 2025
https://doi.org/10.1038/s41556-025-01799-3

Abstract: The mitochondrial proteome is remodelled to meet metabolic demands, but how metabolic cues regulate mitochondrial protein turnover remains unclear. Here we identify a conserved, nutrient-responsive mechanism in which the amino acid leucine suppresses ubiquitin-dependent degradation of outer mitochondrial membrane (OMM) proteins, stabilizing key components of the protein import machinery and expanding the mitochondrial proteome to enhance metabolic respiration. Leucine inhibits the amino acid sensor GCN2, which selectively reduces the E3 ubiquitin ligase cofactor SEL1L at mitochondria. Depletion of SEL1L phenocopies the effect of leucine, elevating OMM protein abundance and mitochondrial respiration. Disease-associated defects in leucine catabolism and OMM protein turnover impair fertility in Caenorhabditis elegans and render human lung cancer cells resistant to inhibition of mitochondrial protein import. These findings define a leucine–GCN2–SEL1L axis that links nutrient sensing to mitochondrial proteostasis, with implications for metabolic disorders and cancer.

25COASDEC34

Title: FSP1-mediated lipid droplet quality control prevents neutral lipid peroxidation and ferroptosis

Mike Lange, Michele Wölk, Vivian Wen Li et.al.

Nature Cell Biology volume 27, November 11, 2025
https://doi.org/10.1038/s41556-025-01790-y

Abstract: Lipid droplets (LDs) are organelles that store and supply lipids, based on cellular needs. Although mechanisms preventing oxidative damage to membrane phospholipids are established, the vulnerability of LD neutral lipids to peroxidation and protective mechanisms are unknown. Here we identify LD-localized ferroptosis suppressor protein 1 (FSP1) as a critical regulator that prevents neutral lipid peroxidation by recycling coenzyme Q10 (CoQ10) to its lipophilic antioxidant form. Lipidomics reveal that FSP1 loss leads to the accumulation of oxidized triacylglycerols and cholesteryl esters, and biochemical reconstitution of FSP1 with CoQ10 and NADH suppresses triacylglycerol peroxidation in vitro. Notably, inducing polyunsaturated fatty acid-rich LDs triggers triacylglycerol peroxidation and LD-initiated ferroptosis when FSP1 activity is impaired. These findings uncover the first LD lipid quality-control pathway, wherein LD-localized FSP1 maintains neutral lipid integrity to prevent the build-up of oxidized lipids and induction of ferroptosis.

25COASDEC35

Title: Enhancer activation from transposable elements in extrachromosomal DNA

Katerina Kraft, Sedona E. Murphy, Matthew G. Jones et.al.

Nature Cell Biology volume 27, November 11, 2025
https://doi.org/10.1038/s41556-025-01788-6

Abstract: Extrachromosomal DNA (ecDNA) drives oncogene amplification and intratumoural heterogeneity in aggressive cancers. While transposable element reactivation is common in cancer, its role on ecDNA remains unexplored. Here we map the 3D architecture of MYC-amplified ecDNA in colorectal cancer cells and identify 68 ecDNA-interacting elements—genomic loci enriched for transposable elements that are frequently integrated

onto ecDNA. We focus on an L1M4a1#LINE/L1 fragment co-amplified with MYC, which functions only in the ecDNA-amplified context. Using CRISPR-CATCH, CRISPR interference and reporter assays, we confirm its presence on ecDNA, enhancer activity and essentiality for cancer cell fitness. These findings reveal that repetitive elements can be reactivated and co-opted as functional rather than inactive sequences on ecDNA, potentially driving oncogene expression and tumour evolution. Our study uncovers a mechanism by which ecDNA harnesses repetitive elements to shape cancer phenotypes, with implications for diagnosis and therapy.

25COASDEC36

Title: TDP-43 skein-like inclusions are formed by BAG3- and HSP70-guided co-aggregation with actin-binding proteins

Shan Lu, Sitao Zhang, Spencer Oung et.al.

Nature Cell Biology volume 27, November 11, 2025

https://doi.org/10.1038/s41556-025-01789-5

Abstract: In multiple neurodegenerative diseases, the RNA-binding protein TDP-43 forms cytoplasmic aggregates of distinct morphologies, including skein-like, small rounded granular and large spherical inclusions. Here, whereas the N-terminal self-oligomerization domain regulates TDP-43 demixing into cytoplasmic droplets, inhibition of N-terminal self-oligomerization domain-mediated oligomerization is shown to promote the formation of skein-like inclusions. Utilizing proximity labelling–mass spectrometry, cellular stresses are shown to induce TDP-43 association with actin-binding proteins that include filamins and α-actinin. Small interfering RNA-mediated reduction of filamin in Drosophila ameliorates cell loss from cytoplasmic TDP-43, consistent with the filamin–TDP-43 interaction enhancing cytotoxicity. TDP-43's association with actin-binding proteins is mediated by BAG3, a HSP70 family nucleotide exchange factor that regulates the proteostasis of actin-binding proteins. BAG2, another HSP70 nucleotide exchange factor, facilitates the formation of small, rounded TDP-43 inclusions. We demonstrate that both TDP-43 self-oligomerization and its binding partners, including HSP70 and cochaperones BAG2 and BAG3, drive the formation of the different types of TDP-43 inclusion.

25COASDEC37

Title: Phase-separated NDF−FACT condensates facilitate transcription elongation on chromatin

Ziwei Li, Francesca Burgos-Bravo, Kevin Xu et.al.

Nature Cell Biology volume 27, November 11, 2025

https://doi.org/10.1038/s41556-025-01778-8

Abstract: How the facilitates chromatin transcription (FACT) complex enables RNA polymerase II to overcome chromatin barriers in cells remains poorly understood—especially given the limited direct interactions of FACT with polymerases, DNA or nucleosomes. Here we demonstrate that phase separation, mediated by nucleosome destabilizing factor (NDF), is a key mechanism enabling the function of FACT during transcription elongation. Through biochemical and single-molecule assays, we found that NDF−FACT condensates create specialized biochemical environments that enhance transcription efficiency approximately 20-fold compared with FACT alone. These dynamic condensates form on transcribing RNA

polymerase II and travel along chromatin, where they promote efficient nucleosome disassembly at barriers while retaining histones on DNA to preserve chromatin integrity. In human stem cells, disruption of these condensates leads to genome-wide transcriptional defects and chromatin instability, mirroring the effects of FACT depletion. By showing that phase separation enhances FACT function during transcription elongation, our study reveals a key mechanism that preserves chromatin integrity and transcriptional homeostasis in human stem cells.

25COASDEC38

Title: Ca2+-driven PDIA6 biomolecular condensation ensures proinsulin folding

Young-Ho Lee, Tomohide Saio, Mai Watabe et.al.

Nature Cell Biology volume 27, November 11, 2025
https://doi.org/10.1038/s41556-025-01794-8

Abstract: The endoplasmic reticulum (ER) plays crucial roles in maintaining protein quality control and regulating dynamic Ca2+ storage in eukaryotic cells. However, the proteostasis system involved in ER-mediated protein quality control has not been fully characterized. Here we show that Ca2+ triggers the condensation of PDIA6, an ER-resident disulfide isomerase and molecular chaperone, into quality control granules. In contrast to the condensation mechanism observed for proteins containing low-complexity domains, our results indicate that transient but specific electrostatic interactions occur between the first and the third folded thioredoxin-like domains of PDIA6. We further show that the PDIA6 condensates recruit proinsulin, thereby accelerating the oxidative proinsulin folding and suppressing the proinsulin aggregation inside quality control granules, essential for secretion of insulin.

25COASDEC39

Title: Epigenetic alterations facilitate transcriptional and translational programs in hypoxia

Kathleen Watt, Bianca Dauber, Krzysztof J. Szkop et.al.

Nature Cell Biology volume 27, November 11, 2025
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Abstract: Adaptation to cellular stresses entails an incompletely understood coordination of transcriptional and post-transcriptional gene expression programs. Here, by quantifying hypoxia-dependent transcriptomes, epigenomes and translatomes in T47D breast cancer cells and H9 human embryonic stem cells, we show pervasive changes in transcription start site (TSS) selection associated with nucleosome repositioning and alterations in H3K4me3 distribution. Notably, hypoxia-associated TSS switching was induced or reversed via pharmacological modulation of H3K4me3 in the absence of hypoxia, defining a role for H3K4me3 in TSS selection independent of HIF1-transcriptional programs. By remodelling 5′UTRs, TSS switching selectively alters protein synthesis, including enhanced translation of messenger RNAs encoding pyruvate dehydrogenase kinase 1, which is essential for metabolic adaptation to hypoxia. These results demonstrate a previously unappreciated mechanism of translational regulation during hypoxia driven by epigenetic reprogramming of the 5′UTRome.

25COASDEC40

Title: The American Cancer Society National Lung Cancer Roundtable strategic plan: Strengthening connections between state-based initiatives

Jessica M. G. Olson PhD, MPH, Jennifer R. Knight DrPH, Amy M. Copeland MPH

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70143

Abstract: Lung cancer is the leading cause of cancer death, accounting for almost 25% of cancer deaths in both men and women. Like many cancers, lowering lung cancer incidence and mortality rates is complicated by challenges across the broad spectrum of risk reduction, screening, diagnosis, treatment, and survivorship. However, lung cancer is uniquely burdened with stigma, nihilism, tobacco industry influence, and a need for streamlined health care planning and delivery.Methods: In 2017, the American Cancer Society National Lung Cancer Roundtable was formed as a consortium of public, private, and voluntary organizations working together to impact lung cancer by engaging in targeted research and initiatives that no single one organization can address individually. Within the American Cancer Society National Lung Cancer Roundtable, the State-Based Initiatives Task Group focuses on similar local and regional implementation challenges to improve care and reduce lung cancer deaths. To accomplish this work, the task group has developed a strategic framework that prioritizes focus areas, establishes a structure to collaborate on projects, provides support, incorporates findings into existing tools, and disseminates results.Results: This strategic framework has been used to create the State-Based Initiatives planning tool, evaluate needs in state-based work, and investigate insurance steerage (the practice of insurance companies directing policyholders to specific health care providers, facilities, or services within their preferred network to control costs and manage care).Conclusions: Strategic planning allows State-Based Initiatives Task Group Members to leverage the successes of individual states through a structured approach and accelerates the dissemination of proven strategies across the United States.

25COASDEC41

Title: Chemoradiotherapy with temozolomide vs. radiotherapy alone in patients with IDH wild-type and TERT promoter mutation histological grade 2/3 gliomas: An extension retrospective analysis of a randomized controlled trial

Jing Zhang PhD, Peng Wang MD, Yin Ren MD et.al.

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70171

Abstract: Given the poor prognosis of IDH wild-type (IDH-wt) and telomerase reverse transcriptase promoter mutation (TERTp-mut) histological grade 2 to 3 gliomas, the World Health Organization has reclassified it as molecular glioblastoma. However, the effectiveness of chemoradiotherapy (CRT) in these patients remains unclear, especially in comparison to radiotherapy alone (RT). This study aims to assess CRT's efficacy in this population.Methods: A prospective randomized study was conducted at Beijing Tiantan Hospital from 2016 to 2019, enrolling 37 patients with histologically confirmed grade 2/3 IDH-wt/TERTp-mutant gliomas. Patients were randomly assigned to receive either RT (n = 18) or CRT (n = 19). After preliminary analysis showed a significant overall survival (OS) benefit in the CRT group, the study cohort was expanded from 2020 to 2022 by recruiting an

additional 21 patients who all received CRT. Primary endpoints were OS and progression-free survival (PFS).Results: The final cohort comprised 58 patients (RT, 18; CRT, 40) with a median follow-up of 43.7 months (range, 7.9–75.1). CRT significantly improved OS compared to RT alone, with a median OS of 25.8 versus 17.2 months (hazard ratio, 0.31; 95% CI, 0.16–0.62; p = .001) and 2-year OS rate of 63.0% versus 16.7%. PFS also favored CRT, showing median PFS of 14.2 versus 7.1 months (hazard ratio, 0.38; 95% CI, 0.21–0.70; p = .002) and 1-year PFS rate of 56.6% versus 33.3%. Multivariable analysis confirmed CRT benefits were independent of O6-methylguanine-DNA methyl-transferase (MGMT) status (OS, p = .001; PFS, p = .002). Treatment was well-tolerated with no grade ≥3 toxicities in the CRT group.Conclusion: CRT significantly improves survival in IDH-wt/TERTp-mut grade 2 to 3 gliomas with favorable safety.

25COASDEC42

Title: Chemotherapy alone for stage II–IVa laryngeal squamous cell carcinoma: A 20-year follow-up

Mateus Trinconi Cunha MD, Matheus Sewastjanow-Silva MD, F. Christopher Holsinger MD et.al.

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70177

Abstract: Current treatment options for nonmetastatic laryngeal squamous cell carcinoma include radiotherapy, chemoradiotherapy, and surgery, which can result in significant morbidity. This study reports the 20-year outcomes of a single-modality chemotherapy as a larynx preservation strategy in patients with stage II–IVa laryngeal squamous cell carcinoma (LSCC).Methods: In this single-institution, single-arm, prospective clinical trial, 31 patients with stage II–IVa LSCC received three or four cycles of paclitaxel, ifosfamide, and a platinum agent (TIP). Patients with a pathologic complete response (pCR) by biopsy assessment received three additional cycles without local therapy. Patients with a partial response underwent conservation laryngeal surgery (CLS). The primary end point was 2-year larynx preservation rate (LPR). Secondary end points included recurrence-free survival (RFS), overall survival (OS), and long-term complications.Results: With a median follow-up time of 21 years, 11 patients (35%) achieved a pCR and were managed with chemotherapy alone. None required laryngectomy, and only one experienced recurrence, which was successfully salvaged with radiotherapy. Among 19 patients who underwent CLS or radiotherapy, seven experienced recurrence and six required laryngectomy. The 20-year LPR was 72%; median OS was 13.5 years, and median RFS was 10.3 years. Patients with a pCR had significantly fewer long-term complications, including lower rates of feeding tube and tracheostomy dependence (p < .01).Conclusions: This long-term follow-up reinforces that TIP alone is an effective larynx preservation strategy in patients with LSCC who achieve a pCR. Further investigations of systemic therapy for laryngeal cancer treatment, including less toxic combinations and immunotherapy as well as incorporating tissue- and blood-based biomarkers, are warranted.

25COASDEC43

Title: Changes in patient-reported primary care engagement in and communication about survivorship care from initial breast cancer treatment to longer-term

survivorship

Megan A. Mullins PhD, MPH, Tianci Wang BS, Allison Furgal et.al.

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70181

Abstract: The objective of this study was to evaluate changes in primary care physicians' (PCPs') engagement and communication from initial breast cancer treatment through longer term survivorship and the patient characteristics associated with low PCP engagement and communication during longer term survivorship.Methods: The iCanCare study is a longitudinal study of women who were diagnosed with breast cancer in 2014–2015 in the Los Angeles and Georgia Surveillance, Epidemiology and End Results registries. Women were surveyed during initial treatment (baseline) and again approximately 6 years later in survivorship (follow-up; overall N = 1412; 60% response rate; n = 825 after exclusions). Respondents were asked how informed their PCP was about their breast cancer care (engagement) and how often they talked with their PCP about their breast cancer care (communication). The authors evaluated changes in PCP engagement and communication from baseline to follow-up and identified patient characteristics associated with low engagement and communication at follow-up using weighted, multivariable-adjusted logistic regression.Results: In this population-based sample of 825 women, 39.5% reported worse PCP communication and 37.9% reported worse PCP engagement during longer term survivorship compared with initial treatment. Women who reported high baseline PCP engagement and communication were one half as likely to report low engagement and communication during longer term survivorship (adjusted odds ratio, 0.50 [95% confidence interval, 0.37–0.68] and 0.43 [95% confidence interval, 0.32–0.58], respectively) compared with women who reported low baseline PCP engagement and communication.Conclusions: Many breast cancer survivors experienced worsening PCP engagement and communication from initial treatment to longer term survivorship despite initially high reports. Promoting sustained PCP engagement and communication could be a promising strategy for improving survivorship care delivery.

25COASDEC44

Title: Clinical characteristics and survival outcomes of thymic mucosa-associated lymphoid tissue lymphoma: A multicenter analysis of 82 patients

Wenyu Shi MD, PhD, Yimin Ren MD, Shu Liu MD, PhD et.al.

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70183

Abstract: The systemic study of thymic mucosa-associated lymphoid tissue (MALT) lymphoma remains lacking. The objective of this study was to characterize the clinical features and outcomes of patients with thymic MALT lymphoma.Methods: The authors conducted a retrospective analysis of patients with thymic MALT lymphoma who were diagnosed at multiple medical centers in China from 2011 to 2024. Clinical, laboratory, therapeutic, and survival data were collected.Results: In total, 82 patients were included. The median age of the cohort was 47 years with a female predominance (female/male ratio = 5.3:1.0). Eighty-two percent of patients presented with limited stage disease. Forty-one patients had a definitive diagnosis of autoimmune disease, with Sjogren's syndrome being the most common (n = 37). Antinuclear antibodies were positive in 42 of 44 (95%) of examined

patients. Management strategies included watch and wait (2%), local therapy alone (surgery, radiotherapy, or both; 71%), a combination of local and systemic therapy (26%), or systemic therapy alone (1%). With a median follow-up of 2.7 years, the 2-year progression-free and overall survival rates for the entire cohort were 98.6% (95% confidence interval, 95.8%–100.0%) and 100% (95% confidence interval, 100.0%–100.0%), respectively. Patients treated with local therapy alone (n = 58) and those who received local and systemic therapy (n = 21) had similar progression-free survival (p = .530). Patients who underwent surgery alone (n = 53) had a 2-year progression-free survival rate of 100% (95% confidence interval, 100.0%–100.0%).Conclusions: Patients with thymic MALT lymphoma have an excellent prognosis. Sjogren's syndrome is closely associated with thymic MALT lymphoma. Routine screening for autoimmune disorders and surgical resection are recommended for patients who have newly diagnosed thymic MALT lymphomas.

25COASDEC45

Title: Optimized dose schedule of rucaparib and liposomal irinotecan/5-fluorouracil in metastatic gastrointestinal cancers: A phase 1 study

Cody Eslinger MD, MS, Daniel Walden MD, Alexandra Krivonos et.al.

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70184

Abstract: This phase 1 study aimed to determine the maximum tolerated dose (MTD) and evaluate the safety and preliminary efficacy of rucaparib (RUB), a poly(adenosine diphosphate ribose) polymerase (PARP) inhibitor, combined with liposomal irinotecan (nal-IRI) and 5-fluorouracil (5-FU) in metastatic gastrointestinal (GI) cancers. RUB targets DNA repair pathways, showing efficacy in tumors with homologous recombination deficiency, such as BRCA mutations. Preclinical data suggest synergy with irinotecan, but overlapping toxicities pose challenges.Methods: Eighteen patients with metastatic GI cancers, who previously progressed on at least one systemic therapy, were enrolled. A novel sequential dosing regimen, informed by nal-IRI pharmacokinetic analysis, was used. Twelve patients were evaluable for dose-limiting toxicity (DLT) and 12 for response per Response Evaluation Criteria in Solid Tumors v1.1 criteria.Results: The MTD was established as RUB 600 mg twice daily, nal-IRI 50 mg/m2, and 5-FU 2400 mg/m2 over 46 hours. The objective response rate (ORR) was 33% (4 of 12), and the disease control rate (DCR) was 75% (9 of 12). Common grade 3 adverse events included diarrhea (33%) and neutropenia (25%), with no grade 4/5 events. Responses were notable in patients with somatic ATM and BRCA mutations, especially those with prior platinum exposure. No DLTs occurred at the recommended phase 2 dose.Conclusions: This optimized dosing schedule successfully established the MTD for RUB with nal-IRI and 5-FU, overcoming prior challenges with PARP inhibitor and irinotecan combinations. The promising ORR and DCR support further evaluation of this regimen in advanced GI malignancies.

25COASDEC46

Title: Self-reported overall well-being and physical function among chemotherapy and surgery patients across six institutions

Michael J. Hassett MD, MPH, Christine M. Cronin MHA, Angela C. Tramontano et.al.

Cancer, Volume131, Issue23, 1 December 2025

https://doi.org/10.1002/cncr.70185

Abstract: Electronic patient-reported outcomes (ePROs) mitigate symptom burden among cancer patients. This study hypothesized that two single-item quality of life measures, overall well-being (OWB) and physical function (PFN), could provide distinct information that augment ePROs.Methods: eSyM, an electronic symptom management program, was deployed across six institutions for patients receiving chemotherapy or surgery for a suspected or confirmed thoracic, gastrointestinal, or gynecologic malignancy. eSyM prompts patients one to three times weekly to complete a 12-item symptom questionnaire and two pictogram questions assessing OWB and PFN. The study identified characteristics associated with OWB/PFN; described correlations between OWB/PFN, severe symptoms, and total symptom burden; and characterized relationships between OWB/PFN and clinical outcomes.Results: From September 2019 to February 2024, 10,176 patients (3669 chemotherapy and 6507 surgery) submitted 78,433 questionnaires. The plurality reported mild impairment for OWB (chemotherapy, 41%; surgery, 45%) and PFN (chemotherapy, 43%; surgery, 39%). OWB and PFN were moderately correlated with each other (chemotherapy, 0.62; surgery, 0.58); with total symptom burden (chemotherapy: OWB 0.57, PFN 0.52; surgery: OWB 0.63, PFN 0.53); and with pain, fatigue, and decreased appetite (0.39–0.61). OWB and PFN varied by employment status and institution, and were associated with emergency department visits, admissions, and survival.Conclusions: Self-reported OWB and PFN were moderately correlated with common symptoms, offered discriminant and face validity, and were associated with clinical outcomes. These measures supplemented information from a multi-item questionnaire and may guide management for cancer patients by contextualizing symptom reports and functioning as a brief screen to identify patients at risk for moderate–severe symptoms or other serious outcomes.

25COASDEC47

Title: Prognostic significance of magnetic resonance imaging-detected extraprostatic extension in localized prostate cancer

Abhishek Kumar MD, MAS, Dominic A. LaBella MD, Michael C. Snider et.al.

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70191

Abstract: Magnetic resonance imaging (MRI) findings are not currently included in prostate cancer (PC) staging. Yet the presence of MRI-detected extraprostatic extension (EPE) may indicate higher risk disease. The purpose of this study was to assess the prevalence of MRI-EPE and prognostic ability in localized PC.Methods: Patients with T1-T2N0M0 PC diagnosed between 2000 and 2021 having a prostate MRI before definitive treatment were identified from the Veterans Affairs Prostate Data Core. MRI reports were assessed for major capsule abutment (MCA), extracapsular extension (ECE), seminal vesicle invasion (SVI), or organ invasion (OI). Any of these findings were considered EPE. Predictors of MRI-detected EPE were assessed with a multivariable logistic regression. The impact of MRI findings on distant metastasis (DM) by multivariable Fine-Gray competing-risks regression was assessed.Results: Overall, 2275 patients were included. Most pretreatment MRIs (85%) occurred after 2016. Approximately half the patients were Black. A total of 480 (21%) patients had palpable disease. Median follow-up time was 5.1 years. The 5-year cumulative incidence of metastasis was 4.8% (95% confidence interval [CI] 3.9%–5.7%). MRI indicated

468 (21%) patients had EPE: MCA (7%), ECE (10%), SVI (3%), and OI (1%). On multivariable analysis, the presence of MCA, ECE, SVI, and OI were each independently associated with worse DM. Findings of a digital rectal examination were also prognostic. Limitations included lack of centralized review of MRI images.Conclusion: MRI-detected EPE, including MCA, is common in localized PC and independently prognostic. MRI findings should be considered in the next iteration of PC staging.

25COASDEC48

Title: Long-term recurrence risk and temporal dynamics after resection of intracranial meningiomas: A multicenter cohort study with up to 15 years of follow-up

Haibo Teng MD, Jiaxin Yu MD, Yilin Pang MD et.al.

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70200

Abstract: Meningiomas are the most common primary intracranial tumors, accounting for approximately one third of central nervous system neoplasms. Although most are benign, recurrence remains a clinical concern, particularly in cases of subtotal resection (STR) where complete tumor removal is not feasible due to involvement of critical structures. Adjuvant Gamma Knife radiosurgery (GKRS) is often considered in these patients, yet the long-term effectiveness of GKRS and the temporal dynamics of recurrence beyond 10 years are not well characterized.Methods: In this multicenter retrospective cohort study, 949 adult patients who underwent surgical resection for intracranial meningiomas between 2009 and 2017 at two tertiary centers in China were followed through 2024. The primary exposure was extent of resection (gross total resection vs subtotal resection [STR]) and postoperative GKRS. The primary outcome was recurrence-free survival (RFS); secondary outcomes included overall survival, annualized recurrence risk, and biomarker-based stratification. Analyses included Cox models and competing-risk approaches.Results: Median follow-up for RFS was 8.8 years. The 15-year RFS rate was 79.2% (95% CI, 74.2–84.6). In STR cases, a second recurrence peak emerged at 7 to 10 years. GKRS was associated with lower recurrence risk (hazard ratio = 0.50; 95% CI, 0.27–0.90), especially in convexity tumors. Ki-67 > 5% and progesterone receptor negativity showed nonsignificant trends toward higher recurrence.Conclusions: In this large cohort with extended follow-up, STR patients exhibited a second recurrence peak at 7 to 10 years postoperatively. Adjuvant GKRS showed long-term benefit, supporting its selective use and long-term surveillance beyond 10 years.

25COASDEC49

Title: Beyond composite measures of regional vulnerability: Rural–urban colorectal cancer mortality disparities mediated by area-level characteristics

Sara Myers MD, Elizabeth S. Davis MSPH et.al.

Cancer, Volume131, Issue23, 1 December 2025
https://doi.org/10.1002/cncr.70098

Abstract: Rural–urban disparities in colorectal cancer (CRC) mortality have been attributed to individual- and population-level factors. Population-level composite measures such as the Social Vulnerability Index (SVI) have been used to investigate rural–urban disparities. However, the contribution of each SVI component to CRC mortality disparities among rural and urban counties is unknown.Methods: Via CRC mortality data for all US counties from

1999 to 2020 from the Centers for Disease Control and Prevention, rural–urban differences in county demographics and in 14 SVI factors were examined. Four-way effect decomposition was used to estimate the proportion of the rural–urban CRC mortality disparity mediated by the SVI.Results: Among 2927 counties (rural, 60.7%; urban, 39.3%), rural counties had 11.8% higher CRC mortality than urban counties; 18.6% of that disparity was mediated by low socioeconomic status (SES), 8.8% by household characteristics, and 2.7% by racial/ethnic minority status. Among all counties, poverty (incidence rate ratio [IRR], 3.2; 95% confidence interval [CI], 2.8–3.5), unemployment (IRR, 5.4; 95% CI, 4.4–6.8), lacking a high school diploma (IRR, 2.7; 95% CI, 2.4–2.9), household crowding (IRR, 3.3; 95% CI, 2.5–4.4), and lacking a vehicle (IRR, 3.4; 95% CI, 3.0–3.8) had the greatest impact on CRC mortality. Compared to urban counties, rural counties with a higher proportion of people without a vehicle had a higher risk of CRC mortality (IRR, 4.3; 95% CI, 3.7–5.0; vs. IRR, 1.9; 95% CI, 1.5–2.4).Conclusions: The rural–urban CRC mortality disparity is largely driven by low SES—higher poverty and unemployment, and lower income and education. The relationship between CRC mortality and the SVI is nuanced, and evaluating each component of the SVI may allow for more targeted area-level interventions than evaluating the SVI alone.

25COASDEC50

Title: Polo-like kinase 4 (PLK4) as a therapeutic target in breast cancer

Armen Parsyan , Harjot Athwal , Vasudeva Bhat et.al.

Carcinogenesis, Volume 46, Issue 4, October 2025
https://doi.org/10.1093/carcin/bgaf067

Abstract: Polo-like kinase 4 (PLK4) is a key kinase regulating centriole duplication, centrosome maturation, cytokinesis and other cellular processes. Growing evidence suggests a critical role of PLK4 in the development and progression of various cancers. In many cancer types, its upregulation leads to pro-oncogenic phenotypes, while its pharmacologic inhibition leads to anticancer effects. Functionally, PLK4 affects cancer cell proliferation, growth, motility, invasion, migration, epithelial-mesenchymal transition, apoptosis and other critical oncogenic processes. In breast cancer, PLK4 is associated with centrosome amplification, aneuploidy and chromosomal instability, promoting invasive phenotypes and resistance to cancer cell death. PLK4 shows great promise as a prognostic and predictive biomarker in breast cancer. It is commonly found to be overexpressed in primary human breast cancers and is associated with poor oncologic outcomes, clinicopathologic parameters, and high-risk subtypes. Various compounds, such as CFI-400945, centrinone B, and others have been developed to inhibit PLK4 activity. Preclinical studies have shown that PLK4 inhibitors lead to decreased proliferation, growth and migration and increased breast cancer cell death. Moreover, PLK4 inhibition can serve to enhance the effects of other treatments, including radiotherapy. Clinical studies have been initiated with some of these compounds in cancer patients, including those with breast cancer. This manuscript discusses the role of PLK4 as a promising therapeutic target in breast cancer, one of the most common causes of morbidity and mortality in women.

25COASDEC51

Title: MAPK3 modulates enhancer–promoter interactions of SKAP2 in acute myeloid

leukemia Available for Purchase Get access Arrow
Yanping Hu , Fang Chen , Tingjie Wang et.al.
Carcinogenesis, Volume 46, Issue 4, October 2025
https://doi.org/10.1093/carcin/bgaf073
Abstract: The regulation of gene expression through chromatin architecture plays a critical role in acute myeloid leukemia (AML). In this study, the influence of MAPK3 on CTCF-mediated chromatin interactions in AML was examined, focusing on gene regulation and chromatin architecture. Immunoprecipitation coupled with mass spectrometry (IP-MS) was conducted to identify CTCF-binding proteins in AML cell lines. Chromatin immunoprecipitation sequencing (ChIP-seq) was used to assess the impact of MAPK3 modulation on CTCF DNA binding, following treatment with an MAPK3 activator or inhibitor. Additionally, chromatin interactions were evaluated using 3C-qPCR, and specific enhancer sites at the SKAP2 locus were deleted using CRISPR-Cas9. Results demonstrated that IP-MS identified MAPK3 as a key CTCF-binding protein, indicating its potential role in AML chromatin regulation. MAPK3 significantly influences CTCF binding at distal intergenic regions upstream of SKAP2, as confirmed by ChIP-seq. Chromatin interaction analyses revealed that CTCF-regulated enhancer–promoter interactions at SKAP2 are modulated by MAPK3 activity. Furthermore, deletion of enhancer regions E4 and E6 led to decreased SKAP2 expression. These findings highlight the critical role of MAPK3 in regulating CTCF-mediated chromatin interactions and suggest that targeting MAPK3-regulated chromatin remodeling could be a novel therapeutic strategy for AML.

25COASDEC52
Title: SRSF3 knockdown-induced cellular senescence as a possible therapeutic strategy for non-small cell lung cancer
Shinji Nakamichi , Natalia von Muhlinen , Leo Yamada et.al.
Carcinogenesis, Volume 46, Issue 4, October 2025
https://doi.org/10.1093/carcin/bgaf082
Abstract: Tyrosine kinase (TK) inhibitors improve clinical outcomes in non-small cell lung cancer (NSCLC) with targetable mutations. However, such NSCLC cases account for only about 50% in the western populations. Inhibition of the splicing factor SRSF3 has been reported to be tumor-suppressive in other cancer cell types. This study for the first time explores the tumor-suppressive activity of siRNA knockdown of SRSF3 in NSCLC cells. The cell lines used were A549 (no TK mutation; TP53 wild type), NCI-H1975 (EGFR L858R/T790M; TP53 R273H mutant), NCI-H322 (no TK mutation; TP53 R248L mutant), and NCI-H596 (no TK mutation; TP53 G245C mutant). In all these cell lines, SRSF3 knockdown increased cellular senescence, as indicated by increased senescence-associated β-galactosidase activity and reduced cell proliferation. In A549 cells, increased apoptotic cleavage of caspase-3 and poly(ADP-ribose) polymerase was also observed. A tumor-suppressive p53 isoform, p53β, was shown to be upregulated by SRSF3 knockdown. However, overexpression of p53β did not induce cellular senescence or apoptosis, suggesting that this p53 isoform is not a primary effector of SRSF3 knockdown in NSCLC cells. Gene expression analyses suggested that the SRSF3 knockdown-induced senescence in NSCLC cells may be mediated by the downregulation of TOP2A, UBE2C, or ASPM, which are known oncogenic factors associated with poor patient prognosis. We also generated SRSF3

siRNA-encapsulating lipid nanoparticles as a future therapeutic tool. This study proposes a therapeutic strategy for NSCLC that is independent of the mutation status of TP53 and TK-encoding genes.

25COASDEC53

Title: BRINP3 promotes lung adenocarcinoma by enhancing CLOCK-mediated transcriptional regulation of CRYZL1 and activating the AKT pathway

Ye Zhang , Cheng Huang , Yeye Chen et.al.

https://doi.org/10.1093/carcin/bgaf039

Abstract: Lung cancer, particularly lung adenocarcinoma (LUAD), is the leading cause of cancer-related death globally. This study investigated the role of BRINP3 in LUAD. Immunohistochemical analysis revealed significantly upregulated BRINP3 expression in LUAD tissues compared to normal tissues, mainly located in the cytoplasm and positively correlated with tumor progression. RNA sequencing data from the TCGA-LUAD database corroborated these findings. Elevated BRINP3 expression was associated with advanced tumor stages, higher malignancy grades, and increased risk of lymphatic metastasis. Functional studies showed that BRINP3 knockdown inhibited cell proliferation, colony formation, and migration, while promoting apoptosis. Conversely, BRINP3 overexpression enhanced these malignant behaviors. Gene expression profiling identified CLOCK and CRYZL1 as potential BRINP3 targets, with BRINP3 interacting with CLOCK to regulate CRYZL1 transcription. Additionally, BRINP3 activated the AKT signaling pathway to promote LUAD progression. In vivo experiments validated the tumor-suppressing effects of BRINP3 knockdown, reducing tumor growth and metastatic potential. In conclusion, BRINP3 played a crucial role in LUAD development and progression by regulating CLOCK-mediated transcriptional regulation of CRYZL1 and activating the AKT signaling pathway. BRINP3 knockdown inhibited LUAD cell malignancy and might represent a potential therapeutic target.

25COASDEC54

Title: An update on the World Trade Center cancer tissue biobank: a scientific resource for molecular and mechanistic studies on WTC-related cancer

Wiley M Turner , Angelo Zegarelli , Tara Ivic-Pavlicic et.al.

https://doi.org/10.1093/carcin/bgaf063

Abstract: World Trade Center (WTC) responders were exposed to a complex mixture of toxins and carcinogens through dust, fumes, and smoke at ground zero. Since then, studies have indicated that WTC responders have elevated cancer rates compared with the general population. While studies have detailed the overarching connection between WTC exposure and cancer, a tissue biobank is needed to enable molecular and mechanistic studies on WTC-related cancers. The cohort includes responders involved in rescue, recovery, or cleanup enrolled in the World Trade Center Health Program (WTCHP) who consented to participate in research. Responders with cancer were identified through WTCHP certification. WTCHP provided data with patients' demographic information, contact details, and cancer diagnoses. Potential participants were contacted by mail, email, or phone for consent and procedure location. If consented, samples were requested from pathology departments. A biobank of cancer tissues from WTC responders has been established with 551 distinct primary cancers

from 521 patients. Of these, prostate makes up 39.0%, thyroid 9.8%, melanoma 8.9%, kidney 6.5%, bladder 6.0%, colorectal 5.8%, breast 5.6%, lung 4.7%, head and neck 4.7%, and other cancers 9%. An additional 343 patients have consented for biobank projects and their samples are being requested. To date, we have created a valuable tissue biobank available to the scientific community for high-impact oncology studies in the unique population of WTC responders. By studying links between carcinogenic exposure and cancer sites, exposure signatures, and markers of cancer aggressiveness, this biobank offers an unprecedented opportunity to advance cancer research in an exposed population.

25COASDEC55

Title: Development of a nomogram for the prediction of postoperative survival in hepatoid adenocarcinoma of the stomach

Kang Wang , Yusong Chen , Xiaoli Li et.al.

https://doi.org/10.1093/carcin/bgaf081

Abstract: This study developed a prognostic nomogram for hepatoid adenocarcinoma of the stomach (HAS) using clinicopathological data from 61 surgically treated patients (First Affiliated Hospital of Zhengzhou University, 2013–2025) and externally validated it with 20 cases from Henan Cancer Hospital. Multivariate Cox regression identified TNM stage, CA125, Ki67, and primary tumor location as independent predictors of overall survival (OS). These factors were integrated into a nomogram and internally validated via bootstrap resampling. Compared to the TNM staging system, the nomogram demonstrated superior predictive performance, as indicated by lower Akaike (160.947 versus 168.746) and Bayesian Information Criterion values (169.391 versus 170.857). The bootstrap-corrected concordance index (C-index) for the nomogram was 0.800 (95% CI: 0.729–0.880), significantly outperforming the TNM system (0.653, 95% CI: 0.559–0.746; P = .001); the external validation C-index was 0.754 (95% CI: 0.638–0.870). Time-dependent C-index and calibration curves confirmed superior discriminative ability and accuracy, while decision curve analysis indicated clinical utility. Patients stratified as high-risk by the nomogram had significantly worse OS versus low-risk groups in both training (P < .0001) and validation cohorts (P = .02). This tool enables risk stratification to guide personalized HAS management.

25COASDEC56

Title: Lung cancer chemo-interception by sulfasalazine and disulfiram codelivered using a nano self-emulsifying drug delivery system in mice

Fekadu Kassie , Kevin Wang , Katherine Bang et.al.

https://doi.org/10.1093/carcin/bgaf075

Abstract: Although preclinical studies consistently indicate that sulfasalazine (SAS) and disulfiram (DSF) are promising agents for the prevention and treatment of lung cancer, their clinical efficacy is limited. This discrepancy is attributed to the poor bioavailability of the drugs. Therefore, in the present study, we explored whether delivery of lower doses of SAS and DSF in nano self-emulsifying drug delivery systems (Nano-SEDDS) improves their potency and efficacy in suppressing malignant progression of lung tumors. Mice were treated with the tobacco smoke carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and once lung adenoma developed, high doses of free SAS (250 mg/kg) + DSF (100 mg/kg)

or SEDDS formulations containing lower doses of SAS + DSF (40 mg/kg SAS + 8, 16 or 40 mg/kg DSF) were administered by oral gavage, every other day, for 10 weeks. Although the doses of SAS and DSF contained in SAS + DSF-SEDDS were about 6-fold and 3–15-fold lower, respectively, than the doses of the respective free drugs, SAS + DSF-SEDDS was more effective than free SAS + DSF in reducing the multiplicity of bigger lung tumors (≥1 mm). These effects were paralleled by significant reductions in the multiplicity of adenoma with progression and adenocarcinoma histopathological lesions. Also, lung tumors from mice treated with SAS + DSF-SEDDS exhibited an increase in the level of 4-hydroxynonenal (4-HNE) and malondialdehyde (MDA), lipid peroxidation products. Overall, our results show that the Nano-SEDDS formulation of SAS + DSF is a promising approach to enhance the potency and efficacy of the drugs for lung cancer chemo-interception and treatment.

25COASDEC57

Title: Non-malignant hematologic conditions and subsequent cancer risk: a prospective cohort study and Mendelian randomization analysis

Weiwei Chen , Jiacong Li , Hengyu Cui et.al.

Carcinogenesis, Volume 46, Issue 4, October 2025

https://doi.org/10.1093/carcin/bgaf085

Abstract: No studies have examined the association between non-malignant hematologic diseases and the risk of various cancers. To examine the associations between non-malignant hematologic diseases and cancer risk, we performed a cohort study and Mendelian randomization analysis. The association between hematologic diseases and incident cancer risk was assessed using time-varying Cox proportional hazards regression with multivariable hazard ratios (HRs) and 95% confidence intervals (CIs). Over a total of 5 031 372 person-years of follow-up in the UK Biobank, 32 589 (6.8%) patients were diagnosed with hematologic diseases, with 2279 incident cancer cases. Multivariable time-varying Cox regression models revealed that any hematologic disease was positively associated with total cancer (HR = 1.19; 95% CI, 1.14–1.24), hematologic cancer (HR = 1.92; 95% CI, 1.69–2.17), and digestive system cancer risks (HR = 1.36; 95% CI, 1.25–1.48). Nine hematologic diseases were associated with higher hematologic cancer risk, and six of the hematologic diseases were also associated with higher risks of four types of digestive system cancer (liver, stomach, esophageal, and small intestine cancers). Mendelian randomization analysis supported the positive association of agranulocytosis with leukemia, coagulation defects and spleen diseases with lymphoma, and unspecified anemia with small intestine cancer. This study indicates that non-malignant hematologic diseases are associated with an increased risk of cancer, particularly cancers in the hematological and digestive systems.

25COASDEC58

Title: A2AR-phospho-STAT1 (Y701)-HLA-E axis as a potential immune modulatory pathway in radiotherapy-resistant triple negative breast cancer

Young Shin Ko , Hana Jin , So Eun Lee et.al.

Carcinogenesis, Volume 46, Issue 4, October 2025

https://doi.org/10.1093/carcin/bgaf069

Abstract: Triple-negative breast cancer (TNBC) patients have lower survival rates and higher recurrence risks than non-TNBC patients. Moreover, radiotherapy-resistant TNBC

(RT-R-TNBC) exhibits enhanced chemotherapy resistance and invasiveness. Therefore, there is a critical need for innovative treatments for RT-R-TNBC and TNBC patients. Our previous study indicated that NK cells exhibit reduced cytotoxicity against RT-R-TNBCs due to human leukocyte antigen class I histocompatibility antigen, alpha chain E (HLA-E) upregulation. Thus, this study aimed to identify the mechanism responsible for the upregulation of HLA-E and suggest potential therapeutic targets for overcoming the RT-resistance of TNBC. We found that HLA-E expression was significantly higher in TNBC tumor tissues than in normal epithelial tissues and non-TNBC tissues, correlating with A2AR levels. In addition, MDA-MB-231 (TNBC) and RT-R-MDA-MB-231 (RT-R-TNBC) showed an A2AR-dependent HLA-E overexpression. NK cell-mediated cytotoxicity against MDA-MB-231 and RT-R-MDA-MB-231 was reduced and restored by A2AR or STAT1 knockdown. Interestingly, STAT1 phosphorylation (Y701) by adenosine (ADO) aligned with the HLA-E expression pattern by ADO, and fludarabine, a STAT1 inhibitor, effectively reduced phospho-STAT1 (Y701) levels but not phospho-STAT1 (S727) levels. Fludarabine also inhibited ADO-induced HLA-E expression in MDA-MB-231 and RT-R-MDA-MB-231, including basal HLA-E expression in RT-R-MDA-MB-231. Additionally, fludarabine reduced tumor progression, lung metastasis, HLA-E expression, and phospho-STAT1 (Y701) in RT-R-MDA-MB-231-injected mice. Moreover, monalizumab, an NKG2A monoclonal antibody, significantly reduced tumor progression and lung metastasis with increased population of cytotoxic NK cells (CD25 + NK1.1+ and CD69 + NK1.1+) in the inguinal lymph nodes of RT-R-MDA-MB-231-injected mice. This study suggests that the A2AR-phospho-STAT1 (Y701)-HLA-E axis may serve as an alternative target for overcoming RT-resistance in TNBC.

25COASDEC59

Title: Δ133p53 isoform enhances TLR4 function to promote tumor growth

Sasini Polwatta Lekamlage , Alexandra N Boix De Jesus , Adriana Machado Saraiva et.al.

Carcinogenesis, Volume 46, Issue 4, October 2025
https://doi.org/10.1093/carcin/bgaf051

Abstract: Tumor protein 53 (TP53) acts as a tumor suppressor and is often mutated in cancer. Isoforms of TP53, such as the Δ133p53 family, can promote tumor growth and metastasis. Therefore, targeting Δ133p53 function may represent a new strategy for preventing tumor metastasis. To inform the identification of proteins to target in Δ133p53-expressing tumors, changes at the cell surface were characterized. Inhibition of cell surface trafficking in a mouse model syngrafted with tumors expressing proteins similar to Δ133p53 (Δ122p53) was associated with reduced tumor growth and metastasis. After confirming that changes at the cell surface were important for Δ133p53 tumor promotion, characterization of protein changes at the Δ133p53/Δ122p53 cell surface revealed increased expression of the toll-like receptor 4 (TLR4) and the TLR4 agonist, apoptosis inhibitor 5. Furthermore, inhibition of TLR4 was sufficient to reduce Δ122p53 tumor growth. Altogether, these results suggest a role for Δ133p53 in contributing to tumor progression by stimulating TLR4 function. Furthermore, targeting changes at the cell surface can reduce Δ133p53 tumor promotion.

25COASDEC60

Title: HS-10296 (almonertinib) enhances radiosensitivity in EGFR-mutant nonsmall cell lung cancer (including T790M) through inhibition of EGFR downstream signaling and DNA damage repair

Weiqi Liu , Yulian Liu , Yun Xie et.al.

Carcinogenesis, Volume 46, Issue 4, October 2025
https://doi.org/10.1093/carcin/bgaf070

Abstract: Nonsmall cell lung cancer (NSCLC) harboring EGFR mutations, including the resistant T790M variant, continues to require improved therapeutic strategies despite the development of EGFR tyrosine kinase inhibitors (TKIs). This study evaluates the radiosensitizing potential of HS-10296 (almonertinib), a third-generation EGFR-TKI, in EGFR-mutant NSCLC models. In vitro studies demonstrated selective growth inhibition in mutant cells (PC-9: half-maximal inhibitory concentration (IC50) = 2.62 μM; H1975: IC50 = 5.22μM at 48 h) compared to wild-type A549 cells (IC50 = 11.42 μM). Clonogenic assays revealed significant radiosensitization in mutant cells (SER: PC-9 = 1.22; H1975 = 1.55) through multiple mechanisms including enhanced DNA damage (1.5–2.0-fold increase in comet tail moments with 4–10× persistent γH2A.X foci), marked suppression of RAD51-mediated DNA repair, and increased apoptosis (combination therapy: 19.53%–20.71% versus monotherapies: 12.08%–14.05%). Mechanistic investigation showed HS-10296 attenuated phosphorylation of EGFR and downstream effectors AKT and ERK, potentially disrupting DNA damage response pathways. In vivo validation using H1975 xenografts demonstrated superior tumor growth inhibition with the combination of HS-10296 and radiotherapy, which correlated with reduced expression of p-EGFR, p-AKT, and RAD51, along with increased γH2A.X levels. These findings establish HS-10296 as a promising radiosensitizer for EGFR-mutant NSCLC through simultaneous targeting of oncogenic signaling via PI3K/AKT and MAPK/ERK pathways and critical DNA repair mechanisms. The study provides compelling preclinical evidence supporting clinical evaluation of HS-10296 combined with radiotherapy for EGFR-driven NSCLC, including tumors with T790M-mediated resistance.

25COASDEC61

Title: Neuromelanin-induced cellular stress and neurotoxicity in the pathogenesis of Parkinson's disease

Md. Jakaria & Jason R. Cannon

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02156-3

Abstract: Neuromelanin is a complex dark brown pigment that primarily accumulates in catecholaminergic neurons, particularly in the substantia nigra and locus coeruleus regions of the brain in primates. Rats and mice are largely devoid of neuromelanin, although it is present in some other non-primate species. This pigment is notable for its age-related accumulation and has been linked to the pathophysiology of various neurodegenerative diseases, especially Parkinson's disease. Research has increasingly suggested that neuromelanin or its precursors trigger cellular stress, including neuroinflammation, apoptosis, oxidative stress, mitochondrial dysfunction, and impaired autophagy. Collectively, these mechanisms significantly contribute to neurodegeneration. Additionally, neuromelanin can interact with various neurotoxic molecules, potentially forming complexes that may provide protective

benefits against neurotoxicity. However, extensive studies also suggest that this interaction can have a double-edged effect; while it may sequester harmful substances, it can simultaneously increase cellular stress and enhance neuronal toxicity, creating a detrimental cycle. We review the multifaceted roles of neuromelanin in the brain, discussing how its properties and interactions contribute to cellular stress and the progression of neurodegenerative processes. In the context of neurotoxic mechanisms, we also address potential therapeutic targets for Parkinson's disease.

25COASDEC62

Title: Do fungi also undergo "ferroptosis"? A microscopic exploration of cellular death

Xingxing Shang, Qian Zhang, Qingli Yang et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02164-3

Abstract: Ferroptosis, a recently identified form of programmed cell death, has shown promising advancements in mammalian cell studies. However, research on ferroptosis in fungi is still in its nascent stages, resulting in limited understanding of its regulatory mechanisms. Given the unique regulatory mechanisms of ferroptosis and its significant implications for fungal research, this review focuses on the regulatory mechanisms of fungal ferroptosis, highlighting key target proteins and potential intervention strategies. Furthermore, the interplay between fungal ferroptosis and organelles is examined, analyzing the molecular logic of organelle-mediated ferroptosis, including their core functions and mechanisms promoting or inhibiting ferroptosis. Based on these findings, potential antifungal agents targeting the fungal ferroptosis pathway are summarized, along with their primary target pathways, key target proteins, and mechanisms of action. We also discuss the main characteristics of fungal ferroptosis and provide perspectives on future research directions. This review aims to provide new insights into the in-depth study of fungal ferroptosis and the development and design of novel antifungal agents targeting fungal ferroptosis. For instance, targeting key proteins or signaling pathways related to fungal ferroptosis may lead to the design of more effective antifungal drugs, overcoming the drug resistance issues of various drug-resistant fungi in current clinical settings.

25COASDEC63

Title: The role of epigenetic regulation in cuproptosis, ferroptosis and NETosis in the pathogenesis of autoimmune diseases

Wenshan Zhao, Leping Wang, Hanru Jia et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02158-1

Abstract: Ferroptosis, cuproptosis and NETosis are various important forms of non-apoptotic programmed cell death, with research involving these subtypes of cell death exponentially increased in recent years. Ferroptosis is a unique iron-dependent form of cell death that involves iron transport as well as redox homeostasis within the cell. Cuproposis is a new phenomenon of cell death, primarily driven by the excessive intracellular accumulation of copper ions, with its occurrence and development closely associated with mitochondrial dysfunction. NETosis on the other hand occurs due to the release of neutrophil extracellular traps by neutrophils upon their stimulation. Currently, various of types of autoimmune

diseases (AD) have been clinically identified, with their etiology established to be multifactorial. In this review, we specifically investigate the correlation between these three non-apoptotic programmed cell deaths and the pathogenesis of AD, as well as elucidate the internal mechanisms involving miRNA, DNA methylation, histone modifications, related transcription factors, and non-coding RNAs from an epigenetic perspective. Additionally, we analyzed the molecular and pathophysiological mechanisms of ferroptosis, cupropopsis, and NETosis in the development of AD. By examining the therapeutic potential of emerging immune checkpoint targets, this review aims to offer novel insights and strategies to address the ongoing challenges in the prevention and treatment of autoimmune diseases.

25COASDEC64

Title: The intersection of mitochondria, lipids, and ferroptosis: a new avenue for dry age-related macular degeneration

Jacob Dohl, Gordon Burns & Mithalesh Singh

Apoptosis, Volume 30, Issue (11-12), 2025

https://doi.org/10.1007/s10495-025-02165-2

Abstract: Age-related macular degeneration (AMD) is currently the leading cause of vision loss in developed countries. Despite decades of research and development, there are currently no treatments for the dry version of the illness. Dry AMD (DAMD) is a multifactorial disease stemming from dysfunction in the complement system, mitochondrial function, and lipid metabolism. While the complement system has been studied in-depth for its involvement in DAMD, mitochondria and lipids are understudied for their potential contributions to this process. Ferroptosis, an iron-dependent cell death mechanism, is associated with mitochondrial dysfunction and lipid dysregulation, and has been implicated as a driver of DAMD. This review describes the pathology of DAMD and the potential role of mitochondria, metabolism, and lipid dysregulation in the disease. We will highlight the intersection of pathways involving mitochondria, lipid dysregulation, and ferroptosis in DAMD progression, as well as the need for future studies to elucidate this connection.

25COASDEC65

Title: Targeting PANoptosis: a promising therapeutic strategy for ALI/ARDS

Mengqi Zhang, Luorui Shang, Fangyuan Zhou et.al.

Apoptosis, Volume 30, Issue (11-12), 2025

https://doi.org/10.1007/s10495-025-02168-z

Abstract: Acute lung injury (ALI) is a complex, high-mortality pulmonary disease triggered by multiple etiological factors, potentially progressing to acute respiratory distress syndrome (ARDS). During the development of ALI/ARDS, a key pathological feature involves the disruption of the intact alveolar-capillary barrier, which is formed by alveolar epithelium, pulmonary interstitium, and microvascular endothelium. Under physiological conditions, cell death removes excess or dysfunctional cells, defends against pathogenic microorganisms, and thus plays a protective role while maintaining homeostasis. However, excessive clearance reactions can lead to pathological loss of pulmonary epithelial cells, endothelial cells, or macrophage-immune cells, eventually exacerbating tissue structural damage. With the discovery of various programmed cell death mechanisms, researchers have consistently uncovered the participation of cell death modes such as apoptosis, pyroptosis, necroptosis,

and PANoptosis in the pathological processes underlying ALI/ARDS. Modulating these critical death pathways presents opportunities for therapeutic intervention in disease progression. Among these, PANoptosis is an independent lytic inflammatory cell death pathway initiated by innate immune sensors and driven by the PANoptosome complex, playing a core role in lung injury and infectious diseases. This review summarizes recent advancements in PANoptosis research in the context of ALI/ARDS, providing a reliable framework and direction for the targeted development of drugs acting on the PANoptosis axis to more effectively prevent and treat ALI/ARDS.

25COASDEC66

Title: Metabolic cell death in cancer: mechanisms and therapeutic potential

Yujinpeng Hao, Jun Shao, Naqi Lian et.al.

Apoptosis, Volume 30, Issue (11-12), 2025

https://doi.org/10.1007/s10495-025-02176-z

Abstract: A defining hallmark of malignant tumours lies in their pronounced resistance to programmed cell death mechanisms. This intrinsic resilience enables cancer cells to circumvent physiological clearance, thereby sustaining unchecked proliferation and survival. Emerging research has revealed that metabolic dysregulation can precipitate a distinctive form of programmed cell death, termed metabolism-linked regulated cell death (RCD), establishing it as a novel paradigm of cellular self-elimination. This systematic review provides an in-depth analysis of the molecular mechanisms orchestrating various metabolic cell death modalities, including pyroptosis, immunogenic cell death (ICD), necroptosis, ferroptosis, cuproptosis, disulfidptosis, lysozincrosis, alkaliptosis, and methuosis. Furthermore, it critically evaluates their therapeutic potential in oncology. By elucidating the intricate interplay among these signalling cascades, this review describes innovative precision medicine strategies that harness metabolism-driven cell death for targeted cancer interventions.

25COASDEC67

Title: HMGB1: a multifaceted mediator of cell death pathways in cardiovascular diseases

Yue Shi, Yixuan Ma, Rong Wang et.al.

Apoptosis, Volume 30, Issue (11-12), 2025

https://doi.org/10.1007/s10495-025-02144-7

Abstract: Cardiovascular diseases (CVDs) are a leading cause of death globally, responsible for 32% of all fatalities. They significantly reduce quality of life and life expectancy, while imposing a substantial economic burden on healthcare systems in different countries. High mobility group box 1 (HMGB1), a location-dependent multifunctional protein, plays a significant role in various cell death pathways associated with CVDs. While its release at the early stages of disease may stimulate immune and inflammatory responses, aiding microbial clearance and wound healing, the accumulation of HMGB1 with disease progression disrupts the balance between autophagy and apoptosis. Excessive intracellular and extracellular HMGB1 is implicated in diverse forms of cell death, including PANoptosis, ferroptosis, and efferocytosis, highlighting its complex role in maintaining cellular homeostasis and responding to injury. Understanding the intricate regulatory functions of HMGB1 in these

processes is critical for developing targeted therapeutic strategies to address cardiovascular pathologies. Preclinical studies have demonstrated the therapeutic potential of targeting HMGB1 release and expression in various CVD models, establishing it as an attractive therapeutic target. Future research focusing on combined strategies that integrate HMGB1 with other targets holds promise for advancing CVD treatment.

25COASDEC68

Title: Oxidative stress and ferroptosis in diabetic cardiomyopathy: mechanistic interplay and therapeutic implications

Shan Li, Yuhe Shu, Shuyu Yang et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02170-5

Abstract: Diabetic cardiomyopathy (DCM) is a severe cardiovascular complication of diabetes mellitus, characterized by pathological changes such as cardiomyocyte hypertrophy, necrosis, and myocardial fibrosis, which can ultimately lead to heart failure. However, its underlying mechanisms remain incompletely understood, limiting the development of effective therapeutic approaches. In recent years, the critical roles of oxidative stress and ferroptosis in the pathogenesis of DCM have attracted increasing attention. Oxidative stress is a state where the imbalance between oxidative and antioxidant systems results in excessive production of reactive oxygen species (ROS), thereby damaging key cellular structures such as cardiomyocyte membranes and mitochondria, and promoting the occurrence and development of DCM. Ferroptosis is an iron-dependent form of regulated cell death, which has been confirmed to be involved in the injury and death of diabetic cardiomyocytes.This article reviews the interaction between oxidative stress and ferroptosis in DCM as well as their molecular mechanisms, explores their complex relationship in the occurrence and progression of the disease, and proposes potential therapeutic strategies based on this mechanistic framework. It aims to provide researchers and clinicians with a comprehensive and up-to-date reference to collectively advance the prevention and treatment of DCM.

25COASDEC69

Title: Harnessing cuproptosis: a new avenue for targeted cancer therapies

Anil Dharavath, Sivkan Kaur, PV Drupad Mohan et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02174-1

Abstract: Copper-induced cell death, referred to as cuproptosis, introduces a new approach for cancer treatment by utilizing the toxic effects of copper. While copper is vital for enzymatic processes, it becomes harmful at excessive concentrations. Cuproptosis is characterized by mitochondrial impairment resulting from copper interacting with lipoylated components of the tricarboxylic acid (TCA) cycle, leading to proteotoxic stress and targeted cell death. This mechanism is distinct from traditional apoptosis and necrosis. Disruption of copper balance and associated genes, such as FDX1, LIAS, and DLAT, has been linked to various types of cancer. In this review, we outline the timeline of cuproptosis discovery and its comparison with other cell death mechanisms. In addition, we discuss copper homeostasis and copper metabolism in normal human physiology. We also reviewed how the disruption of copper balance can lead to cuproptosis and its involvement in tumorigenesis. Furthermore,

we provided an overview of the various genes associated with cuproptosis and their roles in cancer. Given the numerous targets identified, we also provide a thorough overview of the drugs linked to cuproptosis and discuss their clinical relevance and prospects. This review indicates that targeting cuproptosis may serve as a novel therapeutic approach for cancer treatment.

25COASDEC70

Title: Mitophagy: a novel avenue for herbal medicines alleviating myocardial ischemia/reperfusion injury

Mengqi Liao, Ling Men, Ming Gong et.al.

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Abstract: Myocardial ischemia–reperfusion injury (MIRI) has a high incidence and is difficult to cure. Studies have shown that mitophagy is the key mechanism. This review systematically summarizes all documented herbal preparations and bioactive monomers targeting mitophagy for MIRI treatment, which may serve as a valuable reference for future research on herbal medicine-mediated mitophagy regulation. We conducted comprehensive literature searches in PubMed, Embase, Web of Science, and CNKI databases using the keywords “cardiovascular diseases,” “mitophagy,” “myocardial ischemia–reperfusion injury,” “herbal medicine,” “mechanism,” and “therapeutic” for studies published within the last five years up to July 2025. Studies on herbal medicine interventions unrelated to mitophagy were excluded. Our analysis reveals that mitophagy plays a crucial role in attenuating the detrimental effects of MIRI. Furthermore, herbal medicine demonstrates therapeutic efficacy in maintaining homeostatic balance of mitophagy during MIRI. Herbal medicines can precisely regulate mitophagy via the PTEN-induced putative kinase 1 (PINK1)-parkin pathway, and modulate the expression of BCL2 interacting protein 3 (BNIP3), FUN14 domain-containing protein 1 (FUNDC1), NIP3-like protein X (NIX). Herbal medicines exert protective effects against MIRI through diverse mechanisms and signaling pathways by targeting mitophagy. While mitophagy represents a promising frontier for future cardiovascular research, current herbal medicine applications remain predominantly confined to animal and cellular models, with only limited clinical translation. The findings presented herein are anticipated to provide clinicians and cardiovascular researchers with valuable therapeutic strategies and novel research directions.

25COASDEC71

Title: Mechanistic study on the role of multi-pathway autophagy in ovarian aging: literature review

Xinyu Zhu, Huihui Li, Tingting Xue et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02181-2

Abstract: Ovarian aging is one of the common diseases in the female reproductive system. It is characterized by complex etiologies, involving multiple factors such as genetics, environment, metabolism, and cellular stress. In recent years, autophagy, a crucial cellular self-degradation and repair mechanism, has received substantial attention for its role in maintaining and deteriorating ovarian function. This review systematically summarizes the

molecular mechanisms of autophagy and its regulation, as well as the latest research progress of macroautophagy, chaperone-mediated autophagy (CMA) and mitophagy in ovarian aging. Studies have shown that dysregulation of autophagic pathways is closely associated with decreased oocyte quality and reduced ovarian reserve function. Additionally, signaling pathways such as PI3K, AMPK, and mTOR participate in the process of ovarian aging by regulating autophagic activity. Although numerous studies have revealed the critical role of autophagy in ovarian aging, many issues remain to be resolved, such as the crosstalk mechanisms between different autophagic pathways and the precise spatiotemporal dynamics of the autophagic regulatory network. A deep understanding of the regulatory network of multi-pathway autophagy will provide new insights for developing intervention strategies to delay ovarian aging, holding significant scientific and clinical application value.

25COASDEC72

Title: Role of PANoptosis in cancer: Molecular mechanisms and therapeutic opportunities

Wen-Qing Wang, Zi Zhou, Feng-Xin Ge et.al.

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Abstract ◌ PANoptosis is an inflammatory programmed cell death pathway. It integrates apoptosis, pyroptosis, and necroptosis via PANoptosome complexes, thereby coordinating immune responses and remodeling tumor microenvironment (TME). By overcoming limitations of therapies targeting a single-pathway (e.g., those targeting apoptosis), PANoptosis suppresses cancer progression, reverses drug resistance, and synergizes with radiotherapy through immune activation. Mechanistic insights are driving therapeutic strategies that target key regulators (ZBP1, RIPK3) and disease-specific miRNAs to modulate caspase-dependent and caspase-independent cascades. Its pathological duality—acute hyperactivation in tissue injury versus chronic dysregulation in degenerative diseases—highlights the need for context-dependent modulation. PANoptosis activation shows prognostic biomarker potential and universal therapeutic promise for drug-resistant cancers and inflammatory disorders, though clinical translation remains exploratory. This framework positions PANoptosis as a transformative paradigm bridging cell death dynamics and immune regulation.

25COASDEC73

Title: PANoptosis: potential new targets and therapeutic prospects in digestive diseases

Minglin Zhang, Xuelin Zhao, Ting Cai et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02186-x

Abstract: PANoptosis, a newly defined, multifaceted programmed cell death (PCD) pathway, integrates key features of pyroptosis, apoptosis, and necroptosis. It is orchestrated by multiprotein complexes called PANoptosomes (ZBP1-, AIM2-, RIPK1-, and NLRP12-PANoptosomes), which assemble via domain interactions in response to specific pathogen- or damage-associated signals. This integrated pathway plays crucial roles in maintaining tissue homeostasis by eliminating infected and damaged cells and provides potent innate immune defence through the coordinated release of inflammatory cytokines and damage-associated

molecular patterns (DAMPs), offering superior pathogen clearance compared with single PCD modes. Increasing evidence underscores the significant involvement of PANoptosis in digestive diseases. In gastric cancer, it modulates tumour progression, the immune microenvironment and chemoresistance. PANoptosis drives epithelial cell death in ulcerative colitis and Crohn's disease, contributing to mucosal barrier disruption and inflammation. It influences immune infiltration, metabolic reprogramming, and therapeutic response in colorectal cancer. PANoptosis also contributes to the pathogenesis of diverse liver conditions, including failure, fibrosis, metabolic dysfunction-associated steatotic liver disease (MASLD) and hepatocellular carcinoma, and mediates pancreatic injury in acute pancreatitis. While research on oesophageal and pancreatic malignancies is nascent, PANoptosis-based molecular subtyping and therapeutic targeting demonstrate translational potential. This review synthesizes current evidence, highlighting PANoptosis as a critical regulator in digestive pathologies and as a promising target for intervention.

25COASDEC74

Title: The impact of lipid metabolism on ferroptosis in myocardial ischemia–reperfusion injury

Yuxin Li, Zekun Lou, Fang Liu et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02192-z

Abstract: Myocardial ischemia–reperfusion (I/R) injury remains a major challenge in cardiovascular interventions. Although conventional reperfusion therapies restore coronary blood flow, they can often exacerbate myocardial damage. In recent years, ferroptosis, a novel form of regulated cell death characterized by iron-dependent lipid peroxidation, has emerged as a pivotal contributor to myocardial I/R injury. Unlike apoptosis and necrosis, ferroptosis is driven by the accumulation of reactive iron and the peroxidation of membrane phospholipids enriched with polyunsaturated fatty acids (PUFAs), processes that are tightly regulated by lipid metabolism. However, the precise mechanisms linking lipid metabolic reprogramming to ferroptosis during myocardial I/R injury remain incompletely understood. To address this gap, this review systematically examines the interplay between lipid metabolism and ferroptosis in myocardial I/R injury. We highlight the roles of fatty acid uptake, β-oxidation, phospholipid remodeling, cholesterol metabolism, and mitochondria–lipid droplet interactions in forming a deleterious cycle of metabolic disruption, oxidative stress, and membrane damage. Key regulators, such as acyl-CoA synthetase long-chain family member 4 (ACSL4), lysophosphatidylcholine acyltransferase 3 (LPCAT3), and cluster of differentiation 36 (CD36), are emphasized for their roles in contributing to ferroptotic vulnerability. Moreover, the review also explores the protective roles of short-chain fatty acids (SCFAs) and 7-dehydrocholesterol (7-DHC) as emerging anti-ferroptotic agents. Novel yet understudied mechanisms with therapeutic potential are also discussed, including Rab8a–PLIN5-mediated lipid droplet trafficking and 7-DHC reductase (DHCR7) deficiency-induced 7-DHC accumulation. Collectively, this review provides a comprehensive framework for understanding the lipid metabolism–ferroptosis axis in myocardial I/R injury, offering insights for future mechanistic studies and clinical translation.

25COASDEC75

Title: Intermodulation of endoplasmic reticulum stress and ferroptosis in diabetic nephropathy: molecular mechanisms and therapeutic potentials

Jiyang Wang, Fengxia He, Runxiu Wang et.al.

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https://doi.org/10.1007/s10495-025-02195-w

Abstract: Diabetic nephropathy is a prevalent complication of diabetes mellitus, characterized by progressive renal failure, a leading cause of end-stage renal disease. The pathogenesis of diabetic nephropathy is intricate, with recent research highlighting the significant roles of endoplasmic reticulum stress and ferroptosis in its development. Endoplasmic reticulum stress is initiated by the accumulation of misfolded proteins in the endoplasmic reticulum, activating the unfolded protein response. Ferroptosis, an iron-dependent form of programmed cell death, involves iron ion buildup and heightened lipid peroxidation. In diabetic nephropathy, persistent endoplasmic reticulum stress and ferroptosis intensify renal inflammation, fibrosis, and apoptosis, which are crucial processes in the development of the condition. This review seeks to clarify the molecular mechanisms and interactions between endoplasmic reticulum stress and ferroptosis in diabetic nephropathy, as well as anticipate innovative therapeutic strategies that target endoplasmic reticulum stress and ferroptosis to slow down disease advancement and provide hope for individuals affected by diabetic nephropathy.

25COASDEC76

Title: Regulated cell death environments drive fibroinflammatory reprogramming in surviving adipose-derived stem cells

Wilfredo Oliva-Olivera, Tina Ravnsborg, Elisa Le Boiteux et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02191-0

Abstract: Adipose-derived stem cells (ASCs) can shift toward proinflammatory and fibrotic phenotypes, but factors triggering this transition are not fully understood. This study aimed to elucidate the impact of exposure to regulated cell death environments on the fibroinflammatory potential of surviving subcutaneous ASCs (sub-ASCs). Surviving sub-ASCs were characterized by transcriptional analysis of genes associated with inflammation and extracellular matrix remodeling. Phenotypical markers of fibroinflammatory progenitor cells were monitored by immunoblotting and flow cytometry. We determined post-translational modifications (PTMs) of histone proteins by immunoblotting and mass spectrometry, including individual and combinatorial histone marks. Four days after transient exposure to serum starvation- or tumor necrosis factor-alpha (TNFα)-induced cell death, surviving sub-ASCs cultured under hypoxic proliferative conditions showed elevated mRNA levels of inflammatory mediators, fibrillar collagens, matricellular proteins, and cytoskeletal components. This fibroinflammatory transcriptional activation was accompanied by decreased expression of fibroinflammatory progenitor cell markers. Surviving sub-ASCs exhibited variations in histone methylation marks associated with transcriptional regulation. Inhibiting calcium-dependent μ- and m-calpains during TNFα-induced cell death increased histone marks associated with gene activation and repression, altering surviving sub-ASCs transcriptional responses four days later. Middle-down mass spectrometry identified changes

in specific histone mark combinations in surviving sub-ASCs following TNFα-induced cell death. These findings suggest that regulated cell death environments act as reprogramming agents for surviving ASCs, driving fibro-inflammatory transcriptional activation and histone PTM changes, likely as part of an inducible gene expression program promoting cell survival.

25COASDEC77

Title: Integrative analysis of RiboSis-related gene expression in colorectal cancer: implications for prognosis and immunotherapy

Wei Song, Min Zhou, Yatao Wang et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02166-1

Abstract: Colorectal cancer (CRC) is a prevalent and lethal malignancy that imposes significant burdens on patients and healthcare systems worldwide. This study aimed to explore the significance of ribosome biogenesis (RiboSis)-related genes (RRGs) in CRC and their clinical implications. The scRNA-seq data of three CRC tissues were sourced from the Gene Expression Omnibus (GEO) database. Nonnegative matrix factorization (NMF) was employed to categorize cell subtypes associated with RiboSis. An integrative machine learning approach encompassing ten algorithms was subsequently implemented to develop a prognostic signature. Our research revealed 295 differentially expressed RiboSis-related genes (DERRGs) associated with survival outcomes, with a notable RiboSis score that was markedly higher in CRC tissues than in normal counterparts. Univariate Cox analysis revealed 25 DERRGs with significant survival differences ($P < 0.05$). scRNA-seq of 26,961 cells from 13 CRC samples revealed eight major cell types, with T and B cells predominantly enriched in immune response pathways. InferCNV analysis distinguished malignant epithelial cells on the basis of copy number variations, and NMF identified four RiboSis-related cell subtypes. Our RiboSis-related prognostic model, validated across the TCGA, GSE17536, and GSE39582 datasets, demonstrated high predictive accuracy. Notably, low RiboSis signature scores were correlated with reduced immune evasion risk and upregulated immune checkpoint genes, suggesting enhanced responsiveness to immunotherapy. Among the 8 model genes, PFDN2 was considered the hub gene. The experimental results of PFDN2 in this RiboSis signature indicated that PFDN2 expression is elevated in CRC tissues and that PFDN2 knockdown promotes the proliferation, migration, and invasion of CRC cells. This study underscores the potential of RRGs as biomarkers and therapeutic targets, offering new avenues for personalized CRC management.

25COASDEC78

Title: Cathayanon E induces apoptosis and enhances oxaliplatin sensitivity in colorectal cancer through suppression of MCL1

Liang Cen, Xin Hu, Guozhen An et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02167-0

Abstract: Colorectal cancer (CRC) is one of the most common and lethal malignancies worldwide, with treatment failure often attributed to chemoresistance and evasion of apoptosis. Cathayanon E (CE), a natural chalcone derivative isolated from Morus alba, has shown anticancer potential, but its role and mechanism in CRC remain largely unexplored. In

this study, CE significantly inhibited CRC cell proliferation and induced apoptosis both in vitro and in vivo. Mechanistically, CE directly bound to the anti-apoptotic protein MCL1 and promoted its β-TRCP–mediated ubiquitination and proteasomal degradation, thereby inducing mitochondrial apoptotic signaling. Overexpression of MCL1 reversed the antiproliferative and pro-apoptotic effects of CE, validating MCL1 as a functional target of CE. Furthermore, CE markedly enhanced the chemosensitivity of CRC cells to oxaliplatin, resulting in synergistic tumor suppression in xenograft models. These findings highlight CE as a promising natural agent that targets MCL1 to overcome chemoresistance and improve therapeutic outcomes in colorectal cancer.

25COASDEC79

Title: Targeting BACH1 by HPPE inhibits the Wnt/β-catenin pathway and malignant phenotype in glioblastoma cells

Yuzhu Wang, Changxiao Yang, Li Guo et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02183-0

Abstract: BTB domain and CNC homology 1 (BACH1) has been reported to be a vital regulator of tumor progression. However, methods for targeting BACH1 in cancers have not been fully researched. In this study, we identified BACH1 as a poor prognosis-related factor in patients with GBM. Furthermore, a small-molecule compound, HPPE, was found to interact with BACH1 and inhibit the progression of GBM in vitro and in vivo. Molecular dynamics analysis, molecular docking simulation, MST assay, and co-IP experiments revealed that HPPE principally binds to BACH1 at the bZIP domain on the C-terminus and promotes the competitive binding of BACH1 and TCF-4, thus inhibiting formation of the β-catenin/TCF-4 complex. HPPE incubation inhibited proliferation, promoted apoptosis, and induced G2/M arrest, indicating a potential synergistic effect with temozolomide in GBM cells. RNA-seq, qRT–PCR, and gene enrichment analyses revealed that the induction of HPPE repressed the Wnt/β-catenin pathway. Further experiments revealed that BTB domain deletion from BACH1 eliminated its ability to interact with TCF-4 and significantly rescued the inhibition of Wnt/β-catenin signaling and the reduction of malignant phenotype induced by HPPE in GBM cells. In vivo experiments revealed that HPPE prolonged the survival time of mice, inhibited Wnt/β-catenin pathway activity and had a synergistic effect with TMZ in a xenograft model. In summary, these findings provide potential combined therapeutic strategies for glioma by targeting the C-terminus of BACH1 and inhibiting the activation of WNT signaling.

25COASDEC80

Title: RIPK1-targeted therapy alleviates intervertebral disc degeneration via inhibiting nucleus pulposus PANoptosis

Zhenyu Zhu, Fanqi Kong, Feng Jiang et.al.

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https://doi.org/10.1007/s10495-025-02169-y

Abstract: Intervertebral disc degeneration (IVDD) is a major contributor to lumbar diseases, including low back pain, herniation, and stenosis. Despite significant efforts, there have been limited improvements in treatments to alleviate IVDD. The nucleus pulposus (NP) is a crucial

component of the intervertebral disc (IVD), responsible for secreting aggrecan, collagen II, and other extracellular matrix components. Programmed cell death (PCD) of NP cells is believed to play a central role in IVDD. RIPK1 is a key mediator of PCD and recently reported PANoptosis, playing essential role in kidney injury, arteriosclerosis, and acute or chronic inflammation-related diseases. We collected varied degenerated human IVD specimens to examine the expression of RIPK1 and downstream cell death-related markers, including GSDMD, Caspase3, and MLKL, which are indicative of pyroptosis, apoptosis, necroptosis, or the recently denominated PANoptosis. In vitro, we performed RIPK1 knockdown and overexpression to study their effects on IVDD. in vivo, we constructed RIPK1 conditional knockout (CKO) mice to confirm the role of RIPK1 in IVDD. We also utilized a small molecule targeted inhibitor to explore its effects on IVDD in vitro and in vivo. Phosphorylated RIPK1 (p-RIPK1) was significantly increased during IVDD in both human and mouse models. Knockout of RIPK1 effectively alleviated IVDD, as evidenced by the RIPK1 cko mice. Further pathological staining and western blot analysis revealed the overexpression of GSDMD, Caspase3, and MLKL, indicating that RIPK1-mediated PANoptosis plays a crucial role in IVDD. in vitro, overexpression of RIPK1 in NP cells exacerbated PANoptosis and degeneration, while RIPK1 knockdown inhibited these processes. We developed a RIPK1-targeted small molecular inhibitor, compound 3–47, which demonstrated superior efficacy in inhibiting p-RIPK1. Both in vitro and in vivo, 3–47 showed remarkable effects in alleviating IVDD by inhibiting RIPK1-mediated PANoptosis. RIPK1-mediated PANoptosis of NP cells plays a critical role in IVDD. The molecular inhibitor 3–47 could effectively delay IVDD progression in mice, highlighting its therapeutic potential.

25COASDEC81

Title: Endothelial SPRY1 deficiency associates with angiogenic-metabolic reprogramming in pulmonary arterial hypertension: a multi-omics analysis of bulk and single-cell transcriptomic profiles

Yanfei Mo, Desheng Wang, Zhenkun Deng et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
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Abstract: The mechanism underlying vascular remodeling in pulmonary arterial hypertension (PAH) involves complex interactions among various cell types, with dysregulation of endothelial cells (ECs) homeostasis considered a crucial pathological factor. However, their local cellular changes still need to be fully identified during PAH. This study utilized single-cell RNA sequencing data from the GEO database to analyze lung tissue samples from PAH patients and normal controls, revealing significant heterogeneity in lung ECs and dysregulated metabolic pathways. We identified a significant expansion of capillary ECs in PAH patients, linked to dysregulated angiogenesis and glycolysis-tricarboxylic acid cycle metabolic pathways. Through integrative high-dimensional weighted gene co-expression network analysis (hdWGCNA) and machine learning, we identified SPRY1 as a novel key biomarker in PAH pathogenesis and validated its significant downregulation in a monocrotaline-induced PAH rat model. These findings establish capillary ECs expansion and SPRY1 deficiency as pivotal drivers in PAH pathogenesis, providing a foundation for precise therapeutic targeting.

25COASDEC82

Title: CPT1A facilitated ferroptosis by forming feedback loop with Nrf2 via PI3K/AKT pathway in colorectal cancer

Xiao-huan Li, Feng Lv, Si-qi Li et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02171-4

Abstract: Carnitine palmitoyltransferase 1A (CPT1A) has been implicated in the development of colorectal cancer (CRC), yet its role in ferroptosis remains to be fully understood. In this study, we found that CPT1A expression was associated with metastasis of CRC by gene datasets analysis and immunohistochemical staining of clinical samples, and it was upregulated in CRC cells compared with normal colon cell. The CCK-8, Transwell, and wound healing assays demonstrated that overexpression of CPT1A enhanced the viability, invasion, and migratory capacity of CRC cells. CPT1A expression was reduced following induction of ferroptosis in CRC cells, and this downregulation could be reversed by a ferroptosis inhibitor. Moreover, CPT1A overexpression inhibited ferroptosis in CRC cells. Nrf2, a well-known negative regulator of ferroptosis, was found to colocalize with CPT1A in CRC cells. Molecular docking, Co-IP assay and Ch-IP assay further confirmed an interaction between CPT1A and Nrf2. Notably, Nrf2 overexpression upregulated CPT1A expression, whereas Nrf2 knockdown produced the opposite effect. CPT1A overexpression led to activation of PI3K/AKT pathway in CRC cells. Inactivation of the PI3K/AKT pathway by the inhibitor partially reversed the anti-ferroptosis effect of CPT1A overexpression. Furthermore, inhibition of PI3K/AKT pathway suppressed Nrf2 expression, and reduce nuclear translocation of Nrf2, whereas activation of this pathway enhanced Nrf2 expression and nuclear translocation. In vivo experiments corroborated these findings, showing that CPT1A overexpression promoted Nrf2 expression, suppress ferroptosis, facilitated tumor growth, inactivated PI3K/AKT pathway. Taken together, our data suggest that CPT1A associates with metastasis of CRC, and inhibits ferroptosis through a regulatory feedback loop involving Nrf2 and PI3K/AKT pathway.

25COASDEC83

Title: Deciphering macrophage heterogeneity and factors driving M2 polarization in lung adenocarcinoma through single-cell RNA sequencing

Meiling Sheng, Beiwei Yu, Qunzhi Wang et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02172-3

Abstract: Immune checkpoint inhibitors (ICIs) have shown promise in enhancing non-small cell lung cancer (NSCLC) patient prognoses, but their effectiveness is contingent upon the specific tumor microenvironment (TME). In this research, we examined the heterogeneity and plasticity of tumor-associated macrophages in lung adenocarcinoma (LUAD) using single-cell sequencing data GSE207422, identifying genes that may influence their polarization. We identified a positive correlation between BCAT1 expression in immune-resistant patient tissues and M2 macrophage infiltration. Pseudo-temporal analysis revealed a significant overlap between BCAT1 expression dynamics and the trajectory of macrophage M2 polarization. Evidence from both in vitro and in vivo studies indicated that BCAT1 might foster an immunosuppressive environment by driving M2 macrophage polarization, which

could account for the aggressive spread of LUAD and suboptimal responses to immunotherapy. Overall, our findings flagged BCAT1-high-expressing macrophages as a suppressive element in the TME, hinting that targeting BCAT1 could shift macrophage polarization and enhance patient outcomes.

25COASDEC84

Title: VDAC1-interacting proteins: binding site mapping and their derived peptides induce apoptosis and multifaceted cellular effects

Manikandan Santhanam, Venkatadri Babu, Anna Shteinfer-Kuzmine et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02185-y

Abstract: The mitochondrial voltage-dependent anion channel-1 (VDAC1) protein plays a central role in regulating mitochondrial metabolism, energy production, and apoptosis. VDAC1 interacts with over 100 proteins across the cytosol, endoplasmic reticulum, plasma membrane, and mitochondrial membranes. These interactions coordinate metabolism, cell death, and signal transduction, integrating mitochondrial and cellular functions. To identify VDAC1 binding sites, we designed a peptide array of 768 peptides from 19 selected VDAC1-interacting proteins. We focused on three partners: GAPDH, gelsolin, and actin. Their VDAC1-binding sequences as peptides interacted with purified VDAC1 and, as cell-penetrating peptides, induced cell death, and elevated intracellular $Ca2^{+}$ and ROS levels. Despite sequence diversity, the peptides converged on enhancing transcription factors p53 and c-Jun, upregulating VDAC1, promoting its oligomerization, and triggering apoptosis. Other effects related to their originated protein's function include no significant effect of the GAPDH-derived peptide on its catalytic activity, indicating its effects are independent of glycolysis. The gelsolin-derived peptide altered actin organization, increasing filopodia and focal adhesion, and actin-derived peptides reduced actin, gelsolin, and tubulin expression. This study is the first to identify VDAC1 binding sites on 19 interacting partners and to demonstrate their use as cell-penetrating peptides to modulate the VDAC1 network. These findings highlight VDAC1's multifaceted regulatory role and offer a novel approach for targeting VDAC1-protein interactions for therapeutic purposes.

25COASDEC85

Title: Death never dies: increasing impact of programmed cell death

Patrycja Nowak-Sliwinska & Arjan W. Griffioen

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02189-8

Abstract: Programmed cell death has evolved from the classical concept of apoptosis to a diverse repertoire that includes necroptosis, pyroptosis, ferroptosis, cuproptosis, paraptosis, panoptosis, and even the reversal process of anastasis. These pathways have transformed our understanding of health and disease, influencing oncology, neurodegeneration, cardiovascular biology, infection, and immunity. Reflecting this growth, Apoptosis has reached a record Impact Factor of 8.1 in 2024, underscoring both the rising impact of cell death research and the journal's role as its central forum. This success reflects a community effort of authors, reviewers, and editorial board members, and highlights how programmed cell death continues to shape the future of biology and medicine.

25COASDEC86

Title: Integrating pathology genomics and single-cell genomics to identify lactate metabolism-related prognostic features and therapeutic strategies for melanoma

Songyun Zhao, Xiaoqing Liang, Jiaheng Xie et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02190-1

Abstract: Cutaneous melanoma (SKCM) is highly malignant and prone to developing treatment resistance. Lactate metabolism in the tumor microenvironment (TME) plays a crucial role in SKCM progression, immune evasion, and therapy resistance. This study aimed to integrate multi-omics data to systematically characterize the molecular features of lactate metabolism in SKCM, construct an effective prognostic model, and explore potential therapeutic strategies. Quantitative pathological features were extracted using CellProfiler and combined with deep learning features obtained from a pre-trained ResNet50 convolutional neural network. Gene set variation analysis (GSVA) was used to calculate lactate metabolism scores and identify associated pathological features. Single-cell RNA sequencing was applied to assess lactate metabolic activity across different cell types. These data, together with spatial transcriptomics, genomic alterations, immune infiltration profiles, and immunotherapy response data, were integrated to construct a lactate metabolism signature (LMS) prognostic model (comprising 3 pathological features and 11 genes). The model was developed using 101 combinations of 10 machine learning algorithms. Furthermore, RAB32 knockdown experiments were performed to verify its effects on melanoma cell proliferation, migration, invasion, and metabolism. A total of 443 pathological imaging features significantly associated with lactate metabolism were identified. Single-cell analysis revealed that melanoma cells exhibited the highest lactate metabolic activity, with markedly enhanced intercellular communication in the high-metabolism group. The LMS model demonstrated excellent prognostic performance in both the TCGA training and validation cohorts. Patients in the high-LMS group had significantly shorter survival, showed immune evasion features, and exhibited activation of melanoma-related metabolic and signaling pathways (e.g., oxidative phosphorylation). In contrast, the low-LMS group had stronger immune infiltration and higher expression of immune checkpoint molecules. The key gene RAB32 was significantly correlated with all lactate metabolism-related pathological features, was highly expressed in the tumor core, and its high expression predicted poor prognosis. RAB32 knockdown markedly inhibited melanoma cell proliferation, migration, and invasion; reduced lactate production; suppressed the expression of glycolytic enzymes and lactate transporters; and decreased extracellular acidification rate (ECAR) and oxygen consumption rate (OCR). In addition, it significantly inhibited tumor growth in mouse xenograft models. This study developed a multi-omics-integrated prognostic model (LMS) based on lactate metabolism, providing a novel tool for risk stratification and therapeutic decision-making in SKCM patients. It also identified RAB32 as a central player in tumor metabolic reprogramming and invasiveness, with promising potential as a therapeutic target.

25COASDEC87

Title: Multi-omics analysis revealed heterogeneity of AARS1 and AARS2 in pan-cancer and identified AARS1 as a potential prognostic biomarker for urologic neoplasms

Meng Tang, Tingting Huang, Jiayu Wang et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
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Abstract: Lactate, the primary byproduct of glycolysis, has been established as a critical barometer of tumor microenvironment homeostasis and is implicated in tumor progression. Alanyl-tRNA synthetases AARS1 and AARS2 (AARS1/2) have been identified as sensors of intracellular L-lactate and as contributors to cancer development. Nonetheless, investigations into the different roles of AARS1 and AARS2 across various cancer types remain lacking. In this study, we preliminarily explored the correlations between AARS1/2 and the tumor microenvironment in pan-cancer. We first examined the expression patterns of AARS1 and AARS2 across 33 cancer types. Subsequently, we analyzed the relationship of AARS1/2 with clinical features and mutational landscape utilizing the GSCA and cBioPortal databases. Survival outcomes associated with AARS1/2 were assessed through Cox regression and the Kaplan–Meier method. Additionally, we examined the correlations between AARS1/2 and drug sensitivity, as well as immune infiltration, using the GSCA database, TISIDB database, and the CIBERSORT algorithm, respectively. Notably, significant heterogeneity of AARS1 and AARS2 was observed across various dimensions, including expression profiles, clinical outcomes, mutation spectra, and immune infiltration. The expression patterns of AARS1/2 were statistically different in urologic neoplasms. Similarly, survival analysis revealed a close correlation between elevated AARS1 expression and unfavorable prognosis in patients with urologic neoplasms, while AARS2 expression level was not. Interestingly, the results of immune infiltration indicated the statistical heterogeneity of AARS1 and AARS2 in certain urologic neoplasms, especially in bladder urothelial carcinoma (BLCA). Specifically, (1) the correlation between AARS1/2 expression and immune-related scores in BLCA was opposite; and (2) TIDE analysis demonstrated that elevated AARS1 expression was related to a high TIDE score in BLCA, while AARS2 was not. Further detailed analysis of AARS1 and AARS2 in the context of immune infiltration and functional enrichment in BLCA may partially account for these observations. In conclusion, our findings highlighted the heterogeneity of AARS1 and AARS2 across various cancers. Based on our data, AARS1 was identified as a potential prognostic biomarker and a candidate for immunotherapy targeting in urologic cancers, though further validation is needed to confirm its clinical utility.

25COASDEC88

Title: AIM2 regulated by JAK3/STAT1 pathway promotes PANoptosis in intestinal barrier dysfunction caused by concomitant radiation and PD-1 Blockade

Jingru Chen, Yuxuan Tao, Qingxin Wang et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02187-w

Abstract: Intestinal injury is a common and potentially life-threatening complication in patients receiving concurrent radiotherapy (RT) and anti-PD-1 immunotherapy (IO) for pelvic, abdominal, or retroperitoneal malignancies. Despite the therapeutic benefits of RT/IO combinations the mechanisms underlying RT/IO-induced enteritis remain poorly understood. This study investigates the role of Absent in melanoma 2 (AIM2)-mediated PANoptosis in intestinal barrier dysfunction during RT/IO-induced enteritis. Colonic epithelial cell models and murine models were utilized to assess the activation of PANoptosis pathways, barrier function, and inflammation. AIM2 expression was silenced using CRISPR-Cas9-mediated

knockout. Western blotting and immunohistochemistry were employed to assess PANoptosis markers. Barrier function was evaluated using transepithelial electrical resistance (TEER) and FITC-dextran permeability assays. Quasi-targeted metabolomics identified metabolic alterations associated with intestinal injury. Combined RT and IO significantly exacerbated intestinal epithelial damage, as evidenced by increased PANoptosis and compromised barrier function both in vivo and in vitro. AIM2 expression was markedly upregulated following RT/IO treatment. RT/IO treatment activated the JAK3/STAT1 signaling pathway, and pretreatment with the JAK3 inhibitor AG490 inhibited AIM2 expression, while cellular AIM2 knockout attenuated PANoptosis markers, preserved tight junction protein ZO-1, and improved barrier function. Metabolomics analysis showed that RT/IO treatment significantly disturbed intestinal choline metabolism in mice, which may be related to the cell death pathway. Supplementation with choline or its metabolite trimethylamine N-oxide (TMAO), especially TMAO, upregulated JAK3/STAT1 and AIM2-PANoptosis pathways, and aggravated intestinal injury, whereas supplementation of mice with 3,3-Dimethyl-1-butanol (DMB) to reduce the production of TMAO reversed the activation of the choline-induced pathway and inflammatory response. AIM2-driven PANoptosis, activated by the JAK3/STAT1 pathway, plays a key role in RT/IO-induced intestinal damage. Elevated choline metabolism and TMAO accumulation further amplify this pathological process by enhancing JAK3/STAT1 and AIM2 activity. Inhibiting JAK3 or TMAO reduces PANoptosis, offering a potential preclinical treatment to alleviate RT/IO intestinal toxicity.

25COASDEC89

Title: LCN2 drives ferroptosis-associated ischemia–reperfusion injury after renal transplantation: integrated machine learning and in vivo validation

Zhiwei Wu, Bowen Yu, Qing He et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02182-1

Abstract: Renal ischemia–reperfusion injury (IRI) remains a critical obstacle to optimal renal transplant outcomes, driving acute graft dysfunction and long-term allograft failure. While ferroptosis—an iron-dependent form of cell death—has been linked to IRI pathogenesis, the role of lipocalin-2 (LCN2), a regulator of iron homeostasis and inflammation, in transplant-related renal IRI remains uncharacterized. Six murine IRI transcriptomic datasets (83 samples) were integrated using weighted gene co-expression network analysis (WGCNA) and differential expression profiling to screen for IRI-associated hub genes. Findings were validated in two human transplant cohorts (212 samples) via 113 machine learning algorithms, including logistic regression, random forest, and ensemble models. Single-cell RNA sequencing (GSE237429) was used to map gene expression to specific renal cell populations, while a murine warm IRI model evaluated the effects of LCN2 inhibition (ZINC00640089) on tubular injury, ferroptosis markers (MDA, GSH, Fe^{2+}), and inflammatory cytokines (IL-6, TNF-α) across mild (50-minute) and severe (80-minute) ischemia subgroups. WGCNA identified 36 hub genes, with LCN2 emerging as a key node in ferroptosis and immune regulation pathways. A six-gene machine learning model, including LCN2, CLU, and SOX9, demonstrated robust predictive accuracy for IRI (AUC = 0.93). Single-cell analysis revealed elevated LCN2 expression in neutrophils and macrophages in IRI kidneys, correlated with increased immune cell infiltration. In vivo, LCN2 inhibition

significantly reduced severe ischemia-induced tubular injury, suppressed lipid peroxidation (MDA), restored glutathione levels (GSH), and alleviated iron overload (Fe2+) and reactive oxygen species (ROS). Systemic inflammation was mitigated, with IL-6 and TNF-α levels significantly reduced. This study establishes LCN2 as a pivotal mediator of ferroptosis and immune dysregulation in transplant IRI. A machine learning-driven multi-omics approach provides a novel diagnostic framework, while the inhibition of LCN2 is shown to alleviate IRI-induced tissue damage in these models. These findings highlight the utility of integrative analytics in uncovering biological targets and offer new therapeutic avenues for improving kidney transplant outcomes.

25COASDEC90

Title: ERO1A-positive tumor epithelial cells in colorectal cancer progression: a multi-omics perspective

Shangshang Hu, Jinwei Lou, Yuhan Chen et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02184-z

Abstract: Colorectal cancer (CRC) remains a leading cause of cancer-related morbidity and mortality worldwide. Tumor epithelial cells play a crucial role in shaping the tumor microenvironment (TME) and driving cancer progression. This study utilized a multi-omics approach, integrating data from 21 multi-center CRC cohorts (n = 2,767), including single-cell transcriptomics, bulk transcriptomics, spatial transcriptomics, and proteomics. Bioinformatic analyses were combined with in vitro and in vivo experiments for validation. A distinct epithelial subpopulation, ERO1A-positive epithelial cells (ERO1A + Epi), was identified and found to be significantly enriched in advanced-stage CRC, correlating with poor prognosis. ERO1A + Epi cells promoted proliferation, migration, invasion, and epithelial-mesenchymal transition (EMT) in vitro, while in vivo models confirmed their role in tumor growth and liver metastasis. Spatial and intercellular interaction analyses revealed that ERO1A + Epi cells interact with CTHRC1 + cancer-associated fibroblasts (CTHRC1 + CAFs) and SPP1 + macrophages via MDK-LRP1, MIF-(CD74 + CD44), and APP-CD74 signaling pathways, fostering a pro-tumorigenic TME. Co-culture experiments demonstrated that ERO1A + Epi enhances the expression of CTHRC1 and SPP1. A risk prediction model (ETSRM) based on the ERO1A + Epi_TME_Score demonstrated superior prognostic accuracy over 111 existing CRC models. Integrating ETSRM with TNM staging further enhanced survival prediction. Our findings identify ERO1A + Epi as a significant driver of colorectal cancer progression. The ERO1A + Epi_TME_Score-based ETSRM provides a robust prognostic tool, offering new insights into CRC pathogenesis and highlighting potential therapeutic targets for improved patient outcomes.

25COASDEC91

Title: ACTG1 mediates cisplatin resistance in NSCLC through induction of mitochondrial fragmentation

Minghua Xie, Zhiming Yang, Jingyue Zhou et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02177-y

Abstract : Actin gamma 1 (ACTG1) encodes the cytoskeletal protein γ-actin and is

overexpressed in various cancers. Cisplatin-based chemotherapy is the standard first-line treatment for patients with advanced non-small cell lung cancer (NSCLC). However, most patients eventually develop cisplatin resistance. The association between ACTG1 and cisplatin resistance remains unclear. In this study, we found that high expression of ACTG1 was associated with poor prognosis in NSCLC. Knockdown of ACTG1 promoted mitochondrial fragmentation via interaction with the fusion protein MFN2 and induced ferroptosis. Mechanistically, ACTG1 knockdown disrupted mitochondrial dynamics, elevated mitochondrial ROS, reduced glutathione (GSH) levels, and enhanced lipid peroxidation. This cascade significantly inhibited the growth of cisplatin-resistant NSCLC cells and sensitized them to cisplatin. Furthermore, the ferroptosis inducer RSL3 synergized with cisplatin to enhance ferroptosis and mitochondrial fragmentation, effectively sensitizing ACTG1-overexpressing cells both in vitro and in xenograft models. Our findings establish ACTG1 as a critical mediator of cisplatin resistance in NSCLC through regulation of mitochondrial integrity and ferroptosis. Targeting the ACTG1-MFN2 axis combined with ferroptosis induction represents a promising therapeutic strategy to overcome cisplatin resistance.

25COASDEC92

Title: Mechanism of the enterobacterial metabolite sodium butyrate mediating ferroptosis to affect osteogenic ability of BMSCs in mice with estrogen deficiency-caused osteoporosis via the PTEN/PI3K/AKT pathway

Yulin Li, Lan Jiang, Canghai Jin et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02179-w

Abstract: Sodium butyrate (NaB), a major intestinal metabolite, has been suggested to protect against osteoporosis (OP). This study aimed to elucidate the mechanism by which NaB regulates ferroptosis in OP. An ovariectomy-induced mouse OP model was established, and treated with NaB or the ferroptosis inhibitor Fer-1. Bone mineral density, bone microstructure, bone formation and resorption, and ferroptosis markers were assessed. In vitro, mouse bone marrow mesenchymal stem cells (BMSCs) were treated with NaB and the ferroptosis inducer Erastin to evaluate osteogenic differentiation and ferroptosis. Phosphatase and tensin homolog (PTEN) acetylation was detected by co-immunoprecipitation, the phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT) pathway was evaluated by Western blot, and acetylation sites by point mutation. The role of PTEN acetylation was further validated using the p300 inhibitor C646 in vitro and in vivo. NaB treatment enhanced bone formation, suppressed ferroptosis, and promoted osteogenic differentiation in OP mice, mimicking the protective effects of Fer-1. In BMSCs, NaB promoted osteogenesis by inhibiting ferroptosis. Mechanistically, NaB induced acetylation of PTEN at K125/K128, suppressing its phosphatase activity and activating the PI3K/AKT pathway, thereby reducing ferroptosis. C646 partially abolished these effects. NaB promotes PTEN acetylation at K125/K128 to activate PI3K/AKT signaling, thereby inhibiting ferroptosis and alleviating estrogen deficiency-induced OP. These findings highlight NaB as a potential epigenetic metabolic regulator of bone metabolism.

25COASDEC93

Title: His-tagged pro-apoptotic peptides: enhancing cell internalization and anticancer

effect in vitro

Aldo O. González-Cruz, José Juan Pérez-Trujillo, Isaías Balderas-Rentería et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02180-3

Abstract: Epidermal growth factor receptor (EGFR) overexpression is commonly found in various solid tumors, including non-small cell lung cancer, where it is associated with poor prognosis and resistance to treatment. Despite the availability of EGFR-targeted therapies, overcoming drug resistance remains a challenge. Tumor-homing cell-penetrating peptides can selectively target cancer cells and improve drug delivery. In this study, we evaluated the anticancer potential of EGFR-targeted pro-apoptotic peptides, specifically NRPD-KLAK-H and NRPD-CTMP4-H, designed to enhance internalization and overcome drug resistance in EGFR-positive cancers, and compared their effects with those of the free His-tagged peptides NRPD-H, KLAK-H, and CTMP4-H. MTT assays showed that KLAK-H and NRPD-KLAK-H exhibited the strongest anticancer effects, significantly inhibiting cell growth in A-549 cell line, with IC50 values of 33.3 μM and 40.9 μM, respectively. TUNEL assays suggested that KLAK-H and NRPD-KLAK-H induced apoptosis in the tested cell lines. Immunofluorescence revealed successful internalization of KLAK-H/NRPD-KLAK-H, but poor uptake of CTMP4-H/NRPD-CTMP4-H. The His-tag modification improved peptide internalization, suggesting that short poly-histidine sequences can enhance cellular uptake of pro-apoptotic KLAK-derived peptides, particularly in cancer cells. Although the proposed EGFR-targeted proapoptotic peptides did not show the expected effect, our findings indicate that His-tagged pro-apoptotic peptides, especially KLAK-H, hold promise as potential cancer treatments.

25COASDEC94

Title: Mechanism of glycolysis-pyrolysis crosstalk driving vicious circle of intervertebral disc degeneration

Silong Gao, Tao Liu, Xianghan Hou et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02194-x

Abstract: The acidic and inflammatory microenvironment serves as a central pathological feature of intervertebral disc degeneration (IVDD), acting as a critical driving factor in disease progression. However, the interplay between acidic and inflammatory microenvironments remains largely unexplored. In this study, we revealed the molecular mechanism by which crosstalk between glycolysis and pyroptosis exacerbates IVDD. We observed that lactic acid stimulation triggers pyroptosis in NPCs by stimulating the NLRP3 inflammasome, activating the caspase-1 pathway, and upregulating the expressions of IL-1β and IL-18. Acid sensitive ion channel 1a (ASIC1a) expression is positively correlated with extracellular acidosis severity and NPC pyroptosis levels. Furthermore, the knockdown of ASIC1a via siRNA effectively alleviated pyroptosis. After treatment of NPCs with IL-1β, glycolysis levels were increased, accompanied by up-regulation of c-Myc (a key regulator of the Warburg effect) and nuclear translocation, the knockdown of c-Myc effectively alleviated glycolysis. Mechanistically, lactate activates acid-sensing ion channel 1a (ASIC1a), which mediates Ca2+ influx to promote pyroptosis in nucleus pulposus cells (NPCs) and IL-1β release. Secreted IL-1β subsequently induces the nuclear translocation of, thereby

upregulating glycolytic enzyme expression, enhancing glycolysis, and accelerating lactate accumulation. This cascade establishes a vicious cycle that progressively aggravates IVDD. Our findings demonstrate that glycolysis–pyroptosis crosstalk promotes acid–inflammatory microenvironments in degenerated discs, driving disease progression. Targeted inhibition of this crosstalk improves disc biological function and mitigates IVDD progression.

25COASDEC95

Title: KAT2A alleviates the glucose starvation-induced mitochondrial oxidative stress and ferroptosis to promote colon cancer progression

Song Guo, Tianze Zhang, Tao Hao et.al.

Apoptosis, Volume 30, Issue (11-12), 2025

https://doi.org/10.1007/s10495-025-02196-9

Abstract: Beyond its established role as a lysine acetyltransferase, KAT2A has recently been identified to possess succinyltransferase activity. This study aims to investigate the function of KAT2A in mediating succinylation modification of heat shock protein 60 (HSP60) and to elucidate the underlying mechanism through which KAT2A regulates mitochondrial oxidative stress and ferroptosis induced by glucose starvation in colon cancer cells via HSP60 succinylation. Bioinformatic analyses were conducted to assess KAT2A expression in colon cancer and its association with patient prognosis. Protein interaction between KAT2A and HSP60 was examined by co-immunoprecipitation (Co-IP). Intracellular Fe^{2+} levels, lipid peroxidation, and mitochondrial reactive oxygen species (mtROS) were measured using FerroOrange, C11 BODIPY 581/591, and MitoSOX Red fluorescent probes, respectively. Mitochondrial localization and membrane potential were evaluated via immunofluorescence assays. KAT2A is upregulated in colon cancer and correlates with poor prognosis, largely attributable to its ability to enhance cell viability and invasion under glucose deprivation. Overexpression of KAT2A conferred resistance to glucose starvation-induced ferroptosis by mediating HSP60 succinylation. Label-free quantitative proteomic analysis identified three critical succinylation sites on HSP60 (K72, K133, K191), with K191 being the principal site regulating ferroptosis. Succinylated HSP60 interacts with GSTK1 and promotes the mitochondrial translocation of the HSP60–GSTK1 complex, mitigating mitochondrial oxidative stress under glucose starvation. Through this mechanism, KAT2A suppresses ferroptosis and supports colon cancer cell survival and tumor growth. The KAT2A–HSP60–GSTK1 axis attenuates glucose starvation-induced mitochondrial oxidative stress, thereby inhibiting ferroptosis and promoting tumor progression in colon cancer.

25COASDEC96

Title: Astragaloside IV protects against high altitude hypoxia-induced cardiac injury through the CaSR-NF-kB and EGFR-PI3K-AKT-MDM2 pathways

Xiaowen Li, Ruiqi Cao, Ling Zhang et.al.

Apoptosis, Volume 30, Issue (11-12), 2025

https://doi.org/10.1007/s10495-025-02197-8

Abstract: Astragaloside IV (AS-IV), a bioactive compound renowned for its anti-inflammatory, antioxidant, and anti-apoptotic properties, has not yet been investigated for its potential role in modulating cardiac function under high-altitude conditions. This study elucidates the cardioprotective effects of AS-IV against high-altitude-induced cardiac injury

and explores the underlying molecular mechanisms. Under hypobaric hypoxia, we observed significant cardiac dysfunction, hypertrophy, and fibrosis, as confirmed by comprehensive echocardiographic, histopathological, and molecular analyses. Remarkably, AS-IV administration effectively attenuated these pathological changes, restoring cardiac architecture and function while mitigating oxidative stress and apoptosis. Further in vivo and in vitro experiments revealed that AS-IV preserves mitochondrial integrity by enhancing membrane potential, ameliorating mitochondrial impairment, and modulating calcium homeostasis through the calcium-sensing receptor (CaSR)-nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling axis. Network pharmacology-based screening identified key molecular targets, including epidermal growth factor receptor (EGFR), phosphatidylinositol 3-kinase (PI3K), protein kinase B (AKT), and mouse double minute 2 (MDM2), which were subsequently validated via molecular docking studies demonstrating strong binding affinities between AS-IV and these core proteins. Mechanistic investigations further revealed that siRNA-mediated EGFR knockdown or pharmacological activation of CaSR abolished AS-IV's cardioprotective effects, including its anti-apoptotic, antioxidant, and mitochondrial-stabilizing properties. Taken together, our findings demonstrate that AS-IV exerts its therapeutic effects through a dual-pathway mechanism involving (1) the EGFR-PI3K-AKT-MDM2 axis and (2) CaSR-NF-κB signaling. These insights position AS-IV as a promising candidate for the prevention and treatment of high-altitude-related cardiovascular diseases.

25COASDEC97

Title: Multi-omics nominates VDAC2 as a candidate protective locus in sepsis-associated cholesterol dysregulation

Tiezhu Yao, Chengjian Guan, Qian Chen et.al.

Apoptosis, Volume 30, Issue (11-12), 2025
https://doi.org/10.1007/s10495-025-02198-7

Abstract: Sepsis, a life-threatening condition, involves dysregulated cholesterol metabolism critical for immune regulation and cellular processes. This study employed multi-omics and machine learning to explore cholesterol metabolism in sepsis, aiming to identify novel therapeutic targets. Transcriptome and single-cell RNA sequencing data for sepsis were retrieved from the Gene Expression Omnibus (GEO) database. The limma package and WGCNA co-expression network were used to screen genes, hybridized with cholesterol metabolism genes (CMGs) to identify hub genes. Machine learning algorithms screened pivotal genes to construct diagnostic model, validating performance via multi-cohort Receiver Operating Characteristic (ROC) curve. Non-negative matrix factorization (NMF) based molecular typing using CMGs, and integration of 101 machine learning algorithms built prognostic models. Single-cell analysis characterized expression patterns of pivotal genes and key subsets. Causal effects and phenotypic associations of target genes were evaluated using Summary data-based Mendelian Randomization (SMR) and PheWAS. Integrated transcriptomic analysis identified three key genes (VDAC1, VDAC2, and LDLRAP1) associated with dysregulated cholesterol metabolism in sepsis. Machine learning-based diagnostic models exhibited high predictive accuracy. NMF clustering revealed two molecular subtypes, with Cluster 1 characterized by immunosuppression and metabolic reprogramming, linked to poorer prognosis. A machine learning model integrating 101

algorithms predicted 28-day mortality. The single-cell transcriptome atlas identified CD14+CD163+ monocytes as the hub cell population in the immune microenvironment of sepsis, and the active cholesterol metabolic pathway might constitute the core for regulating the immune response. Elevated VDAC2 expression was significantly correlated with reduced sepsis risk, as determined by SMR analysis. This study underscored cholesterol metabolism's critical role in sepsis pathogenesis. Multi-omics nominates VDAC2 as a candidate protective locus in sepsis-associated cholesterol dysregulation.

25COASDEC98

Title: A Universal Solid Reaction Enabling Nanosized Li2S in an Amorphous Matrix for All-Solid-State Li–S Batteries

Xiaoge Hao, Zhi Liang Dong, Jiabin Ma et.al.

J. Am. Chem. Soc., 147, 46, 2025

https://doi.org/10.1021/jacs.4c18340

Abstract: Lithium sulfide (Li2S), a key cathode material for all-solid-state lithium–sulfur (Li–S) batteries, faces challenges such as low electronic and ionic conductivities and limited active material utilization during cycling. In this study, we developed a new cathode featuring nanosized Li2S embedded in an amorphous LiFeS2 matrix (92Li2S@8LiFeS2). Benefiting from the mixed electronic and ionic conductivities of LiFeS2 along with its catalytic effect and the nanosized Li2S that shortens electron and ion transport distances, this 92Li2S@8LiFeS2 cathode exhibits long-term cycling stability with a capacity retention of over 99% after 320 cycles. With an active material content of 48% and a mass loading of 19.1 mg/cm2, the cathode achieves an areal capacity of 13.2 mAh/cm2. This work presents a facile and novel approach to designing Li2S-based cathodes for high-performance, all-solid-state Li–S batteries.

25COASDEC99

Title: Ultrasound-Activatable Lipid Nanoplatform for Region-Confined Innate Immune Stimulation and mRNA Vaccination Therapy of Cancer

Fangmin Chen, Siyuan Ren, Lujia Huang et.al.

J. Am. Chem. Soc., 147, 46, 2025

https://doi.org/10.1021/jacs.5c06028

Abstract: Adjuvant-integrated lipid nanoparticle (LNP) formulations have been extensively investigated to potentiate mRNA vaccine therapy by promoting innate immune stimulation in antigen-presenting cells (APCs). However, these strategies are challenged by the non-specific and "always on" innate immunostimulatory effects of adjuvants, largely impeding their clinical translation. In this study, we developed a novel LNP component, sono-adjuvant lipid, to endow clinically approved LNP formulations with region-confined adjuvanticity. The engineered ultrasound (US)-activatable LNP (ULNP) precisely boosted innate immune responses in the lymph nodes (LN) through US-triggered activation of the cytosolic DNA-sensing pathways in APCs. Compared to conventional LNP integrating toll-like receptor adjuvant, the combination of ULNP with localized US stimulation (ULNP + US) not only enhanced LN-specific mRNA transfection but also elicited 2.5-fold higher antigen-specific CD8+ T cell responses to inhibit established tumor growth. More importantly, the US-activatable adjuvanting strategy was readily applicable to potentiate tumor neoantigen-

encoding circular RNA (circRNA) vaccine therapy. Combining circRNA-loaded ULNP (ci-ULNP) with US stimulation elicited potent antitumor T cell immunity and completely eliminated orthotopic liver tumors in mice. Overall, the sono-adjuvant lipid-integrated ULNP offered a robust platform for spatiotemporally tunable innate immune stimulation and mRNA vaccination therapy of cancer.

25COASDEC100

Title: Atoms and Bonds as Synergisms of Interacting Electrons and Nuclei. The Origin of Chemical Bonds in Polyatomic Molecules

Daniel Del Angel Cruz, Mark S. Gordon, Klaus Ruedenberg

J. Am. Chem. Soc., 147, 46, 2025

https://doi.org/10.1021/jacs.5c07438

Abstract: In quantum mechanical elucidations, the molecular energy of formation from the free atoms is an aggregate of cooperativities (synergisms) of orbital interactions. Frequently, such synergisms are deduced from model wave functions, which are assumed in addition to the actual molecular wave function. By contrast, the present analysis determines synergisms that are embedded in the actual molecular wave function, without arbitrary assumptions. These synergisms are exposed by a resolution of the molecular energy based on intrinsic transformations of the actual molecular wave function. The resolution identifies the modified atoms in the molecule as those quasi-atomic substructures of the wave function that maximally overlap with the free-atom wave function. Bonding results from electron sharing between these quasi-atoms. The antibonding energy increase from the free atoms to the quasi-atoms and the bonding energy lowering through electron-sharing between the quasi-atoms are resolved in terms of synergisms involving quasi-atomic orbitals. The present formulations are based on our previous analyses. The resulting “intrinsic energy decomposition analysis” (IEDA) is quantitatively exemplified by application to the ethane molecule. The IEDA shows that the total theoretical molecular energy of formation is essentially caused by electron sharing in the C–C bond and the six C–H bonds. The bonding energy lowering in each of these bonds is almost entirely due to the lowering of the kinetic energy as a result of the interference of the bonded quasi-atomic orbitals. The results of the analysis suggest that arbitrarily assumed model wave functions do not reliably recover the intrinsic physics of molecule formation.

25COASDEC101

Title: Palladium-Catalyzed Site– and Enantiodifferentiating Allylic C–H Alkylation of Internal Alkenes

Zhi-Peng Shi, Zi-Han Lin, Ye-Xuan Xu et.al.

J. Am. Chem. Soc., 147, 46, 2025

https://doi.org/10.1021/jacs.5c13527

Abstract: The site- and enantioselective transformation of allylic C–H bonds in ubiquitous internal alkenes represents a significant challenge in asymmetric synthesis. Introducing an enzyme-like chiral environment is a crucial strategy to achieve pro-R/S and site-differentiation of allylic C–H bonds, thereby circumventing the formation of complex regio- and stereoisomeric mixtures. In this work, we report a highly site- and enantiodifferentiating allylic C–H alkylation of internal alkenes through pocket-like chiral phosphoramidite-Pd

catalysis. This method is effective for a wide spectrum of cyclic and acyclic internal alkenes. Dispersion interactions are highlighted as playing a pivotal role in stabilizing the enantiodifferentiating transition states of allylic C–H bond cleavage. Within an open pocket delineated by the segments of bulky phosphoramidite ligand, electronically and sterically similar allylic C–H bonds are discriminated. This process culminates in the generation of chiral σ-allylpalladium intermediates that rapidly engage in SN2′-allylation, installing the functional group precisely at the position of the initially cleaved prochiral hydrogen.

25COASDEC102

Title: DNA Nanostructure Self-Assembly in an Aqueous Ionic Liquid Solution with Enhanced Stability and Target Binding Affinity

Dhanush Gandavadi, Hannah Talbot, Abhisek Dwivedy et.al.

J. Am. Chem. Soc., 147, 46, 2025

https://doi.org/10.1021/jacs.5c13969

Abstract: DNA nanostructure-enabled functional constructs have shown potential to improve healthcare outcomes by offering advanced disease diagnostic and therapeutic strategies. Translating this potential of DNA nanostructure-based constructs to real life applications relies on maintaining and enhancing the structural integrity and functions of the surface-anchored moieties. In this study, we explored the possibility of utilizing choline dihydrogen phosphate (CDHP) solution, an aqueous solution of ionic liquid, to assemble DNA nanostructures of different sizes and complexities with enhanced biostability and ligand binding affinity. We show successful formation of the DNA nanostructures in aqueous CDHP solution using gel electrophoresis, atomic force microscopy (AFM), and circular dichroism (CD). Biostability assays reveal that the aqueous CDHP solution may provide passive protection to DNA nanostructures against DNase I and human serum for up to 48 h. We also demonstrate that this enhanced biostability arises both from the structural conformation imparted during CDHP-mediated folding and from the presence of free CDHP ions in the solution. Notably, removal of free ions reduced the passive protection effect, but did not eliminate it, indicating the contribution of both folding and surrounding free ions. Using flow cytometry and surface plasmon resonance assays, we show that the presence of aqueous CDHP solution can enhance the binding of aptamer-functionalized DNA nanostructures to specific receptors on acute myeloid leukemia (AML) cells. Our strategy of using ionic liquid solution for one-pot preparation with enhanced stability and functionality offers a robust, simpler and faster alternative for DNA nanostructure-based constructs.

25COASDEC103

Title: Revealing Solvent-Assisted Li+ Transport in the Solid Electrolyte Interphase operando

Jacob Florian, Hao Lyu, Il Rok Choi et.al.

J. Am. Chem. Soc., 147, 46, 2025

https://doi.org/10.1021/jacs.5c14284

Abstract: The performance of energy-dense lithium metal batteries is critically influenced by the properties of the solid electrolyte interphase (SEI). Yet, progress in understanding this layer has been limited by the lack of accurate operando characterization because the SEI evolves dynamically during cycling. Here, we apply dynamic electrochemical impedance

spectroscopy (dEIS) to resolve the real-time evolution of the SEI on lithium metal in ether-based electrolytes with varying degrees of fluorination. We find that faster stabilization of the compact SEI resistance correlates with improved passivation and higher Coulombic efficiency. Unexpectedly, compact SEI resistance correlates directly with Li+ solvation energy, revealing that weaker Li+ solvation increases not only bulk but also interphase resistance. These findings challenge the conventional view of the SEI as a purely solid-phase conductor and instead support a solvent-assisted Li+ transport mechanism within the compact SEI. This framework emphasizes the need to balance SEI ionic conductivity with the Li+ solvation environment to maximize lithium metal battery performance.

25COASDEC104

Title: Application of Asymmetric Catalysis in the E/Z-Stereodivergent Synthesis of Alkenes

Mingxin Liu, Vibha V. Kanale, Christopher Uyeda

J. Am. Chem. Soc., 147, 46, 2025

https://doi.org/10.1021/jacs.5c15281

Abstract: Catalytic asymmetric reactions are primarily used to install new stereogenic centers highly enriched in either the R or the S configuration. Here, we demonstrate that chiral catalysts can also be used to control the E/Z geometry of an alkene product devoid of chirality. The process is akin to a parallel kinetic resolution in the sense that a chiral catalyst converts two enantiomers of a starting material to two different products, in this case, only differing in the E/Z geometry of an alkene. The reaction is a reductive addition of a 1,1-dichloroalkene to a chiral secondary allylic alcohol. The catalyst controls the facial selectivity of addition to the allylic alcohol, and a subsequent anti-selective β-hydroxide elimination dictates the E/Z geometry of the alkene product. Synthetic applications of the skipped 1,4-diene products and studies probing the origin of stereoselectivity are described.

25COASDEC105

Title: Defect-Driven Redox Interplay on Anatase TiO2: Surface-Structure Dependent Activation for CO2 Hydrogenation CatalysisClick to copy article link

Xiaobo Chen, Yonghyuk Lee, Seunghwa Hong et.al.

J. Am. Chem. Soc., 147, 47, 2025

https://doi.org/10.1021/jacs.5c06076

Abstract: Titanium dioxide (TiO2) is one of the most extensively studied oxides as an active catalyst or catalyst support, particularly in energy and environmental applications, but the atomistic mechanisms governing its dynamic response to reactive environments and their correlation to reactivity remain largely elusive. Using in situ environmental transmission electron microscopy (ETEM), synchrotron X-ray diffraction (XRD), ambient-pressure X-ray photoelectron spectroscopy (AP-XPS), temperature-programmed reduction (TPR), reactivity measurements, and theoretical modeling, we reveal the dynamic interplay between oxygen loss and replenishment of anatase TiO2 under varying reactive conditions. Under H2 exposure, anatase TiO2 undergoes surface reduction via lattice oxygen loss, forming Ti3O5. In contrast, CO2 exposure induces oxygen replenishment, reversing stoichiometry. In mixed H2/CO2 environments, the reverse water–gas shift (RWGS) reaction proceeds selectively on stepped and high-indexed TiO2 surfaces, whereas the thermodynamically stable TiO2(101)

surface remains inactive and intact. Critically, H2 pretreatment generates oxygen vacancies on TiO2(101), transforming it into an active Ti3O5 or defect-rich surface that catalyzes RWGS. By correlating surface structure, defect dynamics, and gas-phase interactions, this work deciphers the competition between H2-driven reduction and CO2-driven oxidation pathways at the atomic scale. These insights establish defect engineering as a strategic lever to activate inert TiO2 facets, advancing the design of adaptive catalysts for sustainable fuel synthesis technologies.

25COASDEC106

Title: Redox Umpolung of Phenalenyl-Based Molecule Inside Water-Soluble Nanocages

Debojyoti Roy, Paramita Datta, Swadhin K. Mandal et.al.

J. Am. Chem. Soc., 147, 47, 2025

https://doi.org/10.1021/jacs.5c11576

Abstract: Phenalenyl (PLY) is the smallest, odd alternant polycyclic hydrocarbon known for its magnetic, conducting, and electronic properties. Such material properties are based on the capability of PLY to act as an electron reservoir. PLY has recently emerged as a reductive catalyst, wherein both its ground and excited states can form long-lived radical anions, driving diverse reductive transformations. However, the rich electronic properties of the π-backbone in PLY systems have never been exploited for oxidative transformations. Here, we incarcerate PLY inside a water-soluble Pd6L412+ nanocavity to provide the first transient absorption signature of PLY-radical cation under photoirradiation, acting as the electron donor instead of its electron acceptor properties; demonstrating redox-umpolung behavior. Photoexciting host–guest charge transfer states, we drive a single electron transfer from PLY to the nanocavity within ∼2 ps, while a solvent-assisted deprotonation of the radical cation within ∼80 ps generates a reactive, long-lived neutral radical (>2 ns). As a proof of concept, utilizing this redox-umpolung photochemistry of PLY, we demonstrate a direct route for the synthesis of aromatic nitriles in water. We envision that our findings will pave the way for advancing water-compatible catalysis using PLY-based molecules, leveraging the unique reactivity of open-shell organic systems.

25COASDEC107

Title: Selection of Ruthenium Polypyridyl Complex-Modified Aptamers for Photodynamic Therapy against Streptococcus Pneumonia

Marie Flamme, Germain Niogret, Luke McKenzie et.al.

J. Am. Chem. Soc., 147, 47, 2025

https://doi.org/10.1021/jacs.5c13224

Abstract: Photodynamic therapy (PDT) harnesses the combination of light, oxygen, and photosensitizers to induce cell death via reactive oxygen species (ROS) formation. Given its intrinsic properties, PDT represents an alluring way of stymieing the increasing surge of antimicrobial resistance (AMR). Despite favorable assets, various hurdles need to be circumvented before PDT can efficiently be used to combat AMR. Here, we have evaluated the possibility of generating aptamers equipped with ruthenium polypyridyl complexes against entire Gram-positive Streptococcus pneumoniae bacteria. This combination is hypothesized to improve the poor specificity of photosensitizers, increase PDT efficiency, and potentially penetrate biofilms. Toward these aims, we first prepared nucleotides equipped

with various ruthenium complexes and investigated their capacity at serving as substrates for polymerases for enzymatic DNA synthesis. Depending on the nature of the polypyridyl ligands, strong intercalation into dsDNA was observed even when connected to negatively charged nucleotide backbones. We then carried out SELEX and identified two unmodified aptamers that bound to the fixed bacterial target with Kd values of 118 nM and 541 nM. The SELEX experiment with the ruthenium-modified nucleotide led to the identification of one aptamer. The enzymatic synthesis of the modified aptamer was complicated by the formation of a very stable secondary structure confirmed by UV melting experiments (Tm of 84 °C). The modified aptamer displayed a high affinity (Kd value of 125 nM) for fixed Streptococcus pneumoniae bacteria. Collectively, these results highlight the possibility of using nucleotides equipped with large modifications such as ruthenium polypyridyl complexes in SELEX to raise potent aptamers against entire bacterial targets. These findings open directions to convert aptamers into potent devices to combat AMR via PDT-based approaches.

25COASDEC108

Title: SSNet: A Spectral Unmixing Framework for Enhancing the Qualitative Sensitivity of SERS to Trace Targets in Complex Mixtures

Si-Heng Luo, Jing Xu, Wei-Li Wang et.al.

J. Am. Chem. Soc., 147, 47, 2025

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Abstract: Surface-enhanced Raman spectroscopy (SERS) is a powerful tool for spectrum–structure correlation across various fields. However, the qualitative and quantitative analysis of SERS to trace targets is often compromised due to the coadsorption and competitive adsorption from nontargets in complex systems. To unmix and identify the SERS signal of a target within a mixture SERS spectrum, we develop SSNet, an intelligent and self-supervised algorithm. Taking the trace detection of gelsemium phytotoxin in various food samples as an example, SSNet performs with high fidelity across the core qualitative and quantitative benchmarks: Raman peak intensity, peak position, and relative intensity. Without any prior knowledge of the matrix, SSNet achieved expert-level qualitative sensitivity. With the knowledge of similar matrices, the sensitivity was an order of magnitude higher than that of an expert, even when the SERS signal of the target is invisible to the naked eye. The ability to unmix SERS signals of multiple targets is further demonstrated using the three structurally similar gelsemium phytotoxins. The exceptional performance and generalizability of SSNet enhance the on-site, in situ, in vivo, and operando applications of Raman/SERS.

25COASDEC109

Title: Unraveling the General Trend of the Reaction of Nitrite with Diiron(II)-polychalcogenides

Kamal Hossain, Arindam Basak, Angshuman Roy Choudhury et.al.

J. Am. Chem. Soc., 147, 48, 2025

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Abstract: Detailed structural and spectroscopic investigation of the reactivity of nitrite (NO2–) with three binuclear Fe(II)-polychalcogenido complexes, [Fe2(BPMP)(En)]1+ (E = S, n = 5; E = Se, n = 4) and [Fe2(BPMP)(S6)(NCS)], in comparison with a Zn(II) analogue, [Zn2(BPMP)(S5)]1+ (BPMP1– is the anion of 2,6-bis[[bis(2-pyridylmethyl)amino]methyl]-

4-methylphenol), establishes, for the first time, a general trend for the product formation and the reaction mechanism. While all the reactions generated nitric oxide (NO) involving the generation of perthionitrite (SSNO–) or its selenium analogue, the reactions involving Fe(II) always produced the dinitrosyl iron complexes (DNICs), [Fe(E5)(NO)2]1– (E = S, Se), and binuclear Fe(II)-chalcogenido/-hydrochalcogenido complexes, which is in sharp contrast to the formation of binuclear Zn(II) complexes featuring the coordinated SnO2– ligand (n = 3, 4). The present study shows that the reaction of diiron(II)-polychalcogenido complexes with NO2– follows a very different path than that followed by the Zn(II) analogues and is not affected by the presence of an additional redox-silent ligand, such as SCN–. Furthermore, the isolation of a unique diiron(II)-trihydrosulfido complex as an analytically pure complex in the reaction of a diiron(II)-pentasulfido complex and NO2– indicated the hitherto unknown prospects of the reactivity of NO2– with coordinated polychalcogenides for new chemical transformations.

25COASDEC110

Title: A General Strategy to Access All Stereosequences in a Synthetic Polymer

Ranajit Barman, Jean-François Lutz

J. Am. Chem. Soc., 147, 48, 2025

https://doi.org/10.1021/jacs.5c15603

Abstract: The control of main-chain stereocenters in synthetic polymers remains a longstanding challenge, with traditional polymerization methods typically yielding only three types of well-defined stereosequences: isotactic, syndiotactic, and heterotactic. Here, we show that a broader range of stereochemical patterns can be accessed using iterative phosphoramidite chemistry. Two monomers bearing opposite configurations at a carbon stereocenter were synthesized and employed in automated solid-phase synthesis to construct poly(phosphodiester amide)s with defined stereosequences. High coupling efficiencies enabled the generation of polymers with exact chain lengths and primary structures. Comprehensive characterization by high-resolution mass spectrometry, ion-exchange HPLC, NMR spectroscopy, and circular dichroism confirmed the high stereochemical fidelity of the resulting materials. This approach enabled the synthesis of perfectly isotactic and syndiotactic polymers (100% m or r dyads), surpassing the precision achievable through conventional polymerization. More importantly, the method also facilitated access to nonclassical and previously unattainable stereosequences, including periodic, stereomutated, and stereocoded arrangements. For polymers with 20 stereocenters, this methodology allows for the theoretical creation of over one million unique stereosequences. These findings establish a new paradigm in stereocontrolled polymer synthesis, expanding the structural and functional landscape of synthetic macromolecules.

25COASDEC111

Title: Direct Interconversion between Bis(borylenes) and Diborenes

Sourav Kar, Koushik Saha, Vailappully Binilkrishna et.al.

J. Am. Chem. Soc., 147, 48, 2025

https://doi.org/10.1021/jacs.5c17540

Abstract: Over the past two decades, the chemistry of borylenes and their formal dimer, diborenes, has witnessed remarkable advances. However, direct evidence for a Wanzlick-type

equilibrium between borylenes and diborenes has remained elusive. Here, we report CAAC-stabilized (CAAC = cyclic (alkyl)(amino)carbene) mono- and disubstituted ferrocene-based borylene systems. The monosubstituted ferrocene-based borylene undergoes intramolecular C–H, CO, and H2 activation, with the C–H activation products existing in equilibrium. Most notably, the disubstituted ferrocene-based bis(borylene) undergoes direct coupling to form a diborene featuring a unique delocalized four-center–two-electron (4c–2e) π bond. Remarkably, this diborene reversibly dissociates back into the bis(borylene), which can be trapped with CO or via intramolecular C–H activation. The electronic and rotational flexibility of the ferrocene scaffold plays a pivotal role in facilitating the reversible coupling and decoupling between these bis(borylene) and diborene species. Furthermore, the ferrocenyl diborene species exhibits distinctive photophysical properties, redox behavior and reactivities.

Diagnostic Services
(Pathology**, C**ancer Screening **& R**adio-diagnosis**)**

25COASDEC01
Title: Genitourinary Pathology Society and International Society of Urological Pathology White Paper on Defining Indolent Prostate Cancer.
Shah, Rajal B. MD*; Paner, Gladell P. MD et.al.
The American Journal of Surgical Pathology 49(12)
https://doi.org/10.1097/PAS.0000000000002425
Abstract: A significant subset of well-differentiated prostatic acinar neoplasms with invasive histologic features will not spread outside of the prostate, become symptomatic, or shorten a patient's life even if the tumor is left untreated. Overdiagnosis and overtreatment of these indolent prostate cancers (PCa) remain a significant health care problem despite the improved risk assessment and uptake in acceptance of conservative management. While detection of indolent PCa on an entirely resected prostate is possible, recognition of indolent PCa on a needle biopsy (NBX) cannot be reliably made as Grade Group 1 (GG1) PCa diagnosis on NBX is not always identical to one from radical prostatectomy due to a variety of reasons. Further, some of the initially diagnosed GG1 PCas on NBX and carefully monitored on active surveillance (AS) are later reclassified with higher grades. At the same time, other GG1 PCas never progressed on long-term follow-up while receiving no therapy. The overarching goal of this white paper by the 2 leading uropathology organizations, Genitourinary Pathology Society (GUPS) and International Society of Urological Pathology (ISUP), is to help identify a path toward a more meaningful multidisciplinary solution addressing the pervasive problem of overdiagnosis of indolent PCa and its downstream negative effects. Herein, GUPS and ISUP jointly release statements that address why recognition of indolent PCa cannot be reliably made in NBX and why various contemporary multidisciplinary approaches are needed to help improve the detection of indolent PCa in NBX.

25COASDEC02
Title: International Society of Urological Pathology Consensus on Cancer Precursor Lesions. Working Group 1
The Prostate
Iczkowski, Kenneth A. MD et.al.
The American Journal of Surgical Pathology 49(12)
https://doi.org/10.1097/PAS.0000000000002430
Abstract: Working Group 1 at ISUP's Cancer Precursors meeting (September 2024) evaluated 5 putative precursors of invasive prostate cancer: high-grade prostatic intraepithelial neoplasia (HGPIN), intraductal carcinoma (IDC), atypical intraductal proliferation (AIP), atypical adenomatous hyperplasia (AAH)/adenosis, and proliferative inflammatory atrophy (PIA). Objectives were to compile recent evidence, interrogate current practices, and vote on recommendations, with 67% approval defined as consensus. Consensus was reached against the reporting of the low-grade form of PIN. HGPIN need not be reported when concomitant cancer or atypical small acinar proliferation suspicious for cancer exists adjacent to it, for biopsy or prostatectomy specimens. Finally, while the clinical significance of unifocal HGPIN in biopsies remains uncertain, there is stronger evidence for multifocal

isolated HGPIN as a predictor of subsequent cancer detection. By consensus, multifocal HGPIN should continue being reported. Slight refinement was achieved regarding IDC criteria. The consensus opinion was that a dense cribriform to solid proliferation need not demonstrate marked nuclear atypia/ pleomorphism to qualify as IDC. The inverse scenario of marked atypia without dense cribriform/solid proliferation fell just short (65%) of consensus for IDC. Redesignating cribriform HGPIN as AIP achieved consensus. AIP found alone or with grade group 1 cancer warrants an explanatory comment. However, agreement was not attained to report AIP in the presence of invasive cancer, in either needle biopsy or prostatectomy. Finally, the optional reporting of PIA or AAH/adenosis in biopsies as pertinent negatives both fell short of consensus. This guidance should help pathologists standardize reporting, staying focused on the clinically actionable aspects of these lesions.

25COASDEC03

Title: Postneoadjuvant Whipple Resections Show Significant Residual Microscopic Tumor Beyond Grossly Identified Tumor Bed

Implications for Accurate Tumor Staging

Wannasai, Komson MD et.al.

The American Journal of Surgical Pathology

https://doi.org/10.1097/PAS.0000000000002465

Abstract: Neoadjuvant chemotherapy plays a vital role in the treatment of pancreatic ductal adenocarcinoma (PDAC), but treatment effect complicates pathologic examination of postneoadjuvant Whipple resections. Institutional practice is variable but current Pancreatobiliary Pathology Society (PBPS) guidelines suggest extensive microscopic examination of the tumor bed (TB). In practice, gross identification of TB is challenging and may lead to an inaccurate assessment of tumor size. The purpose of this study is to evaluate the adequacy of current practice in postneoadjuvant Whipple resections for pathologic staging. A single institutional prospective cohort was assessed, including 29 entirely submitted (ES) specimens and 10 current PBPS guideline-based (CG) specimens. Cases were evaluated for TB gross measurement, TB microscopic tumor, nontumor bed (N-TB) microscopic tumor, overall size assessment by microscopic evaluation, and presence of lymph nodes with metastases. ES and CG specimens showed similar overall residual tumor size measurements under the current PBPS guidelines protocol, but with the entire submission, tumor size increased by an average of 0.5 cm (range: 0.0 to 2.1 cm). Twenty-eight percent had an upstaged ypT due to a significant N-TB tumor. These findings delineate the limitations of gross TB assessment in postneoadjuvant Whipple resections for adequate pathologic staging and appropriate prognostication.

25COASDEC04

Title: Postneoadjuvant Whipple Resections Show Significant Residual Microscopic Tumor Beyond Grossly Identified Tumor Bed: Implications for Accurate Tumor Staging.

Wannasai, Komson MD et.al.

The American Journal of Surgical Pathology 49(12):p

https://doi.org/10.1097/PAS.0000000000002465

Abstract: Neoadjuvant chemotherapy plays a vital role in the treatment of pancreatic ductal

adenocarcinoma (PDAC), but treatment effect complicates pathologic examination of postneoadjuvant Whipple resections. Institutional practice is variable but current Pancreatobiliary Pathology Society (PBPS) guidelines suggest extensive microscopic examination of the tumor bed (TB). In practice, gross identification of TB is challenging and may lead to an inaccurate assessment of tumor size. The purpose of this study is to evaluate the adequacy of current practice in postneoadjuvant Whipple resections for pathologic staging. A single institutional prospective cohort was assessed, including 29 entirely submitted (ES) specimens and 10 current PBPS guideline-based (CG) specimens. Cases were evaluated for TB gross measurement, TB microscopic tumor, nontumor bed (N-TB) microscopic tumor, overall size assessment by microscopic evaluation, and presence of lymph nodes with metastases. ES and CG specimens showed similar overall residual tumor size measurements under the current PBPS guidelines protocol, but with the entire submission, tumor size increased by an average of 0.5 cm (range: 0.0 to 2.1 cm). Twenty-eight percent had an upstaged ypT due to a significant N-TB tumor. These findings delineate the limitations of gross TB assessment in postneoadjuvant Whipple resections for adequate pathologic staging and appropriate prognostication.

25COASDEC05

Title: Aberrant Cytoplasmic p53 Staining in Oral Squamous Cell Carcinoma and Dysplasia: A Clinicopathologic and Molecular Study.

Zhang, Lingxin MD et.al.

The American Journal of Surgical Pathology 49(12)

https://doi.org/10.1097/PAS.0000000000002471

Abstract: p53 cytoplasmic sequestration has been shown to be a mechanism of carcinogenesis. However, until recently, an aberrant p53 cytoplasmic staining pattern by immunohistochemistry (IHC) was under-reported in oral squamous cell carcinoma (OSCC) and oral epithelial dysplasia (OED). Following the identification of a pilot case, the authors studied the clinicopathologic features of 4 OSCCs and 10 OEDs with p53 cytoplasmic staining pattern, 4 of which exhibited co-occurrence of nuclear null/overexpression patterns. Using next-generation sequencing (NGS), we demonstrate that this cytoplasmic staining pattern correlates with *TP53* mutations that disrupt or truncate the C-terminal nuclear localization sequence (NLS) or nuclear exclusion sequence (NES). High-impact NLS-altering mutations in the same region are identified in 8.7% to 11.0% of *TP53*-mutant samples in the TCGA-HNSC cohort. Our study provides a practical definition for aberrant p53 cytoplasmic staining in HNSCC and OED, a diagnostic pitfall with potential biological implication. This study proposes an updated p53 IHC interpretation algorithm to facilitate further data accrual.

25COASDEC06

Title: Tubulocystic Renal Cell Carcinoma With Pure Morphology and Confirmed "Wild Type" FH/2SC Immunophenotype: Clinicopathologic Series of 30 Patients.

Harik, Lara R. MD et.al.

The American Journal of Surgical Pathology ,49(12)

https://doi.org/10.1097/PAS.0000000000002457

Abstract: Tubulocystic renal cell carcinoma is a rare neoplasm, first adopted into the WHO classification of kidney tumors in 2016. The diagnostic criteria were refined in the 2022

WHO classification, requiring “pure morphology” and exclusion of other renal cell carcinoma subtypes with overlapping features. We identified 31 tubulocystic renal cell carcinomas from 30 patients. Median age was 60 years (30 to 77 y) with male:female ratio of 13.5:1. Race was known for 26 patients, and the majority were African American (n = 16/26,62%), followed by white/Caucasian (10/26, 38%). Eleven patients (37%) had a history of chronic or end-stage renal disease. Median tumor size was 2.3 cm (range: 0.4 to 6.3 cm). All tumors were characterized by cysts and tubules, surrounded by fibrotic stroma. Lining epithelial cells had eosinophilic cytoplasm, ranging from flattened to cuboidal to hobnail in arrangement. By definition, solid epithelial nodules and destructive invasion were absent. In addition, all tumors had a normal pattern of FH and 2SC expression by immunohistochemistry. AJCC stage was pT1 for all 31 tumors: 30 pT1a and 1 pT1b. All patients had no evidence of disease at last follow-up (median: 35 mo; range: 1 to 294 mo). We report a large series of tubulocystic renal cell carcinomas with pure morphology and confirmed normal/“wild type” FH/2SC immunophenotype. When these strict definitions are applied, our findings confirm an indolent clinical behavior.

25COASDEC07

Title: Claudin 18.2 and Other Therapeutic Biomarkers in Gastric and Gastroesophageal Junction Adenocarcinomas.

Kolin, David L et.al.

The American Journal of Surgical Pathology 49(12).

https://doi.org/10.1097/PAS.0000000000002464

Abstract: Biomarker-driven therapies have led to several recent advances in treating gastric and gastroesophageal junction (GEJ) cancers, but the overlap of these biomarkers remains unclear. We analyzed coexpression of Claudin 18.2 (CLDN18.2), HER2, PD-L1, and mismatch repair (MMR), focusing on CLDN18.2 staining extent and clinicopathologic correlations in gastric and GEJ adenocarcinomas. A total of 145 cases from 2023 to 2024 were identified from pathology archives. Following published clinical trial criteria, tumors were considered CLDN18.2-positive if ≥75% of tumor cells showed moderate-to-strong membranous staining. CLDN18.2 positivity was observed in 70 cases (48%) and was enriched in tumors with signet-ring-cell features (P=0.0391, univariate; P=0.0113, multivariate). No significant correlation was found with other clinicopathologic features or HER2, PD-L1, or MMR status. The inclusion of CLDN18.2 increased the proportion of cases with at least one actionable biomarker to 92%. Among triple-negative (HER2-negative, PD-L1-negative, and MMR-proficient) tumors, CLDN18.2 was positive in 52% overall and 50% of cases with metastasis, suggesting its potential utility in expanding treatment options. CLDN18.2 appeared to demonstrate relatively low intratumoral heterogeneity, with most tumors (72%) demonstrating either no staining (<10% tumor cells staining) or diffuse staining (≥90% of tumor cells staining). Among tumors classified as CLDN18.2-positive on the above criteria, 84% displayed homogeneous positivity. Nevertheless, heterogeneous expression was observed in a small percentage of tumors (28% of all tumors), indicating that sampling-related misclassification remains a potential concern. Our study provides detailed insights into CLDN18.2 expression and sheds light on the biomarker landscape in gastric and GEJ cancers.

25COASDEC08

Title: Lu-Dotatate versus high-dose long-acting octreotide for the treatment of patients with advanced, grade 1-2, well-differentiated gastroenteropancreatic neuroendocrine tumours (XT-XTR008-3-01): an open-label, randomised, phase III trial☆

J. Xu et.al.

Annals of Oncology, Volume 36, Issue 12
https://doi.org/10.1016/j.annonc.2025.08.3758

Abstract: The phase III trial, XT-XTR008-3-01, was a randomised controlled trial (RCT) that evaluated the efficacy and safety of XTR008, a novel no-carrier-added lutetium-177 (^{177}Lu)–Dotatate, for the first time in a later-line therapy setting for gastroenteropancreatic neuroendocrine tumours (GEP-NETs) of all origins. Patients and methods- Patients with grade 1-2, unresectable, locally advanced or metastatic GEP-NETs who had progressed within the last 12 months before randomisation were randomly allocated 1 : 1 to XTR008 (four cycles every 8 weeks) or octreotide 60 mg (every 4 weeks), stratified by primary tumour site (pancreatic versus non-pancreatic), pathological tumour grade (1 versus 2), and duration of prior somatostatin analogues treatment (≤6 versus >6 months). The primary endpoint was progression-free survival (PFS) by a blinded independent review committee. The key secondary endpoints included overall response rate (ORR); overall survival (OS); quality of life, evaluated using the European Organisation for Research and Treatment of Cancer quality of life questionnaires QLQ-C30 and QLQ-GI.NET21; safety; pharmacokinetics; and dosimetry. Results- Patients (N = 196) were randomized to XTR008 (n = 99) or control (n = 97). Primary tumour sites: pancreas (59%), rectum (28%), midgut (7%). Median follow-up: 11.1 months [interquartile range (IQR) 8.5-11.5, XTR008] versus 10.2 months (IQR 8.5-11.9 months, control). With 78 PFS events, median PFS was not reached [95% confidence interval (CI) 16.13 months to not estimated] versus 5.8 months (95% CI 5.65-8.41 months); stratified hazard ratio (HR) 0.06 (P < 0.0001). ORR: 43.4% (95% CI 33.50% to 53.77%) versus 1.0% (95% CI 0.03% to 5.61%). OS data were immature for both groups, with XTR008 showing a longer survival trend (HR 0.24, P = 0.0550). Treatment-related adverse events: 98% versus 89%; serious adverse events: 16.3% versus 12.5% (6.1% versus 3.1% drug-related). Myelodysplastic syndrome and grade ≥3 renal toxicity occurred in 1% of patients in the XTR008 group; no acute myeloid leukaemia or drug-related deaths occurred. Conclusions- XTR008 monotherapy showed superior efficacy versus high-dose long-acting repeatable (LAR) octreotide monotherapy in advanced GEP-NET tumours of all origins in a later-line treatment setting, with manageable safety, supporting its use as a new treatment option.

25COASDEC09

Title: Effect of 5 years of CT-scan and CEA follow-up on survival endpoints in patients with colorectal cancer: the PRODIGE-13 FFCD phase III trial

C. Lepage et.al.

Annals of Oncology, Volume 36, Issue 12
https://doi.org/10.1016/j.annonc.2025.09.004

Abstract: - Intensive follow-up of patients after curative surgery for colorectal cancer is recommended by various scientific societies. However, these recommendations are based mainly on expert opinions, while the results of the few clinical trials are controversial.

Moreover, no survival benefit has been demonstrated to date. Patients and methods- PRODIGE-13 is a cooperative prospective multicentre controlled phase III trial evaluating by factorial plan the impact of (i) intensive radiological monitoring [alternating abdominal ultrasound (US)/computed tomography (CT) scan/3 months] versus standard monitoring (US/3 months and thoracic radiography/6 months) and (ii) carcinoembryonic antigen (CEA) assessment versus no assessment, in the follow-up of resected stage II or III colorectal cancer with no evidence of residual disease on baseline postsurgical investigation in France and Belgium. The primary endpoint was 5-year overall survival (OS). Results- Altogether, 2009 patients were randomly assigned. Among them, 16% had rectal cancer, and 44% left colon cancer; 75.9% were <75 years old. With a median follow-up of 7.8 years, cancer recurred in 22.3% of patients (local 10.5%, metastatic 72.9%, both 16.6%). The 5-year OS rates were 82.1% [95% confidence interval (CI) 78.5% to 85.2%] in group A (intensive imaging + CEA) versus 84.1% (95% CI 80.5% to 87.0%) in group B (intensive imaging alone), versus 83.6% (95% CI 80.1% to 86.6%) in group C (standard imaging + CEA) versus 79.5% (95% CI 75.7% to 82.8%) in group D (standard imaging alone) [*P* (log-rank) = 0.170]. Median OS was not reached in the four groups. Five-year relapse-free survival (RFS) was 73.8% in the CT-scan surveillance group versus 69.3% in the no-CT-scan group [hazard ratio (HR) 0.89, 95% CI 0.76-1.03, *P* = 0.108]. Five-year RFS was 71.3% in the CEA surveillance group versus 71.8% in the no-CEA group (HR 1.00, 95% CI 0.86-1.16, *P* = 0.959). Conclusions- Among patients with stage II or III colorectal cancer, after curative surgery, the implementation of CEA and/or CT-scan surveillance did not provide any benefit in 5-year OS for the overall population of the study.

25COASDEC10

Title: Phase Ib and dose-expansion study of GSK3326595, a PRMT5 inhibitor as monotherapy and in combination with pembrolizumab in patients with advanced cancers

M.M. Gounder et.al.

Annals of Oncology, Volume 36, Issue 12

https://doi.org/10.1016/j.annonc.2025.08.3757

Abstract: - Protein arginine methyltransferase 5 inhibition often leads to a decrease in cell growth and survival in cancer cell lines. GSK3326595 is a first-generation protein arginine methyltransferase 5 inhibitor.-Patients and methods METEOR-1 was a first-in-human, open-label, multicenter, three-part phase I study (NCT02783300) in patients with solid tumors and non-Hodgkin lymphoma (NHL). The objectives of part 1 were to determine the recommended phase II dose (RP2D), assess safety, evaluate preliminary clinical activity, and study the pharmacokinetics of oral GSK3326595 monotherapy. Part 2 enrolled patients at the RP2D to further evaluate clinical activity and safety. Part 3 explored the RP2D of GSK3326595 with pembrolizumab. Results- A total of 288 patients were treated. In part 1, 69 patients received once daily (od) or twice a day (b.i.d.) GSK3326595 in doses ranging from 12.5 to 600 mg/day. In part 2, 218 patients received either 400 mg or 300 mg od, with the RP2D amended from 400 mg to 300 mg od due to toxicities. In part 3, 10 patients received GSK3326595 at 100 mg/day with pembrolizumab 200 mg intravenously every 3 weeks. Pharmacokinetics revealed that GSK3326595 was rapidly absorbed (T_{max}: 2-3 hours), with a mean terminal half-life of 4-6 hours. Dose-dependent increases in plasma exposure (C_{max} and

AUC) were observed with both od and b.i.d. dosing. The most common adverse events at the RP2D included fatigue (57%), nausea (48%), and anemia (48%). Four partial responses (PRs) were observed in part 1 at doses of 200 mg (n = 2), 300 mg (n = 1), and 400 mg (n = 1). Two complete responses and one PR were seen in NHL [i.e. follicular (n = 2) lymphoma, diffuse large B-cell lymphoma (n = 1)], one PR in adenoid cystic carcinoma, and one PR in HR-positive breast cancer in part 2. No responses were observed in part 3. Conclusions-GSK3326595 monotherapy demonstrated modest antitumor activity. Further research in adenoid cystic carcinoma and NHL is warranted.

25COASDEC11

Title: A-BRAVE trial: a phase III randomized trial with anti-PD-L1 avelumab in high-risk triple-negative early breast cancer patients

P.F. Conte et.al.

Annals of Oncology, Volume 36, Issue 12

https://doi.org/10.1016/j.annonc.2025.08.005

Abstract: - The A-BRAVE trial evaluated the efficacy of avelumab, an anti-programmed death-ligand 1 (PD-L1) antibody, as adjuvant treatment of patients with early triple-negative breast cancer (TNBC) at high risk. Patients and methods-A-BRAVE is a phase III study that randomly assigned patients with high-risk early TNBC to 1 year of avelumab versus observation, after completion of standard surgery and (neo)adjuvant chemotherapy. High-risk was defined as either: (i) ≥pN2/any pT, pN1/pT2, or pN0/pT3 after primary surgery (stratum A); or (ii) invasive residual disease (breast and/or nodes) after neoadjuvant chemotherapy (stratum B). Coprimary endpoints were disease-free survival (DFS) in the intention-to-treat (ITT) and stratum B populations. Secondary endpoints were overall survival (OS) and DFS in PD-L1-positive patients. PD-L1 was evaluated in treatment-naïve tumor samples by immunohistochemistry (73-10 RUO assay, Agilent Technologies) and digital pathology. Results- From June 2016 to October 2020, 466 patients were randomly assigned: 383 entered stratum B (82%) and 83 entered stratum A (18%). At a median follow-up of 52.1 months, avelumab did not significantly improve DFS in the ITT population [hazard ratio (HR) 0.81, 95% confidence interval (CI) 0.61-1.09, P = 0.172; 3-year DFS estimates were 68.3% for avelumab versus 63.2%], or in stratum B (HR 0.80, 95% CI 0.58-1.10, P = 0.170; 3-year DFS estimates were 66.9% for avelumab versus 60.7%). In a descriptive analysis, avelumab reduced the hazard of OS events: HR 0.66, 95% CI 0.45-0.97. The 3-year OS estimates for avelumab and control arm were 84.8% (95% CI 79.5% to 88.8%) and 76.3% (95% CI 70.1% to 81.3%), respectively. PD-L1 status was prognostic but not predictive for avelumab benefit in terms of DFS (test for interaction P = 0.155). Conclusions-For patients with TNBC at high risk of relapse who complete standard treatment with surgery and (neo)adjuvant chemotherapy, 1 year of adjuvant avelumab versus observation did not improve DFS. However, a descriptive analysis suggests a potential favorable impact on OS.

25COASDEC12

Title: Dostarlimab and niraparib in primary advanced ovarian cancer

A.-C. Hardy-Bessard et.al.

Annals of Oncology, Volume 36, Issue 12

https://doi.org/10.1016/j.annonc.2025.05.009

Abstract: -The combination of immunotherapies and poly (ADP-ribose) polymerase inhibitors (PARPis) has been hypothesized to improve outcomes in advanced ovarian cancer (aOC). The FIRST/ENGOT-OV44 trial evaluated adding dostarlimab to first-line platinum-based chemotherapy (PBCT) and niraparib maintenance ± bevacizumab in patients with aOC. Patients and methods- In this randomized, double-blind, phase III trial, patients with newly diagnosed stage III-IV epithelial OC were randomized (1:2) to arm 2 (PBCT–placebo with niraparib maintenance) or arm 3 (PBCT–dostarlimab with dostarlimab–niraparib maintenance); arm 1 (PBCT–placebo with placebo maintenance) enrollment terminated following PARPi approvals. Efficacy was assessed in arms 2 and 3 (intention-to-treat population). The primary endpoint was investigator-assessed progression-free survival (PFS) as per RECIST v1.1. The key secondary endpoint was overall survival (OS). Safety was assessed in patients who received one or more doses of study treatment (arms 1-3; analyzed as per treatment received). Results-From 14 November 2018 to 5 January 2021, 1138 patients were randomized to arms 2 (n = 385) and 3 (n = 753) and included in efficacy analyses. Median follow-up was 53.1 (interquartile range 47.5-59.7) months. There was a statistically significant difference in PFS in arm 3 versus arm 2 (median 20.6 versus 19.2 months; hazard ratio [HR] 0.85, 95% confidence interval [CI] 0.73-0.99, P = 0.0351). OS had reached 57% maturity and was not statistically significant (median 44.4 versus 45.4 months; HR 1.01, 95% CI 0.86-1.19, P = 0.9060). Toxicities observed were consistent with known safety profiles of the agents used in the study. Conclusions-In the first-line treatment of patients with aOC, the addition of dostarlimab to PBCT and niraparib maintenance was associated with a statistically significant, but clinically modest, PFS improvement, with no difference in OS.

25COASDEC13

Title: Randomized phase III trial of adjuvant radiation versus chemoradiation in intermediate-risk, early-stage cervical cancer following radical hysterectomy and lymphadenectomy: results from NRG Oncology/GOG-263/KGOG 1008☆

S.Y. Ryu et.al.

Annals of Oncology, Volume 36, Issue 12

https://doi.org/10.1016/j.annonc.2025.09.003

Abstract: -To determine whether adjuvant chemoradiation (CRT) with weekly cisplatin improves recurrence-free survival (RFS) compared with radiation (RT) in pathologically proven intermediate risk early-stage cervical cancer following radical hysterectomy and lymphadenectomy. Methods- Post-surgical patients with stage I-IIA cervical cancer with pathologically noted intermediate risk factors including combinations of capillary lymphatic space involvement, stromal invasion, and tumor size were randomly assigned in a 1 : 1 ratio to receive either adjuvant CRT or RT (NCT01101451). Patients received conformal RT, or intensity modulated radiation therapy. In the CRT arm, 6 weekly cycles of cisplatin 40 mg/m^2 were administered during RT. RFS was the primary endpoint in randomized and eligible patients. Secondary endpoints included overall survival (OS), quality of life (QoL), and adverse events (AEs). Results- Of the 340 randomized patients, 316 were eligible and most had Federation of Gynecology and Obstetrics (2009) stage IB$_1$ and squamous cell carcinoma histology. Out of 316 patients, 292 (92.4%) received 28 fractions of RT with a median dose of 50.4 Gy and a median treatment duration of 39 days. Three-year RFS was

88.5% in the CRT arm and 85.4% in the RT arm. Both RFS [hazard ratio (HR) 0.698, 95% confidence interval (CI) 0.408-1.192, $P = 0.09$], as well as OS [HR 0.586, 95% CI 0.286-1.199, $P = 0.07$] favored CRT compared with RT alone. Grade 3 or 4 AEs occurred in 43% and 15% in the CRT and RT arms, respectively ($P < 0.01$). A transient decline in QoL occurred in the CRT arm compared with RT after starting treatments and recovered to pre-treatment level by 36 weeks.Conclusion-Although RFS and OS favored CRT, the addition of cisplatin during RT did not statistically improve RFS or OS in cervical cancer patients with intermediate pathological risk factors following radical hysterectomy and lymphadenectomy. CRT increased grade 3 and 4 AEs with a transient decline in QoL.

25COASDEC14

Title: Circulating kidney injury molecule-1 (KIM-1) and association with outcome to adjuvant immunotherapy in renal cell carcinoma

B.I. Rini et.al.

Annals of Oncology, Volume 36, Issue 12

https://doi.org/10.1016/j.annonc.2025.08.007

Abstract: - Adjuvant immunotherapy is currently the standard of care for patients with resected renal cell carcinoma (RCC) at increased risk of recurrence, but there are no biomarkers available to guide treatment. Kidney injury molecule-1 (KIM-1) has previously been described as a potential circulating biomarker in RCC. Patients and methods- Biomarkers and outcomes among patients who participated in a randomized phase III trial of adjuvant atezolizumab versus placebo in resected RCC (IMmotion010) were evaluated. This trial did not meet its primary endpoint of disease-free survival (DFS) in the intention-to-treat population. An affinity-based proximity extension proteomics assay was used to compare levels of circulating proteins among baseline (post-nephrectomy) serum samples and samples taken at the time of recurrence. Results- Serum KIM-1 was the most significantly enriched protein at recurrence versus baseline. Patients with serum KIM-1^{high} at baseline had worse DFS [hazard ratio (HR) 1.68, 95% confidence interval (CI) 1.35-2.09], but also had improved DFS when treated with adjuvant atezolizumab versus placebo (HR 0.72, 95% CI 0.52-0.99). An increase in KIM-1 during follow-up was associated with worse DFS compared with patients with no increase in KIM-1. Within the KIM-1^{high} subgroup, longer DFS following atezolizumab treatment was associated with increased baseline expression of T-effector and Th1 signatures, while shorter DFS was associated with increased baseline expression of matrix remodeling genes and protumor cytokines. Conclusion- These analyses suggest that elevated post-nephrectomy plasma KIM-1 level and kinetics are prognostic, supporting the hypothesis that KIM-1 is a biomarker for minimal residual disease in RCC. As KIM-1^{high} patients are also enriched for benefit from adjuvant immunotherapy, biomarker-driven adjuvant therapy should be evaluated as a potential new paradigm in RCC.

25COASDEC15

Title: Randomized, double-blind, phase III LEAP-003 study of first-line lenvatinib plus pembrolizumab versus placebo plus pembrolizumab for unresectable or metastatic melanoma

A.Arance et.al.

Annals of Oncology, Volume 36, Issue 12

https://doi.org/10.1016/j.annonc.2025.08.008

Abstract: - Lenvatinib plus pembrolizumab demonstrated antitumor activity in advanced melanoma after prior anti-programmed cell death protein or ligand 1 [PD-(L)1] therapy in LEAP-004. Here, we report results from LEAP-003 (NCT03820986) which evaluated first-line lenvatinib plus pembrolizumab versus placebo plus pembrolizumab in unresectable advanced melanoma. Participants and methods- Participants with unresectable stage III or IV melanoma, previously untreated with PD-(L)1 inhibitors were randomly assigned 1 : 1 to pembrolizumab 200 mg intravenously every 3 weeks plus either lenvatinib 20 mg or placebo orally once daily. Dual primary endpoints were progression-free survival (PFS) per RECIST v1.1 by blinded independent central review and overall survival (OS). PFS was formally tested at the first interim analysis; OS at the final analysis. An external data monitoring committee regularly reviewed safety and efficacy. Three interim analyses and a final analysis were planned. Results -Overall, 674 participants were assigned to lenvatinib plus pembrolizumab (n = 334) or placebo plus pembrolizumab (n = 340). Median PFS at first interim analysis was 8.4 months for lenvatinib plus pembrolizumab versus 4.0 months for placebo plus pembrolizumab [hazard ratio (HR) 0.72, 95% confidence interval (CI) 0.59-0.88, P = 0.0008]. This benefit was not maintained at final analysis (HR 0.83, 95% CI 0.69-1.00). Median OS at final analysis was 25.8 months for lenvatinib plus pembrolizumab versus 39.5 months for placebo plus pembrolizumab (HR 1.20, 95% CI 0.97-1.48, P = 0.9521). Grade 3-5 treatment-related adverse events occurred in 58.7% of participants receiving lenvatinib plus pembrolizumab versus 29.0% receiving placebo plus pembrolizumab. Conclusions- Lenvatinib plus pembrolizumab did not provide additional benefit versus placebo plus pembrolizumab in participants with unresectable advanced melanoma. Thus, the trial was terminated early, and the third interim analysis became the final analysis. Immunotherapy remains the standard of care for advanced melanoma.

25COASDEC16

Title: Should a borderline negative HER2 result in a core biopsy of invasive carcinoma of the breast have HER2 assessment repeated in the excision specimen?

Andrew H S Lee et.al.

Journal of clinical pathology, vol.-78, issue 11
https://doi.org/10.1136/jcp-2023-209091

Abstract: The 2015 UK guidelines for HER2 assessment in breast cancer recommended repeat assessment if the core biopsy was scored as 2+ on HER2 immunohistochemistry (IHC) with borderline negative in situ hybridisation (ratio of number of HER2 to chromosome 17 centromere copies of 1.8–1.99). This case series aimed to assess the value of such repeat assessment in the surgical specimen, in particular the proportion that were HER2 positive. Methods Details of biopsies with 2+ IHC and borderline negative in situ hybridisation were extracted from a database. The results of repeat HER2 testing in the surgical specimen for this cohort study were then obtained. Results 112 patients with no preoperative treatment had repeat assessment: 4 were 3+ and 16 were 2+ amplified. Of 14 with preoperative chemotherapy, 1 was 3+ and 4 were 2+ amplified. All the 2+ amplified carcinomas had a HER2 to chromosome 17 ratio less than 4, in 50% the ratio was between 2.0 and 2.2, and in 50% the HER2 copy number was less than 4. Conclusions Repeat assessment yielded 4% 3+ results and 14% 2+ amplified carcinomas but with low level amplification. These results

suggest that retesting of borderline negative HER2 cases should be optional and no longer mandatory.

25COASDEC17

Title: PD-L1 protein expression in breast cancer

Sigurd A Saastad et.al.

Journal of clinical pathology, vol.-78, issue 11

https://doi.org/10.1136/jcp-2023-208942

Abstract: The immune checkpoint marker, Programmed cell death-ligand 1 (PD-L1), is expressed by both cancer epithelial cells and tumour-infiltrating immune cells (TICs) thus constituting a potential target for immunotherapy. This is of particular interest in triple negative breast cancer. In this study, we assessed the prognostic value of PD-L1 expression in tumour epithelial cells and TICs in a series of patients with breast cancer with long-term follow-up, and associations between PD-L1 expression and histopathological type and grade, proliferation and molecular subtype. Methods Using immunohistochemistry for PD-L1 in tissue microarrays, we assessed PD-L1 expression in 821 tumours. Expression of PD-L1 was assessed separately in the epithelial and stromal compartments and classified as <1%, ≥1% to <10% or ≥10% positive staining cells. We correlated PD-L1 expression in tumour epithelial cells and TICs with tumour characteristics using Pearson's χ^2 test, and prognosis by cumulative incidence of death from breast cancer and Cox regression analyses. Results We found membranous staining in ≥1% of tumour epithelial cells in 53/821 cases (6.5%). Of these, 21 (2.6%) were ≥10%. Among TICs, staining (≥1%) was seen in 144/821 cases (17.6%). Of these, 62 were ≥10% (7.6%). PD-L1 was associated with high histopathological grade and proliferation, and the medullary and metaplastic patterns. In TICs, PD-L1 ≥1% found in 22/34 (34.4%) human epidermal growth factor receptor 2 type and 29/58 (50%) basal phenotype. An independent association between PD-L1 expression and prognosis was not observed. Conclusions PD-L1 is expressed more frequently in TICs than tumour epithelial cells. Expression in TICs is associated with aggressive tumour characteristics and non-luminal tumours but not with prognosis.

25COASDEC18

Title: Cross-sectional study to evaluate the utility of elastic tissue staining in primary cicatricial alopecia

Tejas Vishwanath et.al.

Journal of clinical pathology, vol.-78, issue 11

https://doi.org/10.1136/jcp-2022-208745

Abstract: Diagnosing end-stage primary cicatricial alopecia (PCA) on routine histology is challenging since the major diagnostic feature (inflammatory infiltrate) may be minimal or absent. This study aimed to assess various staining patterns and diagnostic utility of elastic tissue staining by Verhoeff-Van Gieson (VVG) method and trichoscopy in PCA. Study design Cross-sectional study. Methods Fifty-three patients clinically diagnosed with PCA underwent biopsy and trichoscopy in this cross-sectional study. Clinically active edge, if present, was biopsied. Twenty serial tissue sections were stained using H&E and VVG stain. Clinicopathological diagnoses were lichen planopilaris (LPP), discoid lupus erythematosus (DLE), folliculitis decalvans and unclassified PCA (UPCA) in 30 (56.6%), 11 (20.75%), 1

(1.9%) and 11 (20.75%) patients, respectively. Utility of VVG stain was ascertained considering clincopathological correlation (CPC) as the reference standard. Association of characteristic trichoscopic and VVG staining patterns was ascertained. Results Diagnostic definition was achieved on VVG staining in 19/30 sections of LPP (wedge-shaped pattern) with 63.33% sensitivity; 7/11 cases of DLE (absent upper and mid dermal elastic fibres) with 63.64% sensitivity and 7/11 cases of UPCA (wedge-shaped pattern-3/7; recoil pattern-4/7). Routine histology suggested diagnosis only in 13/53 sections (24.52%). However, diagnosis on VVG staining corresponded with diagnosis on CPC in 33/53 cases (62.3%). Comparison of H&E versus VVG stain both overall and in the LPP and UPCA cohorts proved utility of VVG staining using Fisher's exact test ($p<0.05$). Statistical significance was also noted when trichoscopy was correlated with patterns on VVG staining ($p<0.05$). Conclusion Increased diagnostic yield is noted with trichoscopy and VVG stain in PCA especially when routine histopathology is non-diagnostic.

25COASDEC19

Title: Low interobserver agreement among subspecialised breast pathologists in evaluating HER2-low breast cancer

Gulisa Turashvili et.al.

Journal of clinical pathology, vol.-78, issue 12

https://doi.org/10.1136/jcp-2023-209055

Abstract: Metastatic HER2-low breast cancer (HLBC) can be treated by trastuzumab deruxtecan. Assessment of low levels of HER2 protein expression suffers from poor interobserver reproducibility. The aim of the study was to evaluate the interobserver agreement among subspecialised breast pathologists and develop a practical algorithm for assessing HLBC. Methods Six breast pathologists (4 juniors, 2 seniors) evaluated 106 HER2 immunostained slides with 0/1+expression. Two rounds (R1, R2) of ring study were performed before and after training with a modified Ki-67 algorithm, and concordance was assessed. Results Agreement with 5% increments increased from substantial to almost perfect (R1: 0.796, R2: 0.804), and remained substantial for three categories (<1% vs 1%–10% vs >10%) (R1: 0.768, R2: 0.764). Seniors and juniors had almost perfect agreement with 5% increments (R1: 0.859 and 0.821, R2: 0.872 and 0.813). For the three categories, agreement remained almost perfect among seniors (R1: 0.837, R2: 0.860) and substantial among juniors (R1: 0.792, R2: 0.768). Binary analysis showed suboptimal agreement, decreasing for both juniors and seniors from substantial (R1: 0.650 and 0.620) to moderate (R2: 0.560 and 0.554) using the 1% cut-off, and increasing from moderate to substantial (R1: 0.478, R2: 0.712) among seniors but remaining moderate (R1: 0.576, R2: 0.465) among juniors using the 10% cut-off. The average scoring time per case was higher (72 vs 92 s). Conclusions Subspecialised breast pathologists have suboptimal agreement for immunohistochemical evaluation of HLBC using the modified Ki-67 methodology. An urgent need remains for a new assay/algorithm to reliably evaluate HLBC.

25COASDEC20

Title: Tumour-infiltrating lymphocyte subsets and their individual prognostic impact in oral squamous cell carcinoma

Aanchal Kakkar et.al.

Journal of clinical pathology, vol.-78, issue 12
https://doi.org/10.1136/jcp-2023-208918

Abstract: Current understanding of oral squamous cell carcinoma (OSCC) is incomplete with regard to prognostic factors that lead to the considerable heterogeneity in treatment response and patient outcomes. We aimed to evaluate the impact of individual tumour-infiltrating lymphocyte (TIL) subsets on prognosis as a possible rationale for this, in a retrospective observational study. Methods Immunohistochemistry was performed to quantitatively assess cell densities of CD3+, CD20+, CD4+, CD8+ and FOXP3+TIL subsets in 50 surgically treated OSCC cases. Results were correlated with disease-free survival (DFS) and overall survival (OS). Receiver operating characteristic curve analysis and Youden index were applied to determine prognostically significant cut-off values. Results Mean counts for CD3+, CD4+, CD8+, CD20+ and FOXP3+TILs were 243, 52, 132, 53 and 116 cells per high power field, respectively. High CD8+ and low FOXP3+TIL counts, and high ratio of CD8:FOXP3 were significantly associated with longer DFS and OS, as well as with improved tumour–host interface parameters. Conclusions Host immune response and its interaction with cancer cells have a significant impact on OSCC outcomes, with some TIL subsets being more clinically relevant than others. High cytotoxic T-cell (CD8) and low Treg (FOXP3) counts, and high cytotoxic T-cell to Treg (CD8:FOXP3) ratio are significantly associated with favourable prognosis. These results may serve as a leading point in identifying novel therapeutic agents that can redesign the tumour immune microenvironment by reducing infiltrating FOXP3-lymphocytes, and modifying their signalling pathways.

25COASDEC21

Title: SSTR2 positively associates with EGFR and predicts poor prognosis in nasopharyngeal carcinoma

Yue Xu et.al.

Journal of clinical pathology, vol.-78, issue 12
https://doi.org/10.1136/jcp-2023-208987

Abstract: Epidermal growth factor receptor (EGFR) belongs to the receptor tyrosine kinases family and overexpression of EGFR has been linked to poor prognosis and cancer progression. Somatostatin receptor 2 (SSTR2) is a G-protein-coupled receptor (GPCR) with diverse biological functions in humans, and it is upregulated through the NF-KB signalling pathway in nasopharyngeal carcinomas (NPC). However, no studies have examined the EGFR and SSTR2 in NPC. This study aimed to investigate whether SSTR2 is associated with EGFR and clinicopathological features in NPC. Methods Bioinformatics analysis was performed to assess the correlation between EGFR and SSTR2 based on the GEO database. The expression of SSTR2 and EGFR was evaluated by immunohistochemistry (IHC) in 491 cases of NPC and 50 cases of non-cancerous nasopharyngeal epithelium. Results The bioinformatics analysis and IHC showed a positive correlation between SSTR2 and EGFR in NPC. High expression of SSTR2 and EGFR was significantly increased in NPC patients compared with non-cancerous nasopharyngeal epithelium. High expression of SSTR2 and/or EGFR was associated with a worse outcome and a higher risk of progression. The study found that patients receiving chemoradiotherapy (CR) with high expression of SSTR2, high expression of EGFR, and high coexpression of SSTR2 and EGFR had a poorer prognosis in both progression-free survival (PFS) and overall survival (OS). Interestingly, NPC patients

with high expression of SSTR2, high expression of EGFR, high coexpression of EGFR and SSTR2, and EGFR/SSTR2 anyone high expression had a better prognosis with CR combined with targeted therapy. Cox multivariate analysis identified SSTR2 and EGFR as independent poor predictors of PFS. Conclusion Our study is the first to shed light on the intricate relationship between SSTR2 and EGFR in NPC and provides new insights into the potential benefits of EGFR targeted therapy for patients with high SSTR2 expression. Additionally, SSTR2 has potential as a new biomarker for poor prognosis in NPC patients**.**

25COASDEC22

Title: Idiopathic granulomatous mastitis: a 5-year retrospective review of cases in a tertiary centre in Dublin, Ireland

Elaine Houlihan et.al.

Journal of clinical pathology, vol.-78, issue 12

https://doi.org/10.1136/jcp-2023-209028

Abstract: Idiopathic granulomatous mastitis (IGM) is a rare, benign, inflammatory breast disorder of unknown aetiology usually affecting women of reproductive age. It classically presents as a unilateral painful breast mass. It is frequently mistaken for carcinoma or other inflammatory breast diseases. Diagnostic investigations include clinical examination, appropriate imaging and tissue sampling. A link between IGM and infection with the *Corynebacterium* species in particular *Corynebacterium kroppenstedtii* has been described. Methods- A retrospective single-centre cohort study was conducted over a 5-year period (2017–2022); all cases of IGM were identified. Results- Forty-one patients were diagnosed with IGM. Breast lump was the most common presenting complaint (n=29). The average age was 45 years. Eighteen patients had samples sent for culture and sensitivity, 11 of which had positive microbiology results indicative of *Corynebacterium* spp infection. An 82% resolution rate (27 of 33) was recorded in those who received either a short-antibiotic course or none at all. Eight patients reported persistent disease at 3 months, five of which had evidence of *Corynebacterium* spp. Discussion- This 5-year review highlights the impact of IGM in a tertiary centre in Dublin, Ireland. Although no treatment guidelines exist, options include antibiotics, immunomodulators and surgery. Due to risk of fistulae and unfavourable cosmetic outcomes, surgery should be reserved for refractory IGM. We suspect that there may be a subset of patients where prolonged antibiotic therapy should be considered. Defining this subgroup requires further study, but likely includes those with cystic neutrophilic granulomatous mastitis, relapsing disease and in whom *Corynebacterium* spp is recovered.

25COASDEC23

Title: Unravelling interobserver variability in gastrointestinal glandular neoplasia: a contemporary study of US and Korean pathologists

Richard R Pacheco et.al.

Journal of clinical pathology, vol.-78, issue 12

https://doi.org/10.1136/jcp-2023-209048

Abstract: Interobserver variability in the assessment of gastric neoplasia biopsies between most Western and Eastern (predominantly represented by Japanese in the literature) pathologists has been documented. It is unknown if such variability exists between the US

and Korean pathologists in the current era. Methods Ten gastrointestinal (GI) pathologists from the USA (n=5) and South Korea (n=5) evaluated 100 scanned images of gastric (n=50) and colorectal (n=50) neoplasia biopsies and answered multiple questionnaires. Consensus was defined as the answer chosen by the majority. Cohen's (κc) and Fleiss' kappa (κf) values were calculated between the consensus of the two groups and among the raters, respectively. Results Both groups reached a consensus in the majority of cases (74%–100%) with slight to perfect intergroup (κc=0.049–1.000) and no to substantial intragroup (κf=−0.083 to 0.660) agreements. For gastric neoplasia, Korean pathologists relied heavily on cytoarchitectural atypia, whereas the US pathologists focused on stromal invasion when diagnosing adenocarcinoma. For colorectal neoplasia, the Korean pathologists identified concurrent intramucosal carcinoma when diagnosing invasive adenocarcinoma, while the presence of desmoplasia was a prerequisite for the diagnosis of invasive adenocarcinoma for the US pathologists. Conclusions For GI neoplasia biopsy interpretation, the diagnostic approach of Korean pathologists is similar to that of Eastern/Japanese pathologists. Consensus outperformed kappa statistics in capturing the magnitude of inter-rater and intergroup reliability, highlighting the potential benefit of consensus meetings to decrease the gap between Western and Eastern diagnostic approaches.

25COASDEC24

Title: Optimal carcinoembryonic antigen (CEA) cutoff values in the diagnosis of neoplastic mucinous pancreatic cysts differ among assays

David Kim et.al.

Journal of clinical pathology, vol.-78, issue 12

https://doi.org/10.1136/jcp-2023-209136

Abstract: Aim Pancreatic cyst fluid carcinoembryonic antigen (CEA) is a pivotal test in the diagnosis and management of neoplastic mucinous cysts (NMC) of the pancreas. Cyst fluid CEA levels of 192 ng/mL have been widely used to identify NMC. However, CEA values are unique to and significantly differ between individual assays with various optimal cutoffs reported in the literature for NMC. Here, we investigate the optimal CEA cut-off value of pancreatic cysts from two different assays to identify differences in thresholds. Methods Pancreatic cyst fluid CEA levels, CEA assay platform (Beckman Dxl (BD) or Siemens Centaur XP (SC)), and clinical/pathological information were retrospectively collected. Cases were categorised into either NMC or non-NMC. Optimal CEA cut-off values were calculated via a receiver operator characteristic curve. Cut-off values were then identified separately by assay platform. Results In total, 149 pancreatic cystic lesions with concurrent CEA values (SC: n=47; BD: n=102) were included. Histological correlation was available for 26 (17%) samples. The optimal CEA cut-off value for all samples at the study institution was 45.9 ng/mL (area under the curve (AUC)=86, Sn=85.7%, Sp=73.8%). When analysed separately by CEA assay, the cut-off values were 45.9 ng/mL (AUC=84.27, Sn=89.7%, Sp=71.4%) for BD and 24.4 ng/mL (AUC=77, Sn=81.8%, Sp=75%) for SC (p=0.48). Conclusions This study showed an optimal pancreas cyst CEA cut-off threshold of 45.9 ng/mL, which is lower than commonly cited literature with different cutoffs on the two separate platforms (BD: 45.9 ng/mL, SC: 24.4 ng/mL).

25COASDEC25

Title: Performance evaluation of a CRISPR Cas9-based selective exponential amplification assay for the detection of KRAS mutations in plasma of patients with advanced pancreatic cancer

Yue Shen et.al.

Journal of clinical pathology, vol.-78, issue 12
https://doi.org/10.1136/jcp-2023-208974

Abstract: Pancreatic ductal adenocarcinoma (PDAC) is highly malignant, with shockingly mortality rates. KRAS oncoprotein is the main molecular target for PDAC. Liquid biopsies, such as the detection of circulating tumour DNA (ctDNA), offer a promising approach for less invasive diagnosis. In this study, we aim to evaluate the precision and utility of programmable enzyme-based selective exponential amplification (PASEA) assay for rare mutant alleles identification. Methods PASEA uses CRISPR-Cas9 to continuously shear wild-type alleles during recombinase polymerase amplification, while mutant alleles are exponentially amplified, ultimately reaching a level detectable by Sanger sequencing. We applied PASEA to detect KRAS mutations in plasma ctDNA. A total of 153 patients with stage IV PDAC were enrolled. We investigated the relationship between ctDNA detection rates with various clinical factors. Results Our results showed 91.43% vs 44.83% detection rate in patients of prechemotherapy and undergoing chemotherapy. KRAS ctDNA was more prevalent in patients with liver metastases and patients did not undergo surgical resection. Patients with liver metastases prior to chemotherapy showed a sensitivity of 95.24% (20/21) with PASEA. Through longitudinal monitoring, we found ctDNA may be a more accurate biomarker for monitoring chemotherapy efficacy in PDAC than CA19-9. Conclusions Our study sheds light on the potential of ctDNA as a valuable complementary biomarker for precision targeted therapy, emphasising the importance of considering chemotherapy status, metastatic sites and surgical history when evaluating its diagnostic potential in PDAC. PASEA technology provides a reliable, cost-effective and minimally invasive method for detecting ctDNA of PDAC.

25COASDEC26

Title: RNA extended interventional nucleic acid longitudinal study: Clinical performance of Aptima messenger RNA HPV testing in cervical cancer screening with a 9-year follow-up

Rosario Granados MD, PhD et.al.

Cancer Cytopathology, vol.-133, issue- 12
https://doi.org/10.1002/cncy.22895

Abstract: - There is a need for additional longitudinal studies with the Aptima messenger RNA human papillomavirus test (AHPV) to support the safety of extended screening intervals. RNA-based extended interventional nucleic acid (REINA) provides relevant information on the clinical performance of AHPV. Methods- This is a longitudinal prospective analysis of 1538 participants after AHPV and liquid-based cytology (LBC) co-test complemented with REINA interventional protocol with a second co-test 4 years after negative screening on 2000 women. Diagnostic accuracy and cumulative risks for CIN2+ up to 9 years were calculated for all test combinations. Results-Sensitivity and specificity for CIN2+ were 96.9% and 88.0% for AHPV and 72.3% and 92.0% for LBC. Negative

predictive value (NPV) and positive predictive value (PPV) of AHPV were 99.9% and 23.6%. The 5- and 9-year risks of AHPV-negative women were 0.4% and 1.0% (CIN2+) and 0.3% and 0.7% (CIN3+), a 73% and 64% lower risk than with negative LBC ($p \leq .002$). REINA participants with an AHPV-positive result at second co-test after a negative AHPV in first round had a significantly lower 5-year risk of CIN2+ (11.1%) than AHPV-positive women with unknown HPV history (29.5%). Conclusions- Currently, this constitutes the longest European longitudinal study with AHPV testing in screening population. It reveals 99.9% NPV and a significant protective effect of a previous negative test 5 years after a new HPV infection. These findings support the safety of Aptima for screening intervals beyond 5 years. The risk of disease is lower 9 years after a negative AHPV test than 3 years after a negative LBC. High specificity and PPV of Aptima may benefit controlling overtreatment and colposcopy referrals.

25COASDEC27

Title: Diagnostic performance of fine-needle aspiration in soft tissue tumors: Application of the World Health Organization System for Reporting Soft Tissue Cytopathology and risk of malignancy assessment

Pawel Gajdzis MD, PhD et.al.

Cancer Cytopathology, vol.-133, issue- 12

https://doi.org/10.1002/cncy.22897

Abstract: - Recently, a new World Health Organization Reporting System for Soft Tissue Cytopathology (WHO System) was introduced. To analyze the value of this system, routine fine-needle aspiration soft tissue tumor (STT) cases were reviewed. Methods- Cytology samples of STTs collected between 1954 and 2022 at the Institut Curie were used (2214 cases, including 1376 primary tumors). All specimens were classified according to the predominant cytomorphological pattern and the WHO System. The diagnostic accuracy and risk of malignancy (ROM) in each category were calculated. Results- Final diagnoses revealed 1236 malignancies and 978 benign or low-risk tumors. The original cytological evaluation led to 21 false-negative results (0.85%) and 29 false-positive results (1.17%). Sensitivity, specificity, positive predictive value, and negative predictive value were 98.3%, 92.1%, 97.5%, and 94.2%, respectively. Overall diagnostic accuracy was 94.2%. The ROM calculated according to the WHO System was 29.87%, 2.49%, 39.62%, 51.43%, 68.42%, and 97.69% in the nondiagnostic, benign, atypical, soft tissue neoplasm of uncertain malignant potential, suspicious for malignancy, and malignant categories, respectively; however, it varied broadly depending on the morphological pattern (62.78% in spindle cell tumors, 84.58% in myxoid tumors, 3.00% in lipomatous tumors, 78.15% in epithelioid tumors, 94.26% in pleomorphic tumors, and 100% in round cell tumors). Conclusions- Cytology of STTs is a powerful diagnostic method. Some cytological patterns overlap in different morphological groups, and the possibility of false-negative and false-positive diagnoses may persist. This analysis evidenced utility of the WHO System, especially when combined with morphological pattern assessment. Subclassification in particular diagnostic categories allowed for calculation of the ROM, which is crucial for optimal patient management.

25COASDEC28

Title: Utilization of an artificial intelligence–enhanced, web-based application to review

bile duct brushing cytologic specimens: A pilot study

Neil B. Marya MD et.al.

Cancer Cytopathology, vol.-133, issue- 12

https://doi.org/10.1002/cncy.22898

Abstract: - The authors previously developed an artificial intelligence (AI) to assist cytologists in the evaluation of digital whole-slide images (WSIs) generated from bile duct brushing specimens. The aim of this trial was to assess the efficiency and accuracy of cytologists using a novel application with this AI tool. Methods- Consecutive bile duct brushing WSIs from indeterminate strictures were obtained. A multidisciplinary panel reviewed all relevant information and provided a central interpretation for each WSI as being "positive," "negative," or "indeterminate." The WSIs were then uploaded to the AI application. The AI scored each WSI as positive or negative for malignancy (i.e., computer-aided diagnosis [CADx]). For each WSI, the AI prioritized cytologic tiles by the likelihood that malignant material was present in the tile. Via the AI, blinded cytologists reviewed all WSIs and provided interpretations (i.e., computer-aided detection [CADe]). The diagnostic accuracies of the WSI evaluation via CADx, CADe, and the original clinical cytologic interpretation (official cytologic interpretation [OCI]) were compared. Results- Of the 84 WSIs, 15 were positive, 42 were negative, and 27 were indeterminate after central review. The WSIs generated on average 141,950 tiles each. Cytologists using the AI evaluated 10.5 tiles per WSI before making an interpretation. Additionally, cytologists required an average of 84.1 s of total WSI evaluation. WSI interpretation accuracies for CADx (0.754; 95% CI, 0.622–0.859), CADe (0.807; 95% CI, 0.750–0.856), and OCI (0.807; 95% CI, 0.671–0.900) were similar. Conclusions- This trial demonstrates that an AI application allows cytologists to perform a triaged review of WSIs while maintaining accuracy.

25COASDEC29

Title: Comparative genomic and immunopathologic analysis of lung adenocarcinomas with and without cytology-proven malignant pleural effusions

Cristiana M. Pineda MD, PhD et.al.

Cancer Cytopathology, vol.-133, issue- 12

https://doi.org/10.1002/cncy.22900

Abstract: - Lung cancer complicated by malignant pleural effusions (MPEs) is associated with significantly increased morbidity and mortality, yet the mechanisms of MPE development remain poorly understood. This study sought to elucidate whether there were specific genomic alterations and/or immunologic biomarkers associated with the presence of MPEs. Methods- Analysis of comprehensive genomic and immunologic profiling for 275 locally advanced (stage III) or advanced (stage IV) lung adenocarcinomas was subcategorized into cytology-confirmed MPE-positive (MPE+; $n = 139$ stage IV) and MPE-negative (MPE−; $n = 30$ stage III + $n = 106$ stage IV) groups. Results- Smoking frequency ($p = .0001$) and tumor mutational burden ($p < .001$) were demonstrated to be lower in the MPE+ group compared to the MPE− group. Median overall survival in the MPE+ group was shorter than in the MPE− group across all data (2.0 vs. 5.5 years; $p < .0001$) and for smokers (1.2 vs. 6.4 years; $p < .0001$). There were a number of differences at the genomic level across all cases and when stratifying by smoking status, including a higher frequency of *EGFR* mutations and a lower frequency of *STK11* mutations in the MPE+ cohort. Finally,

investigation of the comutational profiles of tumors by MPE status revealed differences in *TP53*- and *STK11*-mutant tumors between the two groups. Conclusions- Overall, these findings imply that there are both clinical and genetic factors associated with advanced lung adenocarcinoma MPEs. Future studies of these alterations may prove important both for understanding the pathophysiology of MPE development in advanced cancer and for the earlier detection of at-risk patients.

25COASDEC30

Title: Trichorhinophalangeal syndrome 1 expression in breast and nonbreast metastases from Müllerian, lung, gastrointestinal tract, and pancreatic primary tumors by immunohistochemistry with cytology cell block specimens

Deepak Donthi MD, MPH et.al.

Cancer Cytopathology, vol.-133, issue- 12

https://doi.org/10.1002/cncy.22901

Abstract: -Trichorhinophalangeal syndrome 1 (TRPS1) expression in primary breast and other solid tumors has been investigated but its role as a marker in metastatic tumors is unclear. The objective of this study was to evaluate the sensitivity and specificity of TRPS1 as a breast cancer immunomarker in metastatic tumors that originated from breast, Müllerian, lung, gastrointestinal (GI), and pancreatic primary tumors with cell blocks from fine-needle aspiration (FNA) and effusion specimens. Methods- Cell blocks were immunostained with anti-TRPS1 monoclonal antibody (clone EPR16171). Histochemical scores (H scores) (proportion × intensity; range, 0–300) were assigned; H scores of ≥10 were considered positive. Overall, 160 specimens were examined, including 127 FNAs (35 breast, 25 Müllerian, 36 lung, and 31 GI and pancreatic carcinomas) and 33 effusion specimens (18 breast, 12 Müllerian, one lung, and two GI carcinomas). Results- TRPS1 was positive in 51 of 53 (96%) metastatic breast carcinomas and in 28 of 107 (26.2%) nonbreast metastatic tumors. Metastatic breast carcinoma showed the highest mean H score of 247.35, compared to 45.36 in Müllerian, 8.4 in lung, and 5.88 in GI tumors. The sensitivity and specificity of TRPS1 for identifying a breast origin in metastatic tumors was 96.22% and 72.89%, respectively. Conclusions- Despite high overall sensitivity, TRPS1 showed lower specificity as a breast immunomarker because of its expression in nonbreast tumors. The mean H score in nonbreast tumors was significantly lower than in metastatic breast tumors. It is important to recognize the broad range of expression of TRPS1 in metastatic breast and nonbreast tumors to avoid an incorrect determination of a metastatic tumor's organ of origin.

25COASDEC31

Title: Time to Enhancement of Foci Relative to Parenchymal Enhancement on Ultrafast Breast MRI: A Single-Center Retrospective Study

Helaina C. Regen-Tuero, MD et.al.

American Journal of Roentgenology, Volume 224, Issue 6

https://doi.org/10.2214/AJR.24.32309

Abstract: . Breast mri is a sensitive tool for detecting small cancers. However, differentiating benign and malignant lesions remains challenging, particularly for foci. Studies evaluating other lesion types have identified ultrafast mri (ufmri) parameters associated with malignancy**.** Objective. The purpose of this study was to determine whether kinetic features

of ufmri can differentiate malignant from nonmalignant foci. Methods. This single-center retrospective study selected consecutive ufmri examinations conducted from july 2019 to april 2023 with subsequently performed mri-guided biopsy. Patient characteristics and lesion features were collected from the emr, imaging reports, and imaging review. Focus and parenchymal enhancement (bpe), time to enhancement (tte), and the difference between focus tte and bpe tte were calculated. Associations with malignancy were assessed with univariable and multivariable logistic regression. Results. A total of 124 patients (mean age, 53 years old; range, 29–78 years old) underwent biopsy of 124 foci. Sixty-four patients (51.6%) were postmenopausal, 71 (57.3%) had a personal history of breast cancer, and 81 (65.3%) had a family history of breast cancer. Of the 94 patients who underwent genetic testing, 33 (35.3%) had genetic mutations. Most examinations were performed to evaluate the extent of disease (47.6% [59/124]), followed by screening (41.9% [52/124]). Patients predominantly had heterogeneous fibroglandular tissue (58.1% [72/124]) and mild bpe (57.3% [71/124]). Of 124 lesions, 21 (16.9%) were malignant; of these, 16 were invasive and five were ductal carcinoma in situ. The odds of malignancy increased 5% with each 1-second increase in the difference between lesion tte and bpe tte (95% ci, 2–9%; p = .006). Older age and lower bpe were associated with increased likelihood of malignancy (p = .005 and p = .02, respectively). The odds of malignancy for patients with minimal or mild bpe were 11.69 times the odds for those with moderate or marked bpe (95% ci, 1.51–90.67). No other demographic or lesion characteristics were predictive of malignancy. Conclusion. Earlier visualization of a focus relative to bpe on ufmri was associated with increased likelihood of malignancy; morphologic features showed no association with malignancy. Clinical impact. The difference between focus tte and bpe tte may be a useful parameter for assessing malignancy, which could help reduce unnecessary biopsies.

25COASDEC32

Title: Long-Term Prognostic Implications of Thoracic Aortic Calcification on CT Using Artificial Intelligence–Based Quantification in a Screening Population: A Two-Center Study

Jong Eun Lee, MD, PhD et.al.

American Journal of Roentgenology, Volume 224, Issue 6
https://doi.org/10.2214/AJR.25.32697

Abstract: . The importance of including the thoracic aortic calcification (tac), in addition to coronary artery calcification (cac), in prognostic assessments has been difficult to determine, partly due to greater challenge in performing standardized tac assessments. Objective. The purpose of this study was to evaluate long-term prognostic implications of tac assessed using artificial intelligence (ai)-based quantification on routine chest ct in a screening population. Methods. This retrospective study included 7404 asymptomatic individuals (median age, 53.9 years; 5875 men, 1529 women) who underwent nongated noncontrast chest ct as part of a national general health screening program at one of two centers from january 2007 to december 2014. A commercial ai program quantified tac and cac using agatston scores, which were stratified into categories. Radiologists manually quantified tac and cac in 2567 examinations. The role of ai-based tac categories in predicting major adverse cardiovascular events (mace) and all-cause mortality (acm), independent of ai-based cac categories as well as clinical and laboratory variables, was assessed by multivariable cox proportional hazards

models using data from both centers and concordance statistics from prognostic models developed and tested using center 1 and center 2 data, respectively. Results. Ai-based and manual quantification showed excellent agreement for tac and cac (concordance correlation coefficient: 0.967 and 0.895, respectively). The median observation periods were 7.5 years for mace (383 events in 5342 individuals) and 11.0 years for acm (292 events in 7404 individuals). When adjusted for ai-based cac categories along with clinical and laboratory variables, the risk for mace was not independently associated with any ai-based tac category; risk of acm was independently associated with ai-based tac score of 1001–3000 (hr = 2.14, p = .02) but not with other ai-based tac categories. When prognostic models were tested, the addition of ai-based tac categories did not improve model fit relative to models containing clinical variables, laboratory variables, and ai-based cac categories for mace (concordance index [c-index] = 0.760–0.760, p = .81) or acm (c-index = 0.823–0.830, p = .32). Conclusion. The addition of tac to models containing cac provided limited improvement in risk prediction in an asymptomatic screening population undergoing ct. Clinical impact. Ai-based quantification provides a standardized approach for better understanding the potential role of tac as a predictive imaging biomarker.

25COASDEC33

Title: Attenuation Coefficient for Hepatic Steatosis Using a Single Ultrasound System: Associations of Measurement Parameters With Interoperator Agreement and Diagnostic Performance

Giovanna Ferraioli, MD et.al.

American Journal of Roentgenology, Volume 224, Issue 6

https://doi.org/10.2214/AJR.25.32746

Abstract: . Clinical adoption of ultrasound attenuation coefficient (ac) measurements has been hindered by lack of a uniform measurement protocol and a range of factors that may cause variability. Objective. The purpose of this study was to evaluate associations of roi depth, roi size, and confidence map threshold with interobserver agreement and diagnostic performance of ultrasound ac measurements in detecting and grading hepatic steatosis using mri proton density fat fraction (pdff) as the reference standard. Methods. This prospective study enrolled adults with known steatosis or at risk for steatosis from october 2023 to august 2024. One of two operators obtained videos of ac acquisitions using a single ultrasound unit. Both operators independently reviewed all videos and placed circular rois to obtain ac measurements for all 24 possible combinations of four roi depths (2.0, 2.5, 3.0, and 4.0 cm from liver capsule to roi outer edge), three roi sizes (3.0, 3.5, and 4.0 cm), and two confidence map thresholds (20% and 40%). Participants underwent mri pdff measurement as a reference. Results. The analysis included 101 participants (mean age, 54.5 ± 12.1 [sd] years; 62 women, 39 men). Interoperator agreement was excellent for all combinations (intraclass correlation coefficient, 0.92–0.98). Ac measurements showed strongest correlations (spearman rank correlation coefficient, 0.81 and 0.80 for operators 1 and 2, respectively) with mri pdff at an roi depth of 4.0 cm. The optimal combination considering correlations with mri pdff and auc across steatosis grades included a depth of 4.0 cm, size of 4.0 cm, and threshold of 40%. This combination had an auc for detecting steatosis with grade of greater than 0, greater than 1, and greater than 2 for operator 1 of 0.93, 0.88, and 0.81, respectively, and for operator 2 of 0.92, 0.86, and 0.81, respectively. However, accuracy for detecting steatosis

(grade > 0) was highest for the combination of depth of 3.0 cm, size of 4.0 cm, and threshold of 40% (operator 1, 90.1%; operator 2, 82.2%). Conclusion. Ac measurements showed excellent interoperator agreement across parameter combinations. Correlations with mri pdff were strongest at a depth of 4.0 cm. Combinations yielding highest diagnostic performance were identified. Clinical impact. These results will help determine a standardized optimal protocol for ultrasound ac measurements, facilitating clinical adoption for liver fat quantification.

25COASDEC34

Title: Consensus Reporting Standards for CT, MRI, and MRCP of Pediatric Chronic Pancreatitis

Andrew T. Trout, MD et.al.

American Journal of Roentgenology, Volume 224, Issue 6

https://doi.org/10.2214/AJR.25.32706

Abstract: Chronic pancreatitis is a fibroinflammatory syndrome of the pancreas with a prevalence in children of approximately six per 100,000. Diagnosis of chronic pancreatitis in a child depends on the presence of imaging findings of chronic pancreatitis in the context of specific clinical features. Currently, a standardized reporting system for imaging findings of chronic pancreatitis in children is lacking, and imaging-based thresholds for abnormality have not been defined. Standardized reporting elements were defined for adults in 2019. Not all of the adult criteria are directly applicable to children due to changes in the pancreas with normal growth and development. To address the lack of accepted pediatric chronic pancreatitis reporting standards and encourage standardized communication of imaging findings, we convened a group of experienced pediatric radiologists and pediatric gastroenterologists with expertise in pancreatology and interventional endoscopy to define consensus reporting elements and interpretive criteria for findings of pediatric chronic pancreatitis. On the basis of the existing literature and panel opinion and leveraging a modified Delphi approach, we propose reporting standards for CT, MRI, and MRCP of pediatric chronic pancreatitis.

25COASDEC35

Title: Supporting the Deceased, Their Families, and Their Communities – Part 1: Why Establish an Office of Decedent Affairs

Meagan Chambers, MD, MS, MSc et.al.

Pathology of Archieves and Laboratory Medicine, vol.-149, issue- 12

https://doi.org/10.5858/arpa.2025-0090-OA

Abstract: Decedent affairs offices and programs can serve as an avenue to assist medical centers in facilitating efficient and comprehensive decedent management, despite a paucity of literature on their roles, establishment, and efficacy. Objective- To characterize the motivations and rationales for establishing decedent affairs offices. Design- A survey was administered to 11 established decedent affairs offices/programs, identified through the college of american pathologists autopsy committee and a medical autopsy listserv. The questions comprehensively cover establishment, operations, and outcomes data available by institution. Results- Survey respondents reported the rationale for starting their programs and the benefits such offices can have. Conclusions- Decedent affairs offices and programs

provide a useful option to medical centers to navigate the increasingly complex task of comprehensive decedent management. The present survey helps to delineate the similarities and differences between these programs at 11 institutions, to aid nascent programs in their establishment and growth over time. Despite the need of almost every hospital to have postmortem processes and procedures in effect to handle the care and disposition of decedents, there is limited information in the literature on the establishment and functionality of formal, centralized efforts at decedent care (table). These decedent affairs programs and offices exist in a subset of hospitals, but the rationale for their existence, as well as their benefits, is not widely known.

25COASDEC36

Title: Supporting the Deceased, Their Families, and Their Communities – Part 2: Practical Guidance for Building an Office of Decedent Affairs

Meagan Chambers, MD, MS, MSc et.al.

Pathology of Archieves and Laboratory Medicine, vol.-149, issue- 12
https://doi.org/10.5858/arpa.2025-0094-OA

Abstract: Context. After-death care can be complicated and time-consuming for clinical staff, and frustrating for bereaved families. Delays and errors can have damaging legal and reputational consequences for hospitals. Offices of Decedent Affairs (ODAs) have been proposed as a solution, and their potential benefits have been described in several single institution reports. The literature lacks a contemporary and comprehensive review of existing ODAs and their approaches. Objective. To describe the process of establishing a new ODA and to provide a snapshot of the spectrum of structure, function, and impact of existing ODAs in the United States. Design. A survey was administered to 11 established ODAs spread across the continental United States. Programs were identified through the College of American Pathologists Autopsy Committee and a Medical Autopsy Listserv. Results. Eleven ODAs returned the survey, representing more than 190 cumulative years of experience in decedent care in the hospital setting (median, 10 years). There was a wide range in staffing (both staff size and) as well as scope of services offered. The median ratio of hospital deaths to full-time equivalent (FTE) staffing was 360 deaths per FTE. Respondents reported that ODAs unburden clinical providers and facilitate decedent management. Some respondents reported a quicker turnover of hospital beds and shorter intervals between pronouncement of death and autopsy. ODAs increased autopsy rates when the autopsy services were part of the ODA. Conclusion- This survey provides practical information for hospitals considering establishing a new ODA and useful benchmarks for existing ODA programs. The death of a loved one is a major milestone associated with powerful emotions. It is the last point of in-person contact between the family and hospital staff. The events surrounding death can take on an enormous importance for the family. Miscommunications, delays, and frustrations in decedent care can undo an otherwise positive hospital experience. The tasks surrounding death invariably involve multiple hospital services including clinical staff, pastoral care, social work, security, patient transport, patient experience, and pathologists. Most of these services deal with death episodically and infrequently. Decedent affairs pull them away from their primary mission of patient care and place additional demands on their time.

25COASDEC37

Title: Nonclassic Histologic Variants of Kaposi Sarcoma With Nonspecific Endoscopic Inflammatory Patterns: A Near-Miss Diagnosis Lookout in Gastrointestinal Tract Biopsies

Michael Mitchell et.al.

Pathology of Archieves and Laboratory Medicine, vol.-149, issue- 12
https://doi.org/10.5858/arpa.2025-0085-OA

Abstract: The gastrointestinal (gi) tract is the most frequent extracutaneous site for kaposi sarcoma (ks). However, gi-ks often displays nonspecific endoscopic findings with nonclassic histology in biopsies with a serious potential for a missed diagnosis. There is a paucity of studies discussing the histologic variants of gi-ks, coupled with reportedly high false-negative rates of gi-ks on endoscopic biopsies. Objective-To present our single-institution large case analysis to further elucidate nonclassic histologic variants of gi-ks, with pathologic-endoscopic correlation. Design- A retrospective pathology database search was performed to retrieve 44 gi-ks biopsies from 28 immunocompromised patients. Results-We found that 64% (28 of 44) showed exclusive nonclassic histology mimicking varied inflammatory patterns, namely mucosal hemorrhage–like (n = 10; 23%), mucosal prolapse–like (n = 6; 14%), mucosal inflammation–like (n = 5; 11%), granulation tissue–like (n = 5; 11%), and dilated vascular- or lymphatic-like (n = 2; 5%) patterns. Classic morphology was seen in 16 biopsies (36%), with 11 (25%) also showing concomitant nonclassic histologic patterns. Endoscopically, most cases presented as nodules (n = 16; 36%) or inflammatory patterns (n = 11; 25%). Interestingly, 91% (10 of 11) presenting endoscopically as a nonspecific inflammatory pattern showed nonclassic histology. Gi-ks preceded cutaneous diagnosis in 54% (15 of 28) of patients. Coexisting infectious or drug-associated pathology was seen in 18% (8 of 44) of biopsies, further confounding histologic assessment. Conclusions.- Gi-ks often presents with nonspecific endoscopic and histologic findings, frequently mimicking benign reactive and inflammatory conditions. Awareness of the morphologic diversity of ks on limited biopsy material in the setting of immunosuppression is crucial for pathologists to actively consider this diagnosis even in the absence of known cutaneous ks or an endoscopic masslike lesion.

25COASDEC38

Title: Reproducibility of Equivocal *HER2* In Situ Hybridization Groups 3 and 4, and Comparison With *HER2* mRNA Expression: The Thin Line Between Amplified and Nonamplified Breast Cancers

Ximena Baez-Navarro et.al.

Pathology of Archieves and Laboratory Medicine, vol.-149, issue- 12
https://doi.org/10.5858/arpa.2024-0499-OA

Abstract: Breast carcinomas (bcs) with equivocal HER2 (human epidermal growth factor receptor 2) immunohistochemistry are subjected to in situ hybridization (ISH) to assess *HER2* copy numbers. Infrequently, dual-probe ISH also provides equivocal results, designated as ISH groups 2, 3, or 4. Objective- To evaluate the reproducibility of *HER2* ISH groups 3 and 4, and to compare the integrated immunohistochemistry/ISH HER2 result with *HER2* mrna expression. Design- Dual-probe ISH slides of 50 bcs were re-evaluated by 2 independent observers. Mrna was extracted from microdissected tumor cells. Quantitative

real-time polymerase chain reaction (RT-qpcr) was performed for quantitative evaluation of *HER2* mrna using the mammatyper assay. Results- Reproducibility of ISH groups 1 (amplified; n = 5) and 5 (nonamplified; n = 4) was good with only 1 case differently classified. Many group 4 (n = 28) and group 3 (n = 13) tumors were reclassified after recounting; of 41 patients, 9 and 18 might have been treated differently as based on assessment by observers 1 and 2, respectively. Concordance for mammatyper HER2 status was 56% (n = 18/32) for the original report; 59% (n = 19/32) for observer 1; 72% (n = 23/32) for observer 2; and 63% (n = 20/32) for the majority opinion. Conclusions-The reproducibility of equivocal ISH groups is limited. Although HER2 ISH has long been considered the gold standard to establish the HER2 status in BC, the equivocal "gray zone" between amplified and nonamplified bcs is prone to interobserver variability. Potential solutions could comprise the involvement of at least 3 different observers for assessment of equivocal ISH cases, and/or evaluation of *HER2* mrna as a more objective alternative method.

25COASDEC39

Title: Evaluating Interferon γ to Interleukin 10 Ratio as a Biomarker for Stability and Severity in Vitiligo: A Clinical and Histopathologic Correlation

Geet Bhuyan et.al.

Pathology of Archieves and Laboratory Medicine, vol.-149, issue- 12

https://doi.org/10.5858/arpa.2025-0099-OA

Abstract: Vitiligo is a chronic autoimmune depigmenting disorder characterized by the selective destruction of epidermal melanocytes. Proinflammatory and anti-inflammatory cytokines, such as interferon γ (IFN-γ) and interleukin 10 (IL-10), play a pivotal role in its pathogenesis. Quantifying these cytokines and assessing their ratio may aid in disease prognosis and therapeutic monitoring. Objective- To evaluate the association between the IFN-γ:IL-10 ratio and the clinical as well as histopathologic characteristics of stable and unstable vitiligo. Design- A hospital-based prospective case-control study was conducted during 1 year (2023–2024) on 70 patients with active vitiligo and 30 healthy controls. Serum levels of IFN-γ and IL-10 were quantified, and their correlations with clinical severity, disease stability, and histopathologic grading were analyzed. Results- Unstable vitiligo cases demonstrated significantly higher histopathologic scores (≥3 in 39.62% versus 0% in stable cases, $P = .002$). IFN-γ levels were markedly elevated in unstable vitiligo (11.9 ± 2.56 versus 10.58 ± 1.04 pg/mL, $P = .003$) and in patients with a histopathologic score of 3 or higher (13.35 ± 3.21 versus 10.84 ± 1.34 pg/mL, $P = .002$). The IFN-γ:IL-10 ratio was also significantly higher in these groups. Conclusions- Differentiating stable from unstable vitiligo is essential for optimal disease management. Cytokine profiling, particularly IFN-γ and IL-10 levels, offers a minimally invasive biomarker for assessing disease activity and monitoring therapeutic response.

25COASDEC40

Title: Clinically Relevant Cutoffs for Anti–Extractable Nuclear Antigen Line Immunoassays

Adrian Y. S. Lee et.al.

Pathology of Archieves and Laboratory Medicine, vol.-149, issue- 12

https://doi.org/10.5858/arpa.2025-0061-OA

Abstract: Anti–extractable nuclear antigens (enas) are a form of antinuclear antibody test in the diagnostic laboratory that plays a crucial role in the diagnosis of systemic autoimmune diseases. The line immunoassay (LIA) is one of the most popular assays used to measure these autoantibodies. However, lias suffer from limited diagnostic specificity, and numerous attempts have been made to improve the cutoffs. Objective- To readjust LIA autoantibody cutoffs, using the clinical diagnoses of a large and heterogeneous group of patients. Design- During a 12-month period, 667 discrete patients received an LIA test that had adequate clinical records to determine a diagnosis. Autoantibodies on the Euroimmun LIA (anti-Ro52, anti-Ro60, anti-dsdna, anti-La, anti-mitochondrial antibodies, anti-Sm, anti-RNP, anti-histone, anti-nucleosome, anti–ribosomal P, anti–centromere protein B, and anti-Scl70) were evaluated. Two laboratory physicians independently rated whether the LIA density for each autoantibody was consistent or not consistent with the diagnosis. Receiver operating characteristic curves were constructed for each autoantibody and cutoffs were reestablished to maximize diagnostic specificities of 85% to 90%. Results- New cutoffs were proposed at the diagnostic specificities of 85% and 90%. Overall, there were similar rates of autoantibody detections, using the new cutoffs, compared to the manufacturer's defined cutoff of 10 units for each autoantibody. Conclusions- We have used a novel approach to redefining anti-ENA LIA cutoffs by using clinical diagnoses across a range of pathologic conditions. This ensures that results are clinically relevant to a general laboratory cohort and, when used as a characterizing assay after an initial anti-ENA screen, maximizes diagnostic specificity. Longitudinal evaluation of the new cutoffs is required after implementation to examine clinical impact.

Medical Oncology
(Chemotherapy**, H**ematology **& R**adiotherapy**)**

25COASDEC01
Title: Prospective study comparing acute toxicity and objective response rate between simultaneous integrated boost and sequential boost Intensity-Modulated radiation therapy for locally advanced head and neck squamous cell carcinoma.
EL-Atta, S.S.A., Maria, A.M., Abd-Elaziz, L.M. *et al.*
Med Oncol 42, 553 (2025).
https://doi.org/10.1007/s12032-025-03110-8
Abstract: Patients with locally advanced head and neck squamous cell carcinoma (HNSCC) were included for evaluation of patient characteristics, dosimetric analysis, and plan evaluation of both intensity-modulated radiotherapy (RT) using simultaneous integrated boost (SIB-IMRT) and sequential IMRT (IMRTSEQ) and to compare the response and acute toxicity of both arms. This prospective single-blind randomized clinical comparative study was carried out on 60 patients, clinically and histologically confirmed to have locally advanced HNSCC at the Clinical Oncology Department, Tanta University Hospitals. All patients were randomly divided into two equal groups: Group A was treated with SEQ-IMRT with combined total doses in phases I, II, and III of 70 Gy/35 fractions, 2 Gy/fraction along the entire course, 5 days a week, in 7 weeks by 54 Gy in 27 fractions, and group B was treated with SIB-IMRT dose of 66 Gy to PTV-HR (2.2 Gy/fraction), 60 Gy to PTV-IR (2 Gy/fraction), and 54 Gy to PTV-LR (1.8 Gy/fraction), all were given at the same time in 30 fractions, 5 days a week, over 6 weeks. All patients received 3 cycles of induction chemotherapy with docetaxel (or Taxotere), platinum, and 5-fluorouracil, followed by concurrent chemo-RT with cisplatin or carboplatin. Organ at risk)OAR(was higher for group B (100%) vs. (33.3%) for group A ($p = 0.035$). The 1-year & 2-year OS for the whole group were (98.3% & 61.5%) respectively, while for group A and group B, 1-year OS was 96.7% for group A vs. 100.0% for group B, and the 2-year OS was 53.2% for group A vs. 71.2% for group B. the 2-year PFS was 58.3% for the whole group and 49.4% vs. 69.2% for groups A and B, respectively. The SIB-IMRT arm, with shorter total treatment duration, resulted in comparable treatment outcomes and acute toxicity rates. This reduction in treatment time not only reduces costs but also decreases the workload of busy radiation. The SIB-IMRT is well-tolerated with better treatment compliance for head and neck cancer patients.

25COASDEC02
Title: RPL17 regulates the progression of breast cancer accompanied by MAPK signaling activation.
Cai, Y., Liu, H. & Yin, G.
Med Oncol 42, 550 (2025).
https://doi.org/10.1007/s12032-025-03117-1
Abstract: Breast cancer (BC) is the most frequently diagnosed cancer type and the leading cause of cancer-related mortality among females worldwide. This study aimed to investigate the role of RPL17 in BC. Our findings revealed that the expression of RPL17 in BC tissues and cell lines was significantly elevated compared to normal tissues and cells. The knockout

of RPL17 in BC cell lines profoundly inhibited their proliferation, migration, invasion, and cell adhesion abilities. Furthermore, RPL17 knockout (RPL17-KO) cells exhibited increased apoptosis. Mechanistically, RPL17-KO cells demonstrated decreased MAPK signaling. Finally, the overexpression of RPL17 promoted the epithelial-mesenchymal transition (EMT) process in BC cells. RPL17-overexpressing cells displayed enhanced proliferation, migration, invasion, and cell adhesion abilities, alongside reduced apoptosis and increased MAPK signaling. Collectively, this study suggests that RPL17 functions as an important oncogene and may represent a potential therapeutic target for BC.

25COASDEC03

Title: GLYR1-mediated downregulation of lncRNA HSD11B1-AS1 promotes proliferation, migration, and invasion of breast cancer cells.

Lei, Y., Li, Y., Yu, Y. *et al.*

Med Oncol 42, 549 (2025).

https://doi.org/10.1007/s12032-025-03027-2

Abstract: Long non-coding RNAs (lncRNAs) play important roles in the occurrence and development of multiple cancers, but the role of lncRNAs in breast cancer has not been fully elucidated. We integrated data mining, bioinformatics analysis, and reverse transcription quantitative polymerase chain reaction (RT-qPCR) to pinpoint key lncRNAs that modulate breast cancer development. In vitro functional assays evaluated the impact of lncRNA 11β-hydroxysteroid dehydrogenase type 1-antisense RNA 1 (HSD11B1-AS1) on breast cancer cells proliferation, migration, and invasion. Interactions between HSD11B1-AS1 and Glyoxylate Reductase 1 Homolog (GLYR1) within breast cancer cells were confirmed through bioinformatics prediction, chromatin immunoprecipitation (ChIP), and dual-luciferase reporter assays. Rescue experiments substantiated the involvement of GLYR1 in breast cancer advancement through the regulation of HSD11B1-AS1. HSD11B1-AS1 is markedly downregulated in breast cancer tissues and cell lines, correlating with an unfavorable prognosis for patients. Functional assays revealed that the suppression of HSD11B1-AS1 notably amplified the proliferation, migration, and invasive capabilities of breast cancer cells. Conversely, the overexpression of HSD11B1-AS1 significantly curtailed the proliferation, migration, and invasion of breast cancer cells. Mechanistically, GLYR1 directly binds to the HSD11B1-AS1 promoter and repressess its transcription, thereby enhancing the malignant behaviors of breast cancer cells, including proliferation, migration, and invasion. GLYR1-mediated suppression of HSD11B1-AS1 drives breast cancer progression. The GLYR1/HSD11B1-AS1 axis may represent a promising avenue for diagnostic biomarkers and therapeutic intervention in breast cancer.

25COASDEC04

Title: Anticancer effects of *Commiphora myrrha* extract on colorectal cancer through regulation of metastasis, cell cycle progression, and apoptosis in vitro and in vivo.

Chien, JH., Chang, KF., Chen, YC. *et al.*

Med Oncol 42, 547 (2025).

https://doi.org/10.1007/s12032-025-03050-3

Abstract: *Commiphora myrrha* exhibits multiple pharmacological properties, including antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and anticancer activities.

Although the cytotoxic effects of *C. myrrha* have been observed in various cancer cell lines, the molecular mechanisms underlying its therapeutic potential against colorectal cancer (CRC) remain largely uncharacterized. In this study, we investigated the anticancer effects of *C. myrrha* extract (CMy) on CRC using in vitro and in vivo models. The anticancer properties of CMy were evaluated through MTT assay, colony formation, wound healing assay, invasion assay, cell cycle analysis, and terminal deoxynucleotidyl transferase dUTP nick-end labeling staining. Western blotting was performed to detect the expression of proteins associated with cell cycle progression and apoptosis. The in vivo antitumor efficacy of CMy was investigated in a CRC-bearing BALB/c mouse model. This study revealed that CMy significantly decreased the viability, colony-forming ability, and the migratory and invasive capacities of CRC cells. Mechanistically, CMy induced G0/G1 phase cell cycle arrest through the downregulation of cyclin-dependent kinase 4 and cyclin D1 and promoted apoptosis by upregulating pro-apoptotic markers, including Bcl-2-associated X, caspase-9, and caspase-3. Furthermore, CMy exhibited a synergistic cytotoxic effect when combined with 5-fluorouracil, thereby enhancing its inhibitory activity against CRC cells. In vivo, CMy treatment effectively suppressed tumor progression and prolonged the survival of tumor-bearing mice at well-tolerated doses. Collectively, these findings indicate that CMy is a promising source of cytotoxic phytochemicals with significant anti-CRC activity, supporting its potential application as a therapeutic agent for CRC.

25COASDEC05

Title: miR-770-5p: A novel molecular target regulating KLF4/EGFR signaling through PRMT5 interaction.

Noyan, S., Gur Dedeoglu, B., Can, A. *et al.*

Med Oncol 42, 545 (2025).
https://doi.org/10.1007/s12032-025-03119-z

Abstract: TNBC represents an exceptionally aggressive subtype, distinguished by the absence of targeted therapeutic options. miR-770-5p, a tumor suppressor microRNA, has been shown to regulate critical cancer-associated signaling pathways. PRMT5, is frequently overexpressed in various malignancies and plays a pivotal role in regulating cellular processes, including EGFR signaling, thereby contributing to tumorigenesis. PRMT5 acts as a key modulator of KLF4 transcriptional activity, with its methylation of KLF4, enhancing EGFR expression and promoting tumor progression. In this study, we investigated the regulatory interplay between the PRMT5-KLF4 axis and miR-770-5p in TNBC, focusing specifically on the modulation of EGFR signaling. Bioinformatics analyses identified EGFR as a potential target of miR-770-5p, and experimental validation demonstrated that restoring miR-770-5p expression in TNBC cell lines led to a downregulation of EGFR signaling. Furthermore, our findings unequivocally demonstrate that miR-770-5p directly targets PRMT5, leading to a significant reduction in PRMT5 expression and a notable alteration in KLF4 localization. miR-770-5p treatment increased the cytoplasmic-to-nuclear ratio of KLF4 and disrupted EGFR localization, demonstrating that miR-770-5p disrupts the PRMT5-KLF4-driven activation of EGFR signaling. These findings indicate that miR-770-5p acts as a tumor suppressor in TNBC by modulating EGFR signaling via PRMT5 and KLF4, emphasizing its potential as a therapeutic target.

25COASDEC06

Title: The potential role of BM-MSC-derived exosomes in TUG1 modulation: antileukemic effects on THP-1 cells.

Karimian, F., Loghmani, Z., Vazifeh Shiran, N. *et al.*

Med Oncol 42, 544 (2025).
https://doi.org/10.1007/s12032-025-03103-7

Abstract: Mesenchymal stem cell–derived exosomes (BM-MSC-Exos) have attracted increasing interest for their potential to modulate leukemic cell behavior in acute myeloid leukemia (AML). In this study, the effects of BM-MSC-Exos on the AML cell line THP-1 were evaluated. A dose-dependent reduction in cell viability was observed after 24 h of treatment, as determined by MTT assay. Flow-cytometric analysis revealed a significant increase in apoptotic activity following exposure to BM-MSC-Exos. Cell cycle analysis demonstrated an accumulation of cells in the G0/G1 phase, consistent with growth arrest. Gene-expression profiling by real-time PCR showed upregulation of pro-apoptotic genes (Caspase3, Caspase9, BID, and BAX) and downregulation of the anti-apoptotic gene BCL2. Likewise, expression of cell cycle regulators such as Cyclin D1 and CDK6 was reduced. Importantly, TUG1, an oncogenic long non-coding RNA implicated in leukemogenesis, was also significantly downregulated in exosome-treated cells. Taken together, these results may shed light on the possible role of BM-MSC-Exos in regulating apoptosis, cell-cycle progression, and TUG1 expression in leukemic cells. Further studies are warranted to elucidate the molecular mechanisms underlying these effects and to determine how BM-MSC-Exos–mediated modulation of TUG1 might contribute to leukemic cell regulation.

25COASDEC07

Title: Response evaluations in non-small cell lung cancer patients undergoing immunotherapy: a comparative analysis of RECIST 1.1, iRECIST, and imRECIST criteria.

Shih, YJ., Chen, JH., Yeh, LR. *et al.*

Med Oncol 42, 543 (2025).
https://doi.org/10.1007/s12032-025-03115-3

Abstract: To compare response evaluation criteria using RECIST 1.1, iRECIST, and im RECIST in non-small cell lung cancer (NSCLC) patients treated with PD-1/PD-L1 immune checkpoint inhibitors (ICI) and investigate their discrepancy and impact on survival. This retrospective cohort study included 105 NSCLC patients treated with PD-1/PD-L1 across four hospitals. Response assessments were conducted using RECIST 1.1, iRECIST, and imRECIST criteria after viewing relevant images before and after ICI treatment. The absolute and relative differences on time point (TP) assessments and best overall response (BOR) categories regarding progressive disease (PD) across criteria were reported. The Kaplan-Meier analysis and log-rank test were used to evaluate the differences of overall survival (OS) between concordant or discordant assessments among criteria. Discordant TP assessments were observed in 25 patients (23.8%) across the three criteria. Among them, 15.2% were labeled as PD by RECIST 1.1 and iRECIST but not by imRECIST. Comparing imRECIST with RECIST 1.1, 10 patients (9.9%) had discordant BOR for PD (classified as non-PD by imRECIST but PD by RECIST 1.1). These patients had a median OS of 8.1 months, falling between the concordant disease progression group (2.8 months) and the

concordant disease control group (26.8 months) ($p < 0.001$). In contrast, only 2 patients (1.9%) had discordant BOR for PD between iRECIST and RECIST 1.1. The imRECIST identified 9.9% of NSCLC patients who may potentially benefit from continuing ICI treatment despite a classification of PD with RECIST 1.1. The discordance between iRECIST and RECIST 1.1 was relatively smaller.

25COASDEC08

Title: Empagliflozin mitigates doxorubicin-induced hepatotoxicity by reducing inflammation, oxidative stress, and apoptosis in male NMRI mice.

Asgari, N., Kalhori, Z.

Med Oncol 42, 542 (2025).

https://doi.org/10.1007/s12032-025-03113-5

Abstract: Doxorubicin (DOX) is an effective chemotherapeutic agent widely used against various malignancies; however, its clinical utility is limited by dose-dependent hepatotoxicity. Empagliflozin (EMPA), a sodium-glucose co-transporter-2 (SGLT2) inhibitor, has demonstrated antioxidant, anti-inflammatory, and anti-apoptotic properties. This study aimed to evaluate the protective effects of EMPA against DOX-induced liver injury. Twenty-eight adult male Naval Medical Research Institute (NMRI) (8–12 weeks old) mice were randomly divided into four groups ($n = 7$ per group): the DOX group received 2 mg/kg intraperitoneally on days 1, 7, 14, 21, and 28. DOX + EMPA group, in addition to receiving a 2 mg/kg intraperitoneally on days 1, 7, 14, 21 and 28 of doxorubicin, at the same time received 10 mg/kg/day intraperitoneally empagliflozin for 28 days, the EMPA group received 10 mg/kg/day intraperitoneally empagliflozin for 28 days, and the control group did not receive any medications. Serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), Gamma-glutamyl transferase (GGT), and total bilirubin, interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-α), malondialdehyde (MDA), and ferric reducing antioxidant power (FRAP) were assessed. Liver histology was examined using H&E and Periodic Acid-Schiff (PAS) staining, and hepatocyte apoptosis was quantified via terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay. Co-administration of EMPA attenuated DOX-induced elevations in ALT (1.5 fold), AST (1.4 fold), ALP (1.4 fold), GGT (1.7 fold), total bilirubin (1.6 fold), IL-6 (1.8 fold), TNF-α (1.7 fold), and MDA (1.7 fold) levels, while enhancing FRAP (2.4 fold) levels. Histological evaluation revealed improved hepatic architecture and reduced hepatocyte apoptosis in the DOX + EMPA group compared to the DOX group. Empagliflozin confers hepatoprotective effects against doxorubicin-induced toxicity by modulating oxidative stress, inflammatory cytokines, and apoptotic activity. These findings suggest potential therapeutic benefits of EMPA as an adjuvant in chemotherapy-induced liver injury.

25COASDEC09

Title: Tβ4–17 peptide enhances the chemo-sensitivity of ovarian cancer cells to DDP by affecting NF-κB signaling pathway.

Guo, L., Wang, H., Li, N. *et al.*

Med Oncol 42, 541 (2025).

https://doi.org/10.1007/s12032-025-03106-4

Abstract: Ovarian cancer is a gynecologic malignancy with high mortality and poor prognosis. Chemoresistance is a key cause of ovarian cancer recurrence and metastasis. It has been found that some bioactive peptides can inhibit the growth and metastasis of cancer cells and promote cell apoptosis, thus exerting anti-cancer effects. Tβ4–17 is a small polypeptide that we selected using ITRAQ technology, and its precursor protein is thymosin β4. This study mainly investigated its effect in combination with cisplatin (DDP) on the proliferation, migration and apoptosis of ovarian cancer resistant cells and related molecular mechanisms. Our results showed that Tβ4–17 peptide combined with DDP significantly inhibited the proliferation and migration of drug resistance cells in ovarian cancer, promoted apoptosis, and increased the chemo-sensitivity of ovarian cancer cells to DDP. In addition, qRT-PCR and Western blot showed that NF-κB was significantly highly expressed in DDP-resistant cells of ovarian cancer. After application of NF-κB inhibitors and activators, Western blot, CCK8, EDU fluorescence proliferation assay, and cell scratch assay showed that Tβ4–17 peptide down-regulated NF-κB p65 protein expression and inhibited cell proliferation and migration. In conclusion, our study demonstrates that Tβ4–17 peptide enhances the sensitivity of ovarian cancer cells to DDP by down-regulating NF-κB expression.

25COASDEC10

Title: Essential oil from *Tragopogon dubius* selectively inhibits breast (MCF-7) and glioblastoma (LN-18) cancer cell proliferation; insights into antioxidant, genoprotective potential, and GCMS, GCGCTOFMS-based profiling.

Ahmad, S.S., Chandni, Fouad, D. *et al.*

Med Oncol 42, 540 (2025).
https://doi.org/10.1007/s12032-025-03092-7

Abstract: *Tragopogon dubius* Scop. is consumed as a vegetable and is well known for its numerous ethnomedicinal properties to treat gastrointestinal, kidney, liver dysfunction, inflamed skin, wounds and certain cutaneous diseases. The present study aimed to determine the antioxidant potential, cytotoxicity towards different cancer cells, and genotoxic effect of essential oil of *T. dubius* (Trd-EO) obtained from stem and leaves through hydro distillation. Trd-EO exhibited moderate radical scavenging activity in all antioxidant assays, displayed an effective concentration (EC_{50}) value of 153.77 µg/mL, 126.85 µg/mL, 115.74 µg/mL, and 120.76 µg/mL, in DPPH, ABTS, FRAP, and Superoxide radical scavenging assays respectively. Trd-EO has moderate phenolic (15.86 mg RE/gdw,) and flavonoid (19.88 mg GAE/g dw) contents. Single-cell gel electrophoresis (Comet assay) for genotoxicity of Trd-EO of *T. dubius* showed no significant genotoxic and cytotoxic signs at 25 µg/mL to 200 µg/mL in human lymphocytes. Results through MTT for cytotoxicity analysis showed that *T. dubius* obtained Trd-EO-possessed potent toxicity against human Breast (MCF-7), human glioblastoma (LN-18), human lung (A-549) and human colon (HCT-116) cancer cell lines in a dose-dependent manner. Trd-EO possessed the selective and highest cytotoxicity towards MCF-7 and LN-18 cancer cell lines, reduced over 50% cell growth at the concentration of 24.37 µg/mL and 36.72 µg/mL, and cytomorphological studies indicated the apoptotic effect of the essential oil. GCMS and GCGCTOFMS profiling of Trd-EO revealed 23 and 61 phytoconstituents belonged to fatty acids, aldehydes, alcohols, ketone derivatives, ester derivatives, alkanes and other fatty acid derivatives. As expected for oil extraction, fatty acid derivatives were majorly present.

25COASDEC11

Title: Improving cisplatin chemotherapy in vivo by niosomal propolis and chrysin as nanoadjuvants.

Mohamad, E.A., El-Garhy, M.R. & Rageh, M.M.

Med Oncol 42, 539 (2025).

https://doi.org/10.1007/s12032-025-03105-5

Abstract: Breast cancer remains the most prevalent malignancy among women worldwide, with its incidence steadily increasing. Cisplatin (Cis) is a widely used chemotherapeutic drug. Natural compounds such as propolis and chrysin may help mitigate the toxic side effects of Cis while enhancing its therapeutic efficacy. This study aimed to evaluate the anticancer potential of ethanolic extract of propolis (EEP) and chrysin (Chry) through niosomal encapsulation (Nio). The synergistic effects of Nio formulations in combination with low-dose Cis were also investigated in vivo. EEP was extracted and analyzed for its phytochemical composition using gas chromatography–mass spectrometry (GC–MS). Both EEP and Chry were loaded onto niosomes, which were then characterized by transmission electron microscopy (TEM), dynamic light scattering, zeta potential, UV–Vis, and FTIR spectroscopy. Fifty adult female Swiss Albino mice were induced with Ehrlich carcinoma and randomly divided into ten treatment groups: control, Free Nio, Free EEP, Free Chry, Nio + EEP, Nio + Chry, Nio + EEP + low Cis, Nio + Chry + low Cis, low Cis, and high Cis groups. Treatments were administered intraperitoneally every three days. The study assessed the efficacy of cancer treatments by analyzing tumor histology, tracking growth, and tracking oxidative stress. In addition, the cytotoxicity of kidney and liver tissues was studied. Niosomes improved and enhanced the stability and encapsulation efficiency of EEP and Chry (90%). Combination treatments reduced tumor volume by about 90% compared to the control group and enhanced antioxidant activity. Histopathological evaluation of tumor tissue revealed that Nio + EEP + low Cis and Nio + Chry + low Cis significantly reduced mitotic figures and increased necrotic changes relative to the low and high cis groups. In the liver, these groups exhibited only mild necrobiotic changes and minimal vascular congestion, indicating a protective effect against cisplatin-induced hepatotoxicity. In the kidney, mild interstitial nephritis, limited tubular degeneration, and reduced glomerular hypercellularity were observed. EEP and Chry-loaded niosomes effectively enhanced the antitumor efficacy of low-dose cisplatin while minimizing systemic toxicity. These findings suggest that Nio-based natural adjuvants could be promising nanocarriers for combination cancer therapy.

25COASDEC12

Title: Defeating miR-181a-3p may potentiate the effect of paclitaxel on G2/M arrest in breast cancer stem cells.

Asik, A., Goker Bagca, B., Ozates, N.P. *et al.*

Med Oncol 42, 538 (2025).

https://doi.org/10.1007/s12032-025-03111-7

Abstract: Paclitaxel is a commonly used taxane in breast cancer (BCa) therapy. miRNA-targeted strategies aim to improve treatment efficacy by overcoming suboptimal responses and resistance. This study investigated the effect of miR-181a-3p silencing on paclitaxel sensitivity in triple-negative breast cancer (TNBC) and breast cancer stem cells (BCSCs). miR-181a-3p expression in BCa tissues and its target mRNAs were analyzed using

computational tools. MDA-MB-231 (TNBC model), BCSC, and breast epithelial stem cell (BESC, healthy control) lines were used. RT-qPCR measured gene expression, while Annexin V-FITC and cell cycle kits assessed apoptosis and proliferation. Silencing was achieved via anti-miR-181a-3p transfection, and cells were treated with 10 µM paclitaxel for 48 h. miR-181a-3p silencing significantly enhanced the apoptotic effect of paclitaxel on BCSCs and exhibited a pronounced apoptotic impact independently on these cells. No apoptotic effect was observed in MDA-MB-231 cells. In MDA-MB-231, miR-181a-3p silencing enhanced paclitaxel-induced G2/M arrest, but this effect was not seen in BCSCs. In BESCs, miR-181a-3p silencing decreased the apoptotic and G2/M arrest effects of paclitaxel. Five miR-181a-3p target genes (*CYCS*, *GSK3B*, *BAK1*, *IGF1R*, and *MAPK8*) highly expressed in BCa tissue and implicated in key signaling pathways were computationally identified. Although all were theoretically expected to increase upon silencing, expression changes varied. In BCSCs, apoptotic genes BAK1 and CYCS were upregulated, while proliferative genes IGF1R, MAPK8, and GSK3B were downregulated, consistent with other data. In conclusion, miR-181a-3p modulates apoptotic and cell cycle responses to paclitaxel, positioning it as a promising therapeutic option and biomarker, particularly for addressing BCSC-related resistance and relapse.

25COASDEC13

Title: Ex vivo evaluation of *Allium sativum* extract on acute myeloid leukemia cells and leukemia stem cell populations.

Abdelkarim, M., Kharrat, R., Lakhal, F.B. *et al.*

Med Oncol 42, 536 (2025).

https://doi.org/10.1007/s12032-025-03104-6

Abstract: Despite therapeutic advances, acute myeloid leukemia (AML) remains associated with high relapse rates and poor outcomes, especially in elderly or unfit patients. *Allium sativum* is widely known for its medicinal properties, but its anti-leukemic effects have not been fully explored. This study investigated the cytotoxic and pro-apoptotic potential of an ethyl acetate extract of *Allium sativum* (EAEAS) using ex vivo mononuclear cells from thirteen AML patients. Cytotoxicity was assessed via MTT assay, while mechanisms of cell death were analyzed using annexin V/propidium iodide staining, DNA fragmentation, mitochondrial depolarization, and caspase 3/7 activation. EAEAS induced a dose-dependent decrease in cell viability, with variable IC_{50} values across samples. Apoptosis was confirmed through mitochondrial dysfunction, sub-G1 accumulation, and caspase activation. Additionally, we evaluated the effect of EAEAS on two LSC subpopulations using multicolor flow cytometry. Although no statistically significant changes were observed, some patients showed a decrease in LSC frequencies after treatment, suggesting possible selective activity. These findings indicate that EAEAS triggers intrinsic apoptosis in AML blasts and may exert partial activity on stem-like compartments, warranting further evaluation as an adjuvant therapy in AML.

25COASDEC14

Title: BMP-9 promotes the expression of PD-L1 in osteosarcoma cells through FOXO1.

Zhang, W., Ge, Y. & Xu, X.

Med Oncol 42, 535 (2025).

https://doi.org/10.1007/s12032-025-03097-2

Abstract: Osteosarcoma is the most common primary malignant bone tumor, and its occurrence and development are closely related to the bone microenvironment. Therefore, it is essential to understand the main factors that promote osteosarcoma progression in the bone microenvironment. Our study focused on the effect of BMP-9 on PD-L1 expression in osteosarcoma cells. The expression of PD-L1 was detected western blot and flow cytometry. Using RNA-seq analysis, we explored the mechanism that regulated PD-L1 mRNA expression. Our findings revealed that BMP-9 promoted PD-L1 protein expression in osteosarcoma cells. Further, BMP-9 induced the transcriptional expression of PD-L1 in osteosarcoma cells. RNA sequencing and TCGA database analysis showed that FOXO1 regulates the transcriptional expression of PD-L1. FOXO1 expression was significantly increased under BMP-9 action. Importantly, BMP-9 cannot increase the transcriptional and protein expression of PD-L1 in osteosarcoma cells when FOXO1 is knocked down. Additionally, the expression of BMP-9 was positively correlated with the expression of PD-L1 in clinical samples of osteosarcoma.

25COASDEC15

Title: Anticancer potential of chamaejasmenin B: apoptotic and antioxidant effects on pancreatic cancer cells.

Akçaalan, S., Eroğlu Güneş, C., Asadova, L. *et al.*

Med Oncol 42, 533 (2025).
https://doi.org/10.1007/s12032-025-03099-0

Abstract: The aim of this study was to investigate the effect of Chamaejasmenin B (CHB), a phytochemical, on human pancreatic cancer cell line (MIA PaCa-2). CCK-8 test was performed to evaluate the cytotoxic effect of CHB. To elucidate the molecular mechanism of CHB, expression levels of important genes in the cell cycle and apoptosis pathways were evaluated by qPCR and Western blot analysis. In addition, the effects of CHB on the colony formation capacity of cells, total oxidant and total antioxidant levels were also evaluated. The IC_{50} dose of CHB on MIA PaCa-2 cells was found as 647 µM at 48 h. After CHB treatment in MIA PaCa-2 cells, expressions of BAX, CASP3, CASP7, CYCS, FADD, FAS, CCND2 and P53 genes were significantly increased. However, a decrease in the expressions of CDK4, CDK6, CCND1 and CCND3 genes was observed. In addition, an elevation in CASP3 and P53 protein levels and a decrease in the level of CCND1 protein were determined. CHB treatment significantly suppressed the colony formation capacity in MIA PaCa-2 cells. In addition to these, an increase in total antioxidant levels was observed. These findings suggest that CHB seems to be a promising anticancer therapeutic agent in the treatment of pancreatic cancer.

25COASDEC16

Title: Exploring novel therapeutic strategies: Static Magnetic Fields in combination with doxorubicin induce ROS and apoptosis in acute lymphoblastic leukemia cells.

Nikkhah Bahrami, A., Sadeghian, M.H. & Vazifeh Shiran, N.

Med Oncol 42, 532 (2025).
https://doi.org/10.1007/s12032-025-02999-5

Abstract: Acute lymphoblastic leukemia (ALL), primarily affecting children, is a rare malignancy. This study explores the use of alternative therapies such as Static Magnetic Fields (SMF) and Doxorubicin (Dox) as a novel therapeutic strategy for ALL NALM-6 cells. Viability, apoptosis, cell cycle, ROS, and gene expression were assessed using Trypan blue, MTT, flow cytometry, and qRT-PCR. SMF significantly reduced NALM-6 viability and metabolic activity, increased apoptosis and ROS, and altered gene expression related to apoptosis, ROS, cell cycle, and autophagy. Co-treatment with SMF and Dox enhanced these effects compared to single treatments ($p \leq .05$), with no cytotoxicity to normal PBMCs or L929 cells. SMF alone or with Dox induces ROS-mediated apoptosis and autophagy inhibition, suggesting a potential complementary therapy, though further research is needed.

25COASDEC17

Title: STXBP6 regulates growth, metastasis and lipid metabolism of ovarian cancer cells via the PI3K/AKT signaling pathway.

Wang, M., Xu, H., Li, Q. *et al.*
Med Oncol 42, 531 (2025).
https://doi.org/10.1007/s12032-025-03082-9

Abstract: Ovarian cancer (OC) is the primary cause of mortality related to cancers of the female reproductive system. Early diagnosis remains a major challenge, contributing to a high mortality rate and underscoring an urgent need for novel diagnostic approaches and effective therapeutic strategies. Here, we identify Syntaxin binding protein 6 (STXBP6) as a previously unrecognized oncogenic driver in OC. We demonstrate that STXBP6 expression is markedly elevated in OC tissues and cells and that it promotes OC growth and metastasis both in vitro and in vivo. RNA sequencing revealed that STXBP6 reprograms lipid metabolism, and mechanistic studies confirmed that it enhances OC progression through fatty acid oxidation (FAO). Moreover, activation of the PI3K/AKT signaling pathway was essential for STXBP6-driven FAO and malignant phenotypes. These findings uncover a novel STXBP6/PI3K/AKT axis, providing new insights into OC metabolic reprogramming and potential therapeutic targets.

25COASDEC18

Title: Silencing SOX2OT reduces viability and migration in lung cancer cells via lncRNA and protein regulation.

Zarei, M., Dinari, A., Jahangiri, B. *et al.*
Med Oncol 42, 528 (2025).
https://doi.org/10.1007/s12032-025-03085-6

Abstract: Long non-coding RNAs (lncRNAs) play crucial role in tumor development and are being explored as potential therapeutic targets in lung cancer. Both SOX2OT and SOX2 are consistently overexpressed in lung cancer, suggesting that SOX2OT may play a significant role in its development. This study examines how knocking down SOX2OT affects the expression of specific lncRNAs (LINC00982, LINC00668, SNHG7), the gene P16, and key cell cycle–regulating proteins (HSP90AA1, EP300, YES1) in lung cancer cells. Silencing of SOX2OT in A549 and Calu-3 cells led to a marked reduction in its expression. This downregulation was accompanied by decreased levels of SNHG7 and LINC00668, while LINC00982 and P16 transcripts were strongly induced. At the protein level, EP300,

HSP90AA1, and YES1 were substantially reduced, whereas P16 was notably elevated. Functionally, suppression of SOX2OT impaired cell viability and significantly limited migratory capacity. In parallel, apoptosis assays demonstrated a pronounced increase in apoptotic cell populations following SOX2OT knockdown. SOX2OT regulates specific lncRNAs and proteins involved in lung cancer survival and migration. Silencing SOX2OT significantly reduces viability, migration, and survival of lung cancer cells, suggesting its potential as a therapeutic target. Further in vivo validation and rescue experiments are needed to confirm these mechanisms.

25COASDEC19

Title: A Pragmatic Trial of Glucocorticoids for Community-Acquired Pneumonia

Ruth K. Lucinde et.al.

N Engl J Med 2025, VOL. 393 NO. 22

https://doi.org/10.1056/NEJMoa2507100

Abstract: Adjunctive glucocorticoids may reduce mortality among patients with severe community-acquired pneumonia (CAP) in well-resourced settings. Whether these drugs are beneficial in low-resource settings with limited diagnostic and treatment facilities is unclear. Methods- In this pragmatic, open-label, randomized, controlled trial conducted in 18 public hospitals in Kenya, we assigned adult patients who had received a diagnosis of CAP and who did not have a clear indication for glucocorticoids to receive either standard care for CAP or oral low-dose glucocorticoids for 10 days in addition to standard care. The primary outcome was death from any cause at 30 days after enrolment. Results-A total of 2180 patients underwent randomization (1089 assigned to the glucocorticoid group and 1091 to the standard-care group). The median age of the patients was 53 years (interquartile range, 38 to 72); 46% were women. At day 30, deaths were reported in 530 patients (24.3%): 246 patients (22.6%) in the glucocorticoid group and 284 patients (26.0%) in the standard-care group (hazard ratio, 0.84; 95% confidence interval, 0.73 to 0.97; P=0.02). The frequencies of adverse events and serious adverse events were similar in the two trial groups. Serious adverse events that were considered to be related to glucocorticoid administration occurred in 5 patients (0.5%). Conclusions-In patients with CAP in a low-resource setting, adjunctive glucocorticoid therapy was associated with a lower risk of death than standard care.

25COASDEC20

Title: A Randomized Trial of Shunting for Idiopathic Normal-Pressure Hydrocephalus

Mark G. Luciano, M.D., Ph.D. et.al.

N Engl J Med 2025, VOL. 393 NO. 22

https://doi.org/10.1056/NEJMoa2503109

Abstract: Idiopathic normal-pressure hydrocephalus is a neurologic disorder characterized by impaired gait, balance, cognition, and bladder control in older adults. The disorder is treated with shunt surgery, but the effectiveness of shunting is unclear. Methods-We conducted a double-blind, randomized, placebo-controlled trial involving participants selected for shunt surgery on the basis of gait-velocity improvement with cerebrospinal fluid (CSF) drainage. Participants were randomly assigned to an open-shunt valve setting (opening pressure, 110 mm of water) or a placebo valve setting (opening pressure, >400 mm of water)

of a noninvasively adjustable shunt. The primary outcome was the change in gait velocity 3 months after surgery. Secondary outcomes were the change at 3 months in the Tinetti scale total score (range, 0 to 28; lower scores indicate worse gait and balance), Montreal Cognitive Assessment (MoCA) score (range, 0 to 30; lower scores indicate worse cognition), and Overactive Bladder Questionnaire score (range, 0 to 100; higher scores indicate worse urinary incontinence). Results- A total of 99 participants underwent randomization and received the assigned intervention. At 3 months, gait velocity had increased in the open-shunt group (mean [±SD] change, 0.23±0.23 m per second; assessed in 49 participants) and was unchanged in the placebo group (mean change, 0.03±0.23 m per second; assessed in 49 participants), resulting in a treatment difference of 0.21 m per second (95% confidence interval, 0.12 to 0.31; P<0.001). A significantly greater improvement in the open-shunt group than the placebo group was seen for the Tinetti scale score (mean change, 2.9 points vs. 0.5 points; P=0.003) but not the MoCA score (1.3 points vs. 0.3 points) or the Overactive Bladder Questionnaire score (−3.3 points vs. −1.5 points). The results regarding adverse events were mixed, with more participants in the placebo group reporting falls (46% vs. 24%), an equal percentage having cerebral bleeding (2% in both groups), and more participants in the open-shunt group having subdural bleeding (12% vs. 2%) and positional headaches (59% vs. 28%). Conclusions- Among participants with idiopathic normal-pressure hydrocephalus who had a response to temporary CSF drainage, shunting resulted in significant improvements at 3 months in gait velocity and a measure of gait and balance but not in measures of cognition or incontinence.

25COASDEC21

Title: Trial of Pegcetacoplan in C3 Glomerulopathy and Immune-Complex MPGN

Fadi Fakhouri, M.D., Andrew S. Bomback, M.D

N Engl J Med 2025, VOL. 393 NO. 22
https://doi.org/10.1056/NEJMoa2501510

Abstract: C3 glomerulopathy and primary immune-complex membranoproliferative glomerulonephritis (MPGN) generally result in glomerular C3 deposition and irreversible kidney damage. The efficacy and safety of pegcetacoplan, a C3 and C3b inhibitor, in persons with C3 glomerulopathy or primary immune-complex MPGN are unclear. Methods- We conducted a phase 3, double-blind, placebo-controlled trial involving adolescents and adults with C3 glomerulopathy or primary immune-complex MPGN, including those with native kidney disease and those with disease recurrence after transplantation. Patients were randomly assigned in a 1:1 ratio to receive pegcetacoplan or placebo. The primary end point was the log-transformed ratio of the urinary protein-to-creatinine ratio at week 26 as compared with baseline. Results- A total of 124 patients underwent randomization. The change in proteinuria (as measured by the log-transformed ratio to baseline in the urinary protein-to-creatinine ratio) was significantly greater with pegcetacoplan than with placebo (geometric mean of the urinary protein-to-creatinine ratio, −67.2% [95% confidence interval {CI}, −74.9 to −57.2] vs. 2.9% [95% CI, −8.6 to 15.9]). The difference represents a relative reduction of 68.1% (95% CI, 57.3 to 76.2) as compared with placebo. In hierarchical testing of five secondary end points, significantly higher percentages of patients in the pegcetacoplan group than in the placebo group met the composite renal end-point criteria (stabilization of estimated glomerular filtration rate [eGFR] and ≥50% reduction in urinary protein-to-

creatinine ratio) (49% vs. 3%) and had at least a 50% reduction in the protein-to-creatinine ratio (60% vs. 5%). Among 69 patients with evaluable kidney-biopsy samples, the change in the activity score of the C3 glomerulopathy histologic index did not differ significantly between the two groups; subsequent end points (decrease in C3 staining and change in eGFR) were not formally tested. Pegcetacoplan was not associated with more adverse events than placebo. No serious infections from encapsulated bacteria occurred; 1 patient receiving pegcetacoplan died from coronavirus disease 2019 pneumonia. No allograft rejection or loss occurred. Conclusions- Pegcetacoplan resulted in a significantly greater reduction in proteinuria than placebo among patients with C3 glomerulopathy or primary immune-complex MPGN.

25COASDEC22

Title: Sentinel-Lymph-Node Biopsy Alone or with Lymphadenectomy in Cervical Cancer

Hua Tu, M.D. et.al.

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Abstract: Limited data are available on survival outcomes after sentinel-lymph-node biopsy alone as compared with lymphadenectomy in cervical cancer. Methods-In this multicenter, randomized, noninferiority trial, we enrolled patients with cervical cancer that was stage IA1 (with lymphovascular invasion), IA2, IB1, or IIA1 according to 2009 International Federation of Gynecology and Obstetrics criteria. Sentinel-lymph-node biopsy was performed at the time of surgery and was followed by examination of frozen sections. Patients who had negative sentinel lymph nodes were intraoperatively assigned in a 1:1 ratio not to undergo pelvic lymphadenectomy (the biopsy-only group) or to undergo lymphadenectomy (the lymphadenectomy group). All the patients underwent hysterectomy, and adjuvant therapy was provided according to a unified protocol. The primary end point was disease-free survival at 3 years, with a prespecified noninferiority margin of 5 percentage points in the upper limit of the confidence interval for the difference between the lymphadenectomy group and the biopsy-only group. Secondary end points included retroperitoneal nodal recurrence, cancer-specific survival, and surgical complications. Results- A total of 838 patients underwent randomization: 420 patients were assigned to the biopsy-only group and 418 to the lymphadenectomy group. The median follow-up was 62.8 months. The 3-year disease-free survival was 94.6% in the lymphadenectomy group and 96.9% in the biopsy-only group (difference, −2.3 percentage points; 95% confidence interval [CI], −5.0 to 0.5; P<0.001 for noninferiority); the 3-year cancer-specific survival was 99.2% in the biopsy-only group and 97.8% in the lymphadenectomy group (hazard ratio for death from cancer in competing-risks analysis, 0.37; 95% CI, 0.15 to 0.95). Retroperitoneal nodal recurrences occurred in no patients in the biopsy-only group and in 9 patients (2.2%) in the lymphadenectomy group. The biopsy-only group had a lower incidence of lymphocyst than the lymphadenectomy group (8.3% vs. 22.0%; P<0.001), as well as a lower incidence of lymphedema (5.2% vs. 19.1%; P<0.001), paresthesia (4.0% vs. 8.4%; P=0.009), and pain (2.6% vs. 7.9%; P=0.001). Conclusions- In patients with early-stage cervical cancer, sentinel-lymph-node biopsy alone was noninferior to lymphadenectomy with respect to disease-free survival and was associated with fewer complications.

25COASDEC23

Title: A Phase 3 Trial of Telitacicept for Systemic Lupus Erythematosus

Ronald F. van Vollenhoven, M.D.

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Abstract: Telitacicept, a new dual inhibitor of the cytokines B-lymphocyte stimulator (BLyS) and APRIL (a proliferation-inducing ligand), showed efficacy in adults with active systemic lupus erythematosus (SLE) in a phase 2b trial when added to standard therapy.Methods- We conducted a phase 3 trial in China in which participants with active SLE were randomly assigned (in a 1:1 ratio) to receive telitacicept (160 mg) or placebo subcutaneously once weekly for 52 weeks, in addition to standard therapy. The primary end point at week 52 was a response on the modified SLE Responder Index 4 (SRI-4), with a response on this composite measure defined as a reduction of at least 4 points in the Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score (ranging from 0 to 105, with higher scores indicating greater disease activity), no new disease activity as measured on the British Isles Lupus Assessment Group index, and no worsening in the Physician's Global Assessment score. Results- Of 433 adults screened, 335 underwent randomization (167 to the telitacicept group and 168 to the placebo group). At week 52, significantly more participants receiving telitacicept had a response on the modified SRI-4 than those receiving placebo (67.1% vs. 32.7%; adjusted difference, 34.5 percentage points; 95% confidence interval [CI], 24.3 to 44.7; P<0.001). A reduction of at least 4 points from baseline in the SELENA-SLEDAI score had occurred in 70.1% of the telitacicept group and in 40.5% of the placebo group (difference, 29.6 percentage points; 95% CI, 13.1 to 46.1). Adverse events that were considered by the investigator to be related to the trial regimen were more common with telitacicept than with placebo (74.9% vs. 50.0%). Such events that occurred more frequently in the telitacicept group than in the placebo group included upper respiratory tract infection (31.7% vs. 19.0%), a reduced serum IgG level (15.6% vs. 1.2%), a reduced serum IgM level (15.0% vs. 0.6%), and injection-site reactions (12.6% vs. 0.6%). Conclusions-In this 52-week trial involving participants with active SLE who were receiving therapy, the incidence of a clinical response was higher with telitacicept than with placebo. However, the incidence of upper respiratory infections, reduced immunoglobulin levels, and injection-site reactions was also higher with telitacicept.

25COASDEC24

Title: Long-Term Safety and Efficacy of Gene Therapy for Adenosine Deaminase Deficiency

Claire Booth, M.B., B.S., Ph.D.

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Abstract: Severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency (ADA-SCID) is a life-threatening inborn error of immunity for which lentiviral gene therapy has been investigated in clinical trials. Methods- Between 2012 and 2019, we treated patients who had ADA-SCID with busulfan nonmyeloablative conditioning followed by transplantation with autologous CD34+ hematopoietic stem cells transduced ex vivo with

a lentiviral vector encoding human *ADA*. The primary efficacy end points were overall survival and event-free survival (defined as survival free from rescue allogeneic hematopoietic stem-cell transplantation, reinitiation of enzyme-replacement therapy, and additional gene therapy). Secondary end points included no receipt of immunoglobulin-replacement therapy, the presence of protective titers to tetanus or pneumococcal vaccines, and sustained discontinuation of fungal or viral prophylaxis. We now report the long-term results from this cohort representing 474 patient-years of follow-up, with a median follow-up of 7.5 years. Results-We treated 62 patients with ADA-SCID in the United States (33 patients) and the United Kingdom (29 patients). Overall survival was 100%, and event-free survival was 95% (59 of 62 patients). All 59 patients who had successful gene-marked engraftment at 6 months have continued not to receive enzyme-replacement therapy and have had stable gene marking, ADA enzyme activity, metabolic detoxification, and immune reconstitution through the last follow-up; 58 of these patients (98%) discontinued IgG replacement therapy and have evidence of a robust response to vaccinations. None of the patients had a leukoproliferative event or clonal expansion. Conclusions-These long-term findings in a large patient cohort show the sustained clinical efficacy and safety of autologous CD34+ hematopoietic stem-cell lentiviral gene therapy for ADA-SCID, indicating that it is a curative treatment.

25COASDEC25

Title: Mass Administration of Azithromycin to Infants in Mali to Reduce Mortality

Fadima Cheick Haidara, M.D., Laura Adubra, Ph.D.

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Abstract: Mass administration of azithromycin to children 1 to 59 months of age has been shown to reduce mortality among infants and children in this age group in some areas of sub-Saharan Africa. The largest effects have appeared to be among infants younger than 12 months of age, within 3 months after treatment; this observation motivated the design of the current trial. Methods- In this trial, we randomly assigned villages in Mali, West Africa, in a 3:4:2 ratio to receive distributions of placebo, azithromycin two times a year, or azithromycin four times a year. Infants 1 to 11 months of age received, in doses of 20 mg per kilogram of body weight, placebo every 3 months (control group); azithromycin at two quarterly visits from January through June and placebo at two quarterly visits from July through December (twice-yearly azithromycin group); or azithromycin every 3 months (quarterly azithromycin group). The primary outcome was death within 3 months after eligibility had been confirmed, analyzed in the intention-to-treat population. Results- From December 2020 through December 2022, a total of 1151 villages were enrolled in the trial; 386 villages were randomly assigned to the control group, 511 to the twice-yearly azithromycin group, and 254 to the quarterly azithromycin group. Among all the villages, 149,090 infants received at least one dose of placebo or azithromycin, with a total of 82,600 person-years of follow-up; 968 deaths were recorded. Mortality was 11.9 deaths per 1000 person-years at risk in the control group, 11.8 deaths per 1000 person-years in the twice-yearly azithromycin group (incidence rate ratio, 1.00; 95% confidence interval [CI], 0.83 to 1.19), and 11.3 deaths per 1000 person-years in the quarterly azithromycin group (incidence rate ratio, 0.93; 95% CI, 0.75 to 1.15). Adverse events were rare, and the percentages of infants with adverse events were similar in

the three groups. Mortality among untreated children 12 to 59 months of age was similar across groups. Conclusions- Mass administration of azithromycin in Mali, limited to infants 1 to 11 months of age, did not result in lower infant or child mortality than placebo, regardless of whether azithromycin was delivered twice yearly or quarterly.

25COASDEC26

Title: Hypertonic Saline or Carbocisteine in Bronchiectasis

Judy M. Bradley, Ph.D.

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Abstract: Bronchiectasis guidelines are inconsistent with regard to the effectiveness of mucoactive agents, and their use varies geographically. Large trials are needed to assess safety and effectiveness. Methods- For this open-label, randomized, two-by-two factorial trial at 20 sites in the United Kingdom, we enrolled participants with non–cystic fibrosis bronchiectasis who had frequent pulmonary exacerbations and daily sputum production. Current smokers and persons who had recently received mucoactive treatments were excluded. All participants received standard care and were also assigned either to one of three mucoactive-drug groups — hypertonic saline (the hypertonic-saline group), hypertonic saline and carbocisteine (the combination group), or carbocisteine (the carbocisteine group) — or to standard care alone. The comparisons were between hypertonic saline and no hypertonic saline and between carbocisteine and no carbocisteine, with each category consisting of two groups. The primary outcome was the number of pulmonary exacerbations over a 52-week period. Key secondary outcomes were scores on disease-specific health-related quality-of-life assessments, time to next pulmonary exacerbation, and safety. Results- A total of 288 participants underwent randomization. No treatment interactions were found. The mean number of adjudicated fully qualifying pulmonary exacerbations over the 52-week period was 0.76 (95% confidence interval [CI], 0.58 to 0.95) with hypertonic saline as compared with 0.98 (95% CI, 0.78 to 1.19) with no hypertonic saline (adjusted between-group difference in the means, −0.25 [95% CI, −0.57 to 0.07; P=0.12]) and 0.86 (95% CI, 0.66 to 1.06) with carbocisteine as compared with 0.90 (95% CI, 0.70 to 1.09) with no carbocisteine (adjusted between-group difference in the means, −0.04 [95% CI, −0.36 to 0.28; P=0.81]). Secondary outcomes and the incidence of adverse events, including serious adverse events, were similar across the groups. Conclusions- In participants with bronchiectasis, neither hypertonic saline nor carbocisteine significantly reduced the mean incidence of pulmonary exacerbations over a period of 52 weeks.

25COASDEC27

Title: Aspirin in Patients with Chronic Coronary Syndrome Receiving Oral Anticoagulation

Gilles Lemesle, M.D., Ph.D.

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Abstract: The appropriate antithrombotic regimen for patients with chronic coronary syndrome who are at high atherothrombotic risk and receiving long-term oral anticoagulation remains unknown. Methods- We conducted a multicenter, double-blind, randomized,

placebo-controlled trial in France involving patients with chronic coronary syndrome who had undergone a previous stent implantation (>6 months before enrollment) and were at high atherothrombotic risk and currently receiving long-term oral anticoagulation. The patients were randomly assigned in a 1:1 ratio to receive aspirin (100 mg once daily) or placebo; all the patients continued to receive their current oral anticoagulation therapy. The primary efficacy outcome was a composite of cardiovascular death, myocardial infarction, stroke, systemic embolism, coronary revascularization, or acute limb ischemia. The key safety outcome was major bleeding. Results- A total of 872 patients underwent randomization; 433 were assigned to the aspirin group, and 439 to the placebo group. The trial was stopped early at the advice of the independent data and safety monitoring board after a median follow-up of 2.2 years because of an excess of deaths from any cause in the aspirin group. A primary efficacy outcome event occurred in 73 patients (16.9%) in the aspirin group and in 53 patients (12.1%) in the placebo group (adjusted hazard ratio, 1.53; 95% confidence interval [CI], 1.07 to 2.18; P=0.02). Death from any cause occurred in 58 patients (13.4%) in the aspirin group and in 37 (8.4%) in the placebo group (adjusted hazard ratio, 1.72; 95% CI, 1.14 to 2.58; P=0.01). Major bleeding occurred in 44 patients (10.2%) in the aspirin group and in 15 patients (3.4%) in the placebo group (adjusted hazard ratio, 3.35; 95% CI, 1.87 to 6.00; P<0.001). A total of 467 and 395 serious adverse events were reported in the aspirin group and placebo group, respectively.Conclusions- Among patients with chronic coronary syndrome at high atherothrombotic risk who were receiving an oral anticoagulant, the addition of aspirin led to a higher risk of cardiovascular death, myocardial infarction, stroke, systemic embolism, coronary revascularization, or acute limb ischemia than placebo, as well as higher risks of death from any cause and major bleeding.

25COASDEC28

Title: Common Diseases in Clinical Cohorts — Not Always What They Seem

Fedik Rahimov, Ph.D.

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Abstract: Misdiagnosis or underdiagnosis of rare diseases in patients with diagnoses of common diseases can lead to delayed or inappropriate treatments, thereby complicating the management of both rare and common conditions. Despite advances in molecular diagnostic techniques, the effect of rare diseases on the diagnosis of common diseases in research and clinical trials has not been comprehensively investigated. Methods- We used exome- and genome-sequencing data from participants in the U.K. Biobank, a research study, and five clinical trials involving patients who had received a primary diagnosis of multiple sclerosis, inflammatory bowel disease, or atopic dermatitis to assess the incidence of monogenic rare diseases that often manifest with clinical symptoms overlapping with those of these common diseases. Results- We identified 153 U.K. Biobank participants who carried a rare variant that contributes to a molecular diagnosis of a monogenic disorder — 53 of 1850 (2.86%) with a diagnosis of multiple sclerosis, 75 of 6681 (1.12%) with a diagnosis of inflammatory bowel disease, and 25 of 998 (2.50%) with a diagnosis of atopic dermatitis. We replicated the findings regarding such rare disease–causing variants in two independent cohorts — one including patients with a diagnosis of multiple sclerosis, and the other patients with a diagnosis of inflammatory bowel disease — who had undergone genome sequencing for

research and for clinical trials, respectively. By combining genome and transcriptome analyses, we showed that molecular diagnosis can potentially elucidate mechanisms of inadequate response to therapeutic intervention. Conclusions- Our study shows the value of systematic genome sequencing in understanding the phenotypic heterogeneity of common diseases and identifying failure to diagnose rare diseases and highlights the benefits of deep molecular phenotyping in clinical trials and patient care.

25COASDEC29

Title: Sotatercept for Pulmonary Arterial Hypertension within the First Year after Diagnosis

Vallerie V. McLaughlin, M.D., Marius M. Hoeper, M.D., Ph.D

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Abstract: Sotatercept, an activin-signaling inhibitor, reduces morbidity and mortality among patients with long-standing pulmonary arterial hypertension. Its effects in patients with pulmonary arterial hypertension within the first year after diagnosis are unclear. Methods- In this phase 3 trial, we enrolled adult patients with World Health Organization functional class II or III pulmonary arterial hypertension who had received the diagnosis less than 1 year earlier, had an intermediate or high risk of death, and were receiving double or triple therapy. Patients were randomly assigned to receive add-on therapy with subcutaneous sotatercept (starting dose, 0.3 mg per kilogram of body weight; escalated to target dose, 0.7 mg per kilogram) or placebo every 21 days. The primary end point was clinical worsening, a composite of death from any cause, unplanned hospitalization lasting at least 24 hours for worsening of pulmonary arterial hypertension, atrial septostomy, lung transplantation, or deterioration in performance in exercise testing due to pulmonary arterial hypertension, assessed in a time-to-first-event analysis. Results -The trial was stopped early owing to loss of clinical equipoise after the reporting of positive results from previous sotatercept trials. A total of 320 patients were included (160 each in the sotatercept and placebo groups). The median duration of follow-up was 13.2 months. At least one primary end-point event occurred in 17 patients (10.6%) in the sotatercept group and in 59 patients (36.9%) in the placebo group (hazard ratio, 0.24; 95% confidence interval, 0.14 to 0.41; P<0.001). Deterioration in performance in exercise testing due to pulmonary arterial hypertension occurred in 8 patients (5.0%) in the sotatercept group and in 46 patients (28.8%) in the placebo group; unplanned hospitalization for worsening of pulmonary arterial hypertension occurred in 3 patients (1.9%) and 14 patients (8.8%), respectively; and death from any cause occurred in 7 patients (4.4%) and 6 patients (3.8%). No cases of atrial septostomy or lung transplantation occurred. The most common adverse events with sotatercept were epistaxis (31.9%) and telangiectasia (26.2%).Conclusions- Among adults with pulmonary arterial hypertension who had received the diagnosis less than 1 year earlier, the addition of sotatercept to therapy resulted in a lower risk of clinical worsening than placebo.

25COASDEC30

Title: Association of 2024–2025 Covid-19 Vaccine with Covid-19 Outcomes in U.S. Veterans

Miao Cai, Ph.D.

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Abstract: Amid the declining clinical severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and diminishing public uptake of annual coronavirus disease 2019 (Covid-19) vaccines, contemporary evidence on vaccine effectiveness against clinically relevant outcomes is needed. Methods- We conducted an observational study that used the electronic health records of the Department of Veterans Affairs to evaluate the effectiveness of the 2024–2025 Covid-19 vaccine among veterans who received the Covid-19 and influenza vaccines on the same day (164,132 participants) and in an active-comparator group of veterans who received the influenza vaccine only (131,839 participants), between September 3 and December 31, 2024. Participants were followed for 180 days or until the occurrence of an outcome, whichever came first. We used inverse-probability–weighted models to estimate vaccine effectiveness (calculated as 1 minus the risk ratio) against Covid-19–associated emergency department visits, hospitalizations, and deaths at 6 months. Results- At 6 months of follow-up, the estimated vaccine effectiveness was 29.3% (95% confidence interval [CI], 19.1 to 39.2) against Covid-19–associated emergency department visits (risk difference per 10,000 persons, 18.3; 95% CI, 10.8 to 27.6), 39.2% (95% CI, 21.6 to 54.5) against Covid-19–associated hospitalizations (risk difference per 10,000 persons, 7.5; 95% CI, 3.4 to 13.0), and 64.0% (95% CI, 23.0 to 85.8) against Covid-19–associated deaths (risk difference per 10,000 persons, 2.2; 95% CI, 0.5 to 6.9). Vaccine effectiveness against a composite of these outcomes was 28.3% (95% CI, 18.2 to 38.2), with a risk difference per 10,000 persons of 18.2 (95% CI, 10.7 to 27.5). The Covid-19 vaccine was associated with decreased risks of these outcomes across prespecified subgroups defined according to age (<65 years, 65 to 75 years, and >75 years), the presence or absence of major coexisting conditions, and immunocompetence status. Conclusions- In this national cohort of U.S. veterans, the receipt of the 2024–2025 Covid-19 vaccine was associated with decreased risks of severe clinical outcomes.

25COASDEC31

Title: European Study of Prostate Cancer Screening — 23-Year Follow-up

Monique J. Roobol, Ph.D.

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Abstract: The European Randomized Study of Screening for Prostate Cancer (ERSPC) was initiated in 1993 to assess the effect of prostate-specific antigen (PSA) testing on prostate cancer mortality. Because deaths from prostate cancer are expected to rise worldwide owing to increased life expectancy and population growth, a final analysis of the long-term outcomes of prostate cancer screening is essential to understanding the benefits and harms of PSA testing. Methods- We updated the findings from ERSPC, a multicenter, randomized study conducted across eight European countries with a focus on a predefined core age group of 162,236 men who were 55 to 69 years of age at the time of randomization. Participants were randomly assigned to the screening group and offered repeated PSA testing or to the control group and not invited for screening. The primary outcome was prostate cancer mortality. Results- After a median follow-up of 23 years, prostate cancer mortality was 13% lower in the screening group (rate ratio, 0.87; 95% confidence interval [CI], 0.80 to 0.95),

and the absolute risk reduction was 0.22% (95% CI, 0.10 to 0.34). The cumulative incidence of prostate cancer was higher in the screening group than in the control group (rate ratio, 1.30; 95% CI, 1.26 to 1.33). At a median of 23 years of follow-up, one death from prostate cancer was prevented for every 456 men (95% CI, 306 to 943) who were invited for screening, and one death from prostate cancer was averted for every 12 men (95% CI, 8 to 26) in whom prostate cancer was diagnosed, as compared with one death from prostate cancer prevented for every 628 men (95% CI, 419 to 1481) and one death averted for every 18 men (95% CI, 12 to 45) at 16 years of follow-up. Conclusions- Long-term follow-up confirms a sustained reduction in deaths from prostate cancer with PSA testing, alongside an improved harm–benefit ratio. Future screening strategies should adopt risk-based approaches to minimize overdiagnosis while maintaining clinical benefits.

25COASDEC32

Title: Overall Survival with Amivantamab–Lazertinib in *EGFR*-Mutated Advanced NSCLC

James Chih-Hsin Yang, M.D., Ph.D

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Abstract: Previous results from this phase 3 trial showed that progression-free survival among participants with previously untreated *EGFR* (epidermal growth factor receptor)–mutated advanced non–small-cell lung cancer (NSCLC) was significantly improved with amivantamab–lazertinib as compared with osimertinib. Results of the protocol-specified final overall survival analysis in this trial have not been reported. Methods- We randomly assigned, in a 2:2:1 ratio, participants with previously untreated *EGFR*-mutated (exon 19 deletion or L858R substitution), locally advanced or metastatic NSCLC to receive amivantamab–lazertinib, osimertinib, or lazertinib. Overall survival (assessed in an analysis of the time from randomization to death from any cause) in the amivantamab–lazertinib group as compared with the osimertinib group was a key secondary end point. Additional end points included safety. Results- A total of 429 participants each were assigned to receive amivantamab–lazertinib or osimertinib. Over a median follow-up of 37.8 months, amivantamab–lazertinib led to significantly longer overall survival than osimertinib (hazard ratio for death, 0.75; 95% confidence interval, 0.61 to 0.92; P=0.005); 3-year overall survival was 60% and 51%, respectively. At the clinical cutoff date, 38% of participants in the amivantamab–lazertinib group and 28% in the osimertinib group were still receiving the assigned treatment. Adverse events of grade 3 or higher were more common with amivantamab–lazertinib (in 80% of participants) than with osimertinib (in 52%), particularly skin-related events, venous thromboembolism, and infusion-related events; these findings were consistent with the established safety profile of each treatment. No new safety signals were observed with additional follow-up. Conclusions- Amivantamab–lazertinib led to significantly longer overall survival among participants with previously untreated *EGFR*-mutated advanced NSCLC than osimertinib but was associated with an increased risk of adverse events of grade 3 or higher.

25COASDEC33

Title: A Randomized Trial of Physical Therapy for Meniscal Tear and Knee Pain

Jeffrey N. Katz, M.D., Jamie E. Collins, Ph.D
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Abstract: Physical therapy is routinely recommended for knee pain attributed to a degenerative meniscal tear, but its efficacy has not been established. Methods- We randomly assigned participants 45 to 85 years of age with knee pain, osteoarthritis, and meniscal tear to one of four groups: home exercise (3-month home-exercise program), home exercise plus text messages to encourage exercise adherence, home exercise plus text messages plus sham physical therapy (in-clinic sham manual therapy and sham ultrasound therapy), and home exercise plus text messages plus standard physical therapy (supervised strengthening, functional, and stretching exercises and manual therapy). The primary outcome was the change in the Knee Injury and Osteoarthritis Outcome Score (KOOS) pain subscore (range, 0 to 100, with higher scores indicating more pain) between baseline and 3 months, with adjustment for trial site, baseline KOOS pain subscore, and radiographic grade. Results- A total of 879 participants underwent randomization (mean [±SD] age, 59.2±7.8 years). The difference in the 3-month change in the KOOS pain subscore between home exercise and home exercise plus text messages was −0.1 points (98.3% confidence interval [CI], −3.8 to 3.7) and between home exercise and home exercise plus text messages plus standard physical therapy was 2.5 points (98.3% CI, −1.3 to 6.2); the difference between home exercise plus text messages and home exercise plus text messages plus standard physical therapy was 2.5 points (98.3% CI, −1.4 to 6.5). Adverse events were generally nonserious and evenly distributed overall across groups. Conclusions- For patients with degenerative meniscal tear and knee pain, the addition of physical therapy or text messages to encourage adherence to home exercises was not superior in reducing pain to a home-exercise program alone.

25COASDEC34

Title: Safety, Efficacy, and Immunogenicity of a Salmonella Paratyphi A Vaccine

Naina McCann, M.R.C.P.
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https://doi.org/10.1056/NEJMoa2502992
Abstract: *Salmonella enterica* serovar Paratyphi A (also known as S. Paratyphi A) is responsible for more than 2 million cases of enteric fever annually. There are no licensed vaccines against S. Paratyphi A. Methods- In a double-blind, randomized, placebo-controlled trial, we evaluated an orally administered live, attenuated S. Paratyphi A vaccine (CVD 1902) using a controlled human infection model. Healthy U.K. adults were assigned in a 1:1 ratio to receive two doses of CVD 1902 or placebo 14 days apart. Twenty-eight days after the second dose, participants were challenged orally with S. Paratyphi A. The primary end point was a diagnosis of S. Paratyphi A infection within 14 days after challenge. Secondary end points included safety and immunogenicity. Results- A total of 72 participants underwent randomization, of whom 34 in the CVD 1902 group and 36 in the placebo group were challenged with S. Paratyphi A. The median age of the participants was 32 years (range, 20 to 54), and 46% were women. The number of adverse events was generally similar in the two groups, and no vaccine-related serious adverse events were identified. CVD 1902 induced serum IgG and IgA responses to the O antigen of S. Paratyphi A. No increases in serum IgG or IgA titers occurred in the placebo group. In the intention-to-treat population, an S.

Paratyphi A infection was diagnosed within 14 days after challenge in 21% of the participants in the CVD 1902 group and in 75% of those in the placebo group (P<0.001), resulting in a vaccine efficacy of 73% (95% confidence interval [CI], 46 to 86). The vaccine efficacy was 69% (95% CI, 42 to 84) in the per-protocol analysis. Conclusions- In healthy U.K. adults who were challenged with S. Paratyphi A in a controlled human infection model, a two-dose series of CVD 1902 led to protection against S. Paratyphi A infection without safety concerns.

25COASDEC35

Title: Ten-Year Survival after Postmastectomy Chest-Wall Irradiation in Breast Cancer

Ian H. Kunkler, F.R.C.R., Nicola S. Russell, M.D., Ph.D.

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Abstract: The role of postmastectomy chest-wall irradiation in patients with breast cancer classified as pN1 (with involvement of one to three axillary nodes) or pN0 (pathologically node negative) with additional risk factors is uncertain. Methods- In this international, phase 3, randomized trial, we evaluated the omission of chest-wall irradiation in women with "intermediate-risk" breast cancer — defined as cancer that was stage pT1N1, pT2N1, or pT3N0 or stage pT2N0 with a histologic grade of 3, lymphovascular invasion, or both (tumor size: T1, ≤2 cm; T2, >2 cm to 5 cm; or T3, >5 cm) — that was treated with mastectomy, an axillary procedure, and systemic therapy. Patients were assigned to undergo chest-wall irradiation (40 to 50 Gy; the irradiation group) or not to undergo chest-wall irradiation (the no-irradiation group). The primary end point was overall survival, with 10 years of follow-up. Chest-wall recurrence, regional recurrence, disease-free survival, distant metastasis–free survival, causes of death, and radiation-related adverse events were also assessed. Results- The intention-to-treat population included 808 patients in the irradiation group and 799 in the no-irradiation group. The median follow up was 9.6 years. Overall survival was 81.4% with chest-wall irradiation and 81.9% with no chest-wall irradiation according to 10-year Kaplan–Meier estimates (hazard ratio for death, 1.04; 95% confidence interval [CI], 0.82 to 1.30; P=0.80). A total of 29 patients had a chest-wall recurrence — 9 (1.1%) in the irradiation group and 20 (2.5%) in the no-irradiation group (between-group difference, <2 percentage points; hazard ratio, 0.45; 95% CI, 0.20 to 0.99). Disease-free survival was 76.2% in the irradiation group and 75.5% in the no-irradiation group (hazard ratio for recurrence or death, 0.97; 95% CI, 0.79 to 1.18), and distant metastasis–free survival was 78.2% and 79.2%, respectively (hazard ratio for distant metastasis or death, 1.06; 95% CI, 0.86 to 1.31). Conclusions- In this trial, chest-wall irradiation did not result in higher overall survival than no chest-wall irradiation among patients with intermediate-risk, early breast cancer treated with mastectomy and contemporary adjuvant systemic therapy.

25COASDEC36

Title: Oral Icotrokinra for Plaque Psoriasis in Adults and Adolescents

Robert Bissonnette, M.D., Jennifer Soung, M.D.

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Abstract: Icotrokinra, a targeted oral peptide that selectively binds the interleukin-23 receptor, is under investigation for the treatment of plaque psoriasis. Methods- We conducted a phase 3, double-blind, randomized, placebo-controlled trial involving adults and adolescents (≥12 years of age) with moderate-to-severe plaque psoriasis, as defined by all the following: a total body-surface area of psoriasis involvement of at least 10%, a Psoriasis Area and Severity Index (PASI) score of at least 12 (range, 0 to 72, with higher scores indicating a greater extent or severity of psoriasis), and an Investigator's Global Assessment (IGA) score of at least 3 (range, 0 [clear skin] to 4 [severe disease]). Participants were assigned in a 2:1 ratio to receive icotrokinra at a dose of 200 mg once daily through week 24 or placebo through week 16 followed by transition to icotrokinra. The coprimary end points were an IGA 0/1 response (IGA score of 0 or 1 with ≥2-point reduction from baseline) and a PASI 90 response (≥90% reduction from baseline in the PASI score) at week 16 Results-A total of 684 participants underwent randomization (456 to the icotrokinra group and 228 to the placebo group). At week 16, a total of 65% of the participants receiving icotrokinra and 8% of those receiving placebo had an IGA 0/1 response, and 50% and 4%, respectively, had a PASI 90 response (P<0.001 for both comparisons). Complete clearance of skin at week 16 was significantly more likely with icotrokinra than with placebo (IGA score of 0, 33% vs. 1%; PASI 100 response [100% reduction from baseline in the PASI score], 27% vs. <1%; P<0.001 for both comparisons). The percentage of participants with at least one adverse event through week 16 was 49% in each group; the most common adverse events in each group were nasopharyngitis and upper respiratory tract infection. The exposure-adjusted incidence of adverse events was consistent through week 24. Conclusions- Selective blockade of the interleukin-23 receptor with the targeted oral peptide icotrokinra resulted in a significantly higher incidence of skin clearance at week 16 than placebo among adults and adolescents with moderate-to-severe plaque psoriasis. Longer-term data will provide a more complete understanding of the benefit–risk profile of icotrokinra.

25COASDEC37

Title: Sevabertinib in Advanced *HER2*-Mutant Non–Small-Cell Lung Cancer

Xiuning Le, M.D., Ph.D., Tae Min Kim, M.D., Ph.D et.al.

Abstract: *HER2* gene mutations occur in 2 to 4% of patients with non–small-cell lung cancer (NSCLC). Sevabertinib is an oral, reversible tyrosine kinase inhibitor that has shown anti-HER2 activity in preclinical models. Methods- We conducted an open-label, multicenter, multicohort, phase 1–2 study to evaluate sevabertinib at a twice-daily dose of 20 mg in patients with locally advanced or metastatic *HER2*-mutant NSCLC. Three cohorts were defined according to previous therapy: cohort D comprised previously treated patients who had not received HER2-targeted therapy; cohort E, patients who had previously received HER2-directed antibody–drug conjugates; and cohort F, patients who had not previously received treatment. The primary end point was an objective response, as assessed by blinded independent central review. Secondary end points were duration of response and progression-free survival. Results- A total of 209 patients received sevabertinib (as of June 27, 2025, the data-cutoff date); the median duration of follow-up was 13.8 months in cohort D, 11.7 months in cohort E, and 9.9 months in cohort F. Among 81 patients in cohort D, an objective response was observed in 64% (95% confidence interval [CI], 53 to 75); the median duration of response was 9.2 months (95% CI, 6.3 to 13.5), and the median progression-free survival

was 8.3 months (95% CI, 6.9 to 12.3). Among 55 patients in cohort E, an objective response was observed in 38% (95% CI, 25 to 52); the median duration of response was 8.5 months, and the median progression-free survival was 5.5 months. Among 73 patients in cohort F, an objective response was observed in 71% (95% CI, 59 to 81), and the median duration of response was 11.0 months; data on progression-free survival were immature. Grade 3 or higher drug-related adverse events occurred in 31% of the patients. The most common adverse event was diarrhea (in 84 to 91%), with diarrhea of grade 3 or higher occurring in 5 to 23%. Treatment was discontinued by 3% of the patients owing to drug-related adverse events. Conclusions- Sevabertinib showed antitumor activity in patients with locally advanced or metastatic *HER2*-mutant NSCLC. Diarrhea was the most common adverse event.

25COASDEC38

Title: Association of serum metabolites and breast cancer risk: A population-based case–control study in black urban South African women

Yahya Mahamat-Saleh

International Journal of Cancer, Volume157, Issue8

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Abstract: The incidence of breast cancer has been steadily increasing in South Africa over the past decades, but this rise can only be partially attributed to changes in known modifiable risk factors. Metabolomics may help to elucidate novel biological pathways and identify potential biomarkers associated with cancer. We investigated the association between serum metabolites and breast cancer risk in black women from Soweto, South Africa. An untargeted ultra-high-performance LC–MS method was used to measure molecular features in serum samples from a total of 396 breast cancer cases and 396 population-based controls matched on age and demographic settings, enrolled in the South African Breast Cancer study. A total of 5820 features were detected from metabolomics analyses and 1732 were retained for statistical analysis after data pre-processing and imputation. Multivariable conditional logistic regression was used to estimate odds ratios (ORs) and false discovery rate-adjusted (FDR) confidence interval (CI) for the association of metabolite features and breast cancer risk. Overall, 12 molecular features were significantly associated with odds of breast cancer (FDR <0.05); 11 features were associated with increased odds of breast cancer, and 1 feature was associated with decreased odds of breast cancer. Of these, 7 metabolic features corresponding to 3 individual metabolites were identified. Serum levels of cortisol (OR = 1.63, 95% CI = 1.18-2.25 per 1 SD increase), kynurenine (OR = 1.38, 95% CI = 1.01-1.88), and octenoylcarnitine (OR = 1.46, 95% CI = 1.02-2.08) were associated with higher odds of breast cancer. This study suggests that metabolic pathways related to cortisol, kynurenine, and carnitine metabolism may play a role in black African women with breast cancer. These results need to be explored in prospective studies.

25COASDEC39

Title: Maternal hormonal contraceptive use and childhood central nervous system tumor risk in a large Scandinavian cohort

Caroline H. Hemmingsen

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Abstract: An association between maternal hormonal contraception use and childhood central nervous system (CNS) tumors has been suggested, but findings are inconclusive. This population-based cohort study includes Scandinavian nationwide registry data on liveborn children (1996–2018). Children were followed from birth until CNS tumor (<20 years) or censoring (other cancer, emigration, death, 20th birthday, or end of follow-up in 2017–2020). Cox proportional hazards models estimated hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the association between maternal hormonal contraception use (any type, type-specific) and CNS tumor risk (any, any malignant, type-specific). Maternal use was categorized as "recent use" (0–3 months before or during pregnancy, except for non-oral progestin-only types), "previous use" (before recent use), and "no use". A total of 3,183,316 children were followed for 29,455,528 person-years, during which time 1384 children developed a CNS tumor (610 malignant). Compared with no use, maternal previous or recent use of any hormonal contraception (HR 0.93, 95% CI 0.82–1.05; HR 0.99, 95% CI 0.83–1.19), combined and progestin-only types (oral, non-oral), were not associated with childhood CNS tumor risk. However, maternal recent progestin-only injection use was associated with malignant childhood CNS tumors (HR 3.95, 95CI % 1.46–10.68), compared with no use (number needed to harm: 1 per 14,577 person-years). In conclusion, no association was found between maternal use of common types of hormonal contraception and CNS tumors in children. The rarely used progestin-only injections (medroxyprogesterone acetate) were associated with malignant CNS tumor risk in children, though based on few children.

25COASDEC40

Title: Future of population-based cancer registries: A global perspective—A survey of population-based cancer registries

Liesbet J. Van Eycken

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Abstract: Population-Based Cancer Registries (PBCRs) play a fundamental role in cancer control. They collect data to compile information on the occurrence, extent, and outcome of cancer in geographically defined populations. Whilst the basic reporting on cancer incidence and survival by cancer type is extremely useful, other prognostic factors including stage, biomarkers, comorbidities, treatment, and socio-economic parameters are crucial to evaluate, understand, and ultimately reduce the variation of outcomes observed in different populations. To explore current data collection practices of the PBCRs worldwide and comprehend their challenges and future directions, we conducted a web-based survey in collaboration with the Global Initiative for Cancer Registry Development (GICR) led by the International Agency for Research on Cancer (IARC), the International Association of Cancer Registries (IACR), and the North American Association of Central Cancer Registries (NAACCR). Of the 268 invited PBCRs, 141 PBCRs responded to our survey. Although almost all PBCRs reported collecting the basic variables for each cancer (incidence date, basis of diagnosis, topography, morphology and tumour behaviour), fewer collect date of death, stage, treatment, biomarkers, and socio-economic parameters, this issue being more pronounced in LMIC. Most PBCRs confirmed reporting on cancer incidence, but only 60%

publish survival results. Other outcomes such as recurrence and patient-reported outcome measures were rarely available. There is a clear need for development and sustained support to maximize the PBCRs' ability to collect data and/or expand coverage area, ideally through significant investment in legislation, financial, human, and technological resources to secure and optimize their potential in cancer control.

25COASDEC41

Title: Plasma proteomic profiles for early detection and risk stratification of non-small cell lung carcinoma: A prospective cohort study with 52,913 participants

Renjia Zhao

International Journal of Cancer, Volume157, Issue8
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Abstract: Early detection of non-small cell lung cancer (NSCLC) can improve survival rates, and plasma proteomics may provide effective tools for risk prediction. The population for this study included 52,913 participants and 2911 plasma proteomics from UK Biobank. The cohort was divided into discovery and validation cohorts based on their countries. Cox regression, XGBoost, and SHAP analysis were used to identify key NSCLC-associated proteins. Machine learning (ML) models were developed and validated across different timeframes. Risk stratification was performed using protein levels. Temporal change analysis and two-sample Mendelian Randomization (MR) were conducted to assess the early prediction ability and causal relationships, respectively. Twenty-five proteins were significantly associated with NSCLC. ML identified CXCL17, CEACAM5, and WFDC2 as having the highest predictive power. The three-protein panel plus epidemiological indicators exhibited superior performance in 5- and 10-year predictions, achieving AUROC of 0.904 (95%CI: 0.839–0.968) and 0.873 (95%CI: 0.815–0.931), respectively. Risk stratification identified a high-risk group with a 9.18-fold higher risk than the general population and a 16.75-fold higher risk than the low-risk group, respectively. Temporal change analysis revealed that protein expression levels in cases were globally higher than in controls up to 10 years before diagnosis. MR implied a suggestive causal relationship between CXCL17 and NSCLC. Our findings suggest three plasma proteins possess robust predictive capabilities for NSCLC, allowing for predictions up to 10 years in advance. Incorporating these biomarkers into risk models enhances early detection, providing a foundation for targeted screening and precision medicine in NSCLC.

25COASDEC42

Title: Global trends in the incidence of cancer attributable to human papillomavirus infection: A population-based study

Tian Tian

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https://doi.org/10.1002/ijc.35520

Abstract: Human papillomavirus (HPV) plays a significant role in cancers of the head, neck, and anogenital areas. This study aimed to estimate the burden and trends of HPV-related cancers in 44 selected countries from 1990 to 2017. Data on cancers attributable to HPV infection from 1990 to 2017 were extracted from the Cancer Incidence in Five Continents (CI5) plus database. The population-attributable fraction (PAF), age-standardised incidence

rates (ASIR), and average annual percentage change (AAPC) were analyzed to identify trends. From 1990 to 2017, 3,560,554 new HPV-attributed cancer cases were recorded across 44 countries, with an ASIR of 4.6 per 100,000 population. Site-specific ASIRs were: cervical (5.8), penile (1.2), vulvar (4.0), vaginal (1.5), anal (1.9), oropharyngeal (3.1), oral (1.3), and laryngeal (1.4). While ASIRs decreased in most countries, significant increases occurred in China, Uganda, and Latvia. HPV-related cancers remain a global health challenge with marked regional variations.

25COASDEC43

Title: The potential role of environmentally associated DNA methylation in childhood acute lymphoblastic leukaemia subtypes

Jessica R. Saville

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Abstract: Various genetic aberrations are suggested to initiate the development of acute lymphoblastic leukaemia (ALL) but alone are insufficient for disease onset. Epigenetic alteration, such as DNA methylation changes, plays a key role in human health. Evidence suggests DNA methylation may be an intermediate mechanism through which the environment contributes to ALL manifestation. ALL is categorized into subtypes based on leukaemia-associated genetic events, and it is plausible that different exposures pose differing risks for given subtypes. Using our previously established meet-in-the-middle approach, we performed CpG-level analysis to investigate DNA methylation as an intermediate mechanism between risk exposures and ALL. Differentially methylated CpGs (DMCs) were integrated, identifying overlapping methylation, with hypergeometric tests used to assess the probability of concurring methylation considering directionality. DMC analysis reinforced previous gene-level findings suggesting altered DNA methylation associated with maternal radiation exposure, alcohol intake, and plasma folate during pregnancy is also present in the disease. Whilst maternal folate-associated and leukaemia-associated methylation appear consistent across most subtypes, the effect of other exposures appears subtype-specific. We suggest environmentally associated methylation includes driver and/or 'navigator' changes, the latter influencing biological pathways contributing to ALL. This analysis aids understanding of which risk factors may contribute to specific subtypes or which influence ALL risk more generally.

25COASDEC44

Title: Managing hydrocephalus in patients with leptomeningeal disease: A multicenter retrospective analysis

Obada T. Alhalabi

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Abstract: Leptomeningeal disease (LMD) represents a terminal condition of tumor cell seeding that can cause symptomatic hydrocephalus. With improved survival rates under systemic therapy, the role of cerebrospinal fluid (CSF) drainage through ventriculo-peritoneal shunt (VPS) or Rickham reservoir (RR) placement in LMD patients is gaining more relevance. This study aimed to compare outcomes of both modalities in a multicentric

contemporary cohort. A retrospective analysis of medical charts in patients receiving VPS for LMD and malresorptive hydrocephalus in two neurosurgical centers between 2006 and 2021 yielded 64 patients. The most common underlying oncological conditions were breast ($n = 32$, 49%) and non-small cell lung cancer (NSCLC, $n = 16$, 25%). The median time between primary and LMD diagnosis was 23.3 months (11.2 to 43.4 months). Symptoms of intracranial hypertension were relieved in 79% of cases ($n = 50$) after shunting, with 42 (66%) and 32 patients (50%) receiving systemic and intrathecal therapy, respectively. A further multicenter analysis comparing patients receiving VPS with patients receiving RR (with regular tapping) included 155 patients (VPS: $n = 80$, 52%; RR: $n = 75$, 48%). Compared to VPS, RRs were associated with a lower surgical revision rate (8% vs. 24%, $p = 0.009$). There was no difference in median overall survival in VPS patients (118 days) compared to RR patients (80 days, $p = 0.180$). Given this data showing a short and comparable survival of patients under both modalities with a lower RR complication rate, a rationale for an initial Rickham implantation in LMD patients with hydrocephalus, with later VPS conversion for long-term surviving patients, could be contemplated.

25COASDEC45

Title: Performance of thermoablation among women treated for high-risk human papillomavirus in a screen-and-treat program in South Africa

Melanie Jenkins

International Journal of Cancer, Volume157, Issue8

https://doi.org/10.1002/ijc.35519

Abstract: Thermal ablation is a simple treatment option for HPV-associated, pre-cancerous disease, has a low risk of complications and can be undertaken by non-specialists. For these reasons, it is one of the recommended treatment modalities for cervical cancer screening programs. As part of a screen-and-treat demonstration study, 3060 women living with and without HIV, aged 30–65 years, were recruited at an urban site in South Africa. HPV testing stratified the population into those at highest risk for precancerous disease, identifying 529 (17.3%) women with high HPV viral loads on select HPV genotypes and multi-channel infections indicating their need for treatment. Among this group, visual assessment criteria further stratified this at-risk population into those suitable versus unsuitable for ablative therapy. 483 (91.3%) of 529 women met visual criteria defining their suitability for ablative treatment and all were treated with thermoablation. Women were followed at 6- and 12-months where HPV testing and colposcopy with histological sampling were performed. HPV persistence at 12 months despite treatment was 51.8%, and detection of histologically confirmed cervical intraepithelial neoplasia grade 2 or higher occurred in 24.0%. Being HIV-positive, older age, multi-channel infection, high HPV viral load, and low CD4 count were associated with these indicators of treatment failure. Cervical cancer screening programs that target treatment to the highest risk women are likely to observe higher indicators of treatment failure than less focused programs. Although thermoablation is an approved treatment modality, our results highlight the urgency of finding more effective but safe and practical treatment options for precancerous disease.

25COASDEC46

Title: Preeclampsia and risk of breast cancer: A longitudinal cohort study of tumor histology

Shu Qin Wei

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Abstract: Patients with preeclampsia have a reduced risk of breast cancer, but it is not clear if the protective effect extends to all types of breast tumors. Our objective was to determine the association of preeclampsia with ductal, lobular, and other breast cancer histology. We conducted a longitudinal cohort study of 1,459,716 patients who had pregnancies between 1989 and 2022 in Quebec, Canada. The main exposure measure was preeclampsia. The outcome was breast cancer, including ductal, lobular, and other histological subtypes diagnosed up to 34 years after childbirth. We included in situ, localized invasive, and metastatic breast cancer. We used Cox regression models to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between preeclampsia and breast cancer histology, adjusted for maternal characteristics. Patients with preeclampsia had a lower incidence of breast cancer than patients without preeclampsia (82.1 vs. 111.7 per 100,000 person-years). Preeclampsia was associated with a 16% lower risk of breast cancer compared with no preeclampsia (HR 0.84, 95% CI 0.79–0.89), including a 14% lower risk of ductal (HR 0.86, 95% CI 0.81–0.93) and 31% lower risk of lobular tumors (HR 0.69, 95% CI 0.55–0.87). The protective association was present for in situ, localized invasive, and metastatic breast tumors. Preeclampsia was not associated with mucinous, medullary, papillary, or other breast cancer histology. We conclude that patients with preeclampsia are less likely to develop ductal and lobular breast cancer than patients with normotensive pregnancies, but do not have a reduced risk of other types of breast cancer.

25COASDEC47

Title: Risk factors for low-risk prostate cancer: A retrospective cohort study within the FinRSPC trial

Uzoamaka E. Okwor

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Abstract: Overdiagnosis of low-risk prostate cancer (PC), often accompanied by overtreatment, remains an important harmful consequence of prostate-specific antigen (PSA)-based screening. Although PSA screening can reduce PC mortality and metastatic PC, the balance of benefits and harms remains controversial. This retrospective cohort study of 80,144 men from the Finnish Randomized Study of Screening for Prostate Cancer, with a median follow-up of 18.0 years, compared determinants of low-risk PC with determinants of high-risk PC. Low-risk PC ($N = 1774$) was classified according to the European Association of Urology guidelines, excluding cases with subsequent PC death. A secondary analysis excluded cases with post-diagnosis disease progression. Intermediate, high-risk, and advanced cases were classified as high-risk PC ($N = 6466$). Poisson regression was used to analyze PC incidence. Low-risk PC was more common in the screening than the control arm (1.9 vs. 1.2 cases per 1000 person-years), whereas high-risk PC was more frequent in the control arm (5.7 vs. 5.4 cases per 1000 person-years in the screening arm). The risk of low-

risk PC remained stable across screening rounds, while the risk for high-risk PC declined after the first screen. Age was associated with an increased risk of high-risk PC, but no clear trend by age was observed for low-risk PC. Family history and use of 5-alpha reductase inhibitors showed stronger associations with low-risk PC than high-risk PC, though less so for screen-detected cancers. These suggest that risk factors for low-risk PC differ from those for high-risk PC, with determinants of low-risk PC being more closely related to medical service use.

25COASDEC48

Title: Physical activity and risks of recurrence and progression among patients with non-muscle invasive bladder cancer

Ivy Beeren

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https://doi.org/10.1002/ijc.70030

Abstract: Previous studies in solid tumors link high physical activity (PA) levels to lower cancer recurrence risk, but evidence is lacking for patients with non-muscle invasive bladder cancer (NMIBC). We evaluated the association between (changes in) PA (total, moderate-to-vigorous PA, leisure-time PA, and Dutch PA guideline adherence) and risks of NMIBC recurrence and progression. Patients diagnosed between 2014 and 2021 were recruited for the multi-center prospective cohort UroLife. Participants reported prediagnosis PA at 6 weeks ($n = 1414$) and postdiagnosis PA at 3 and 15 months after diagnosis ($n = 1275$). Multivariable proportional hazards models were used to assess the association of PA levels with risk of first and multiple recurrence(s) and progression. During a median total follow-up time of 4.6 years, 501 patients had ≥1 recurrence, 144 had ≥2 recurrences, and 157 had progression. Higher pre- and postdiagnosis PA levels were not significantly associated with risks of first recurrence, multiple recurrences, and progression. Pre-to-postdiagnosis increases of 10 metabolic equivalent of task hour/week in leisure-time PA, equivalent to 3–4 h/week of walking or 1 h/week of running, were significantly associated with lower progression risk (hazard ratio at 3 months: 0.94, 95% confidence interval: 0.89–0.99). The self-reported and relatively high PA levels could have limited the detection of associations. In conclusion, higher PA levels before or after NMIBC diagnosis were not significantly associated with lower recurrence or progression risk. Although pre-to-postdiagnosis increases in leisure-time PA were associated with lower progression risk, further research is necessary before specific PA recommendations can be formulated for patients with NMIBC.

25COASDEC49

Title: Toxicities in long-term survivors of head and neck cancer—A multi-national cross-sectional analysis

Katherine J. Taylor

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https://doi.org/10.1002/ijc.70033

Abstract: Head and neck cancer (HNC) patients may experience toxicities as a result of their treatment modality. While acute toxicities have been well documented, the prevalence of toxicities at long-term follow-up of HNC survivors is less clear. As part of a multi-national, cross-sectional study, HNC survivors at least 5 years post-diagnosis were invited to undergo a

toxicity examination. Using the Common Terminology Criteria for Adverse Events (version 5), 33 toxicities were assessed. From 2019 to 2021, 1094 survivors from 26 sites in 11 countries completed the assessment. Eighty-seven percent were from Europe, and most were survivors of oropharynx (35%), oral cavity (21%), or larynx cancer (19%). The majority had been diagnosed at stage III or IV (62%), and the median time since diagnosis was 8 years (range 5–36). Most had been treated with surgery and radiotherapy with or without chemotherapy (38%). Six percent had no toxicities, and 26% had only mild toxicities. 68% had at least one moderate or severe late toxicity. Overall, the most frequent late toxicities at any grade were dry mouth (67%), soft tissue fibrosis (52%), dysphagia (51%), and voice alterations (39%). Fistulae, neck and face edema, and osteonecrosis of the jaws were present in very few survivors. Our study shows that the majority of HNC survivors experience moderate or severe late toxicities, but that the problems are concentrated in a small group of specific toxicities. Understanding the problems experienced in the long term can help better inform newly diagnosed patients as well as inform survivorship follow-up initiatives**.**

25COASDEC50

Title: Integrating multi-ancestry genomic and proteomic data to identify blood risk biomarkers and target proteins for breast cancer genetic risk loci

Guochong Jia et. al.

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Abstract: Genome-wide association studies (GWAS) have identified more than 200 risk loci for breast cancer. However, target genes and their encoded proteins in these loci remain largely unknown. In this study, we utilized genetic prediction models for 1349 circulating proteins derived from individuals of African ($n = 1871$) and European ($n = 7213$) ancestry to investigate genetically predicted protein levels in association with breast cancer risk among females of African ($n = 40{,}138$), Asian ($n = 137{,}677$), and European ($n = 247{,}173$) ancestry. We identified 51 blood protein biomarkers associated with breast cancer risk, overall or by subtypes, at a false discovery rate (FDR) < 0.05, including 27 proteins encoded by genes located at least 1 Mb away from any of the known risk loci identified in GWAS. Of them, 32 proteins showed significant associations with breast cancer risk at the Bonferroni-corrected significance level ($p < 2.45 \times 10^{-4}$). Of the 24 proteins located at GWAS-identified risk loci, associations for 14 proteins were significantly attenuated after adjustment for the index risk variant of each respective locus, suggesting that these proteins may be target proteins for the risk loci. Encoding gene expression levels in normal breast tissue could be genetically predicted for 23 of the 51 identified proteins, and 13 encoding genes were associated with breast cancer risk in the same direction ($p < .05$). Our study identified potential protein targets of GWAS risk loci and biomarkers for breast cancer risk and provided additional insights into breast cancer genetics and etiology.

25COASDEC51

Title: Negative impact of corticosteroid use on outcome in patients with advanced BTCs treated with cisplatin, gemcitabine, and durvalumab: A large real-life worldwide population

Federica Lo Prinzi

International Journal of Cancer, Volume157, Issue8
https://doi.org/10.1002/ijc.70009

Abstract: In recent years, there has been increasing interest in the possible prognostic impact of concomitant medications in patients with cancer treated with immunotherapy combinations. This real-world analysis aims to evaluate the impact of concomitant medications on survival outcomes in patients with advanced biliary tract cancer (BTCs) treated with cisplatin, gemcitabine and durvalumab (CGD) therapy. The study cohort included patients with a diagnosis of advanced BTCs who were taking concomitant medications for their comorbidities before the start of CGD. The primary objectives were overall survival (OS) and progression-free survival (PFS). The initial population consisted of 666 patients, who were retrospectively collected from 41 sites in 12 countries. Data on concomitant medications were available for 493 patients. After a median follow-up of 8.8 months (95% CI: 7.8–9.8), patients who did not take steroids (prednisone >10 mg/day or equivalent) or nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids, before the start of CGD, had longer OS and PFS in univariate analysis. The multivariate analysis confirmed longer OS for patients who did not take steroids. Patients who did not take steroids had an OS of 14.8 months (95% CI: 13.1–29.1) versus 5.0 months (95% CI: 2.14–11.32) of patients who took prednisone >10 mg/day or equivalent. No differences were reported in terms of overall response rate (ORR), disease control rate (DCR) ($p = 1.0$ and $p = .16$, respectively), and safety profile between the two groups. Our analysis suggests that patients who did not receive steroids before the start of GCD had longer survival and highlighted the relevance of balancing concomitant medications and chemoimmunotherapy.

25COASDEC52

Title: Optimizing surveillance strategies for sacrococcygeal teratoma: A Midwest pediatric surgery consortium multi-institutional study

Shachi Srivatsa

International Journal of Cancer, Volume157, Issue8
https://doi.org/10.1002/ijc.70010

Abstract: Sacrococcygeal teratomas (SCTs) are the most common germ cell tumors in neonates and infants. While typically benign, SCTs carry an undefined risk of recurrence and malignant transformation, making post-resection surveillance critical. However, no consensus guidelines exist to direct post-resection surveillance. We conducted a multi-institutional retrospective cohort study across 11 pediatric institutions in the Midwest Pediatric Surgery Research Consortium. The study included patients 18 years or younger who underwent SCT resection from January 2010 to December 2020, excluding those with Currarino syndrome. The primary outcome was SCT recurrence, assessed via clinical exams, imaging, and tumor markers. Secondary outcomes included recurrence histology and surveillance practices. Cox proportional hazards modeling evaluated recurrence risk factors. Of the 178 patients, 10% experienced recurrence during a median follow-up period of 2.88 years (IQR: 1.52, 4.80). Overall recurrence-free survival for the entire cohort was 93.7%, 88.8%, and 88.8% at 1, 3, and 5 years, respectively. Malignant histopathology was the only factor significantly associated with recurrence (HR 5.83, $p = .014$). The timing of SCT diagnosis, completeness of resection, and Altman classification were not significantly associated with recurrence. Surveillance strategies varied significantly across institutions, with no standardized protocol

for follow-up. The majority of recurrences occurred within the first 3 years post-resection, with malignant histopathology being the strongest predictor. For lower risk tumors (mature and immature teratomas), a minimum of 3 years of surveillance, including imaging, tumor markers, and clinical exams, is recommended. Standardized surveillance protocols could improve consistency and early detection.

25COASDEC53

Title: Clinical impact of real-time androgen receptor alteration monitoring on metastatic castration-resistant prostate cancer treatment in real-world settings

Regina Stitz

International Journal of Cancer, Volume157, Issue 9

https://doi.org/10.1002/ijc.70019

Abstract: Androgen receptor (*AR*) alterations contribute to resistance against androgen receptor signaling inhibitors (ARSi) in metastatic castration-resistant prostate cancer (mCRPC). This study evaluated *AR* alteration monitoring via liquid biopsy in routine clinical practice. To this end, we enrolled 39 mCRPC patients in a real-world clinical setting and monitored disease progression with progression-free survival (PFS) and overall survival (OS) analyzed in relation to *AR* status. *AR* alterations were detected in 8 of 39 patients (20.5%) at baseline, with five additional cases emerging during progression (total 33.3%). AR-V7 was identified in 12.8%, and *AR* amplification and/or hotspot mutations in 20.5%. Patients with *AR* alterations had significantly lower PSA response rates to ARSi (37.5% vs. 80.7%; $p = 0.0276$). All *AR* alteration-positive patients experienced disease progression, compared to 34.6% of *AR*-negative cases. PFS was significantly shorter in *AR* alteration-positive patients (11 vs. 52 months; $p = 0.001$), while OS showed a non-significant trend toward shorter survival (41 vs. 74 months; $p = 0.0619$). Univariate analysis confirmed *AR* alterations as an independent predictor of PFS ($p = 0.0035$). This real-world study demonstrates that *AR* monitoring via liquid biopsy predicts treatment response and progression in mCRPC. Continuous monitoring is essential, as *AR* alterations emerge over time. Patients with *AR* alterations have poorer ARSi responses and shorter PFS, emphasizing the need for adaptive treatment strategies in real-world clinical practice.

25COASDEC54

Title: Differential effects of *RAS* mutations on chemoradiotherapy and total neoadjuvant therapy in locally advanced rectal cancer

Erina Haraguchi

International Journal of Cancer, Volume157, Issue8

https://doi.org/10.1002/ijc.70040

Abstract: Limited data are available on the impact of *RAS* mutations in patients with locally advanced rectal cancer treated with total neoadjuvant therapy (TNT). This retrospective study aimed to evaluate the effect of *RAS* mutations on treatment efficacy in 290 patients with locally advanced rectal cancer without distant metastasis, treated between 2015 and 2021 with neoadjuvant long-course chemoradiotherapy (CRT) with or without neoadjuvant systemic chemotherapy. *RAS* mutations were analyzed using pretreatment biopsy specimens. Associations between mutations and clinical outcomes were assessed separately in 146 patients who underwent conventional CRT and 144 patients who underwent

TNT. *RAS* mutations were identified in 42.5% and 51.4% of the CRT and TNT groups, respectively. No significant association was observed in either group between *RAS* mutation and complete response (CR, defined as pathological CR or sustained clinical CR after non-operative management). However, in the multivariable analysis, *RAS* mutations were significantly associated with a high neoadjuvant rectal score and worse recurrence-free survival in the CRT group. Yet, no such associations were observed in the TNT group, suggesting that TNT may mitigate the adverse effects of *RAS* mutations. Although further prospective, multicenter studies are required, our data suggest that *RAS* mutations may predict poor responses and higher recurrence risk among patients with locally advanced rectal cancer, and that TNT may be the better treatment option for these patients.

25COASDEC55

Title: The anti-aging Klotho protects glioblastoma macrophages from radiotherapy-induced inflammation and predicts immunotherapy response

Andrea Galluzzo

International Journal of Cancer, Volume157, Issue 9

https://doi.org/10.1002/ijc.70038

Abstract: Immunosuppressive myeloid cells, such as microglia and macrophages, play a key role in mediating resistance to immunotherapy in glioblastoma patients. Bulk RNA sequencing analysis revealed elevated expression of *Klotho* (*Kl*) in gliomas derived from irradiated glioma-bearing mice. *Klotho*, which encodes an anti-aging protein, was found to be upregulated in glioma-associated microglia/macrophages (GAMs) exhibiting an M1 pro-inflammatory phenotype. This upregulation appeared to enhance the antitumor efficacy of a combination of radiotherapy and dendritic cell (DC) immunotherapy. Furthermore, transcript levels of *KL* in tumor specimens and corresponding serum levels in glioblastoma patients undergoing DC immunotherapy were correlated with favorable prognostic outcomes and improved treatment responses. Given its expression in human M1-like GAMs, serum KL levels can offer valuable insights into the immune microenvironment and hold clinical significance as a peripheral biomarker. These findings highlight the pivotal role of Klotho as a prognostic biomarker for predicting responses to immunotherapy, with potential applications for monitoring tumor progression or regression through changes in serum levels.

25COASDEC56

Title: Baseline vitamin D status, genetic susceptibility, and the risk of incident hepatocellular carcinoma

Chengxiao Yu

International Journal of Cancer, Volume157, Issue9

https://doi.org/10.1002/ijc.70003

Abstract: High vitamin D concentrations may reduce the incidence of hepatocellular carcinoma (HCC), though results have been inconsistent. This study aimed to evaluate the association between serum 25-hydroxyvitamin D (25(OH)D) levels and HCC, and to assess whether the genetic risk of HCC modifies this association. The prospective cohort study involved 447,028 individuals free of liver diseases in the UK Biobank. Serum 25(OH)D concentrations were measured by the chemiluminescent immunoassay method. The associations were evaluated using the Cox proportional hazards model, estimating hazard

ratios (HRs) and corresponding 95% confidence intervals (CIs). Additionally, the weighted polygenic risk score (PRS) of HCC was calculated by 5 SNPs reported in a previously published genome-wide association study (GWAS). During a median follow-up of 12.5 years, 377 cases of HCC were documented. Compared to the lowest quartile of serum 25(OH)D, the HR (95% CI) of HCC was 0.52 (0.38–0.70) in the highest quartile. Per 10 nmol/L increase in serum 25(OH)D was associated with a 12% lower HCC risk (95% CI: 7%–17%). A joint effect of genetic and serum 25(OH)D on HCC risk was observed. Those with low genetic risk of HCC and the highest serum 25(OH)D had a HR (95% CI) of 0.22 (0.11–0.45) compared to those with high genetic risk of HCC and the lowest 25(OH)D serum levels, but there was no interaction (p interaction = 0.529). Our findings emphasize that higher serum 25(OH)D levels are linked to a reduced risk of HCC, indicating the potential role of 25(OH)D in the primary prevention of HCC.

25COASDEC57

Title: Understanding delays in breast cancer diagnosis in Africa: Key insights and contributing factors

Liza A. Hoveling

International Journal of Cancer, Volume157, Issue9
https://doi.org/10.1002/ijc.70008

Abstract: Africa has the highest age-standardized breast cancer (BC) mortality rates, largely due to diagnostic delays. Therefore, this scoping review aims to identify individual-level factors that contribute to diagnostic delay of BC in African women. We conducted a global scoping review on cancer diagnostic delays in women, following PRISMA-ScR guidelines. In this scoping review, diagnostic delay is defined as the time from first symptom recognition to pathological diagnosis. Qualitative and quantitative studies involving cancer patients or healthcare professionals published between 2018 and November 28, 2023, were included. We searched PubMed/MEDLINE and Scopus, excluding non-English studies and those focused solely on screening. Two reviewers independently screened titles, full texts, and extracted data. Disagreements were resolved by discussion. Consultations followed Arksey and O'Malley's framework, with input from a general practitioner, psychologist, and epidemiologist. Factors were classified using Bronfenbrenner's ecological model to analyze BC diagnostic delays in Africa. Of 9699 studies, 128 were relevant; 30 focused on African BC patients. Delays were linked to microsystem factors: lack of awareness, fear, young age, low education, finances, mesosystem factors: family duties, limited access, delayed care, symptom disclosure, exosystem factors: traditional healers, mistrust, referral inefficiencies, and macrosystem factors: religious beliefs, education gaps, cultural norms. Diagnostic delays in women with BC in Africa are mainly due to low awareness, cultural beliefs, and reliance on traditional healers. Expanding current interventions and integrating them into healthcare systems, along with engaging religious leaders, is important. Future research should focus on culturally tailored strategies to improve early detection and outcomes.

25COASDEC58

Title: Genetic variants linked to type 2 diabetes in *CDKN1B* and *TCF7L2* influence survival outcomes in metastatic colorectal cancer

Raffaella Ruggiero

https://doi.org/10.1002/ijc.70035

Abstract: Evidence suggests that metastatic colorectal cancer patients with type 2 diabetes (T2D) experience a poorer prognosis in contrast to their non-diabetic counterparts. Considering the multifactorial genetic nature of colon cancer development, we examined whether gene polymorphisms associated with T2D could affect the clinical outcome of metastatic colon cancer. Using in silico analysis, we evaluated gene variants linked to both T2D and colon cancer utilizing data from The Cancer Genome Atlas (TCGA). Subsequently, we assessed the prognostic relevance of polymorphisms in *CCND2*, *CDKN1B*, *CDKN2A*, *CDKN2B*, *EML4*, *HNF1A*, *ID3*, *IGF1*, *IGF1R*, *IGF2*, *INHBA*, *INSR*, *IRS1*, *IRS2*, and *TCF7L2* in a cohort of 99 consecutive metastatic non-diabetic colon cancer patients with favorable clinical conditions. Primary colon cancer DNA was sequenced using the TruSight Oncology 500 kit, followed by sequencing on an Illumina NovaSeq 6000 platform. Notably, patients carrying the *CDKN1B* p.V109G and *TCF7L2* p.P370R polymorphisms exhibited significantly shorter median survivals compared to wild-type counterparts, with adjusted hazard ratios (covariates: age, gender, metastatic extent, *RAS*/*BRAF* mutations, and response to therapy) of 2.28 (95% CI: 1.18–4.41) and 4.45 (95% CI: 1.26–15.70), respectively. Our findings provide scientific evidence of T2D genetic polymorphisms' involvement in determining the aggressiveness of metastatic colon cancer, identifying *CDKN1B* p.V109G and *TCF7L2* p.P370R as novel unfavorable prognostic markers.

25COASDEC59

Title: Evaluating ChatGPT's recommendations for systematic treatment decisions in recurrent or metastatic head and neck squamous cell carcinoma: Perspectives from experts and junior doctors

Danfang Yan

International Journal of Cancer, Volume157, Issue9
https://doi.org/10.1002/ijc.70001

Abstract: This study evaluates ChatGPT-4's potential as a decision-support tool in the treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC). The study involved 12 retrospectively chosen patients with detailed clinical, tumor, treatment history, imaging, pathology, and symptomatic data. ChatGPT-4, along with six experts and 10 junior oncologists, assessed these cases. The AI model applied the 8th edition AJCC TNM criteria for tumor staging and proposed treatment strategies. Performance was quantitatively rated on a 0–100 scale by both expert and junior oncologists, with further analysis through statistical scoring and intraclass correlation coefficients. Findings revealed that ChatGPT-4 achieved an 83.3% accuracy rate in tumor staging with two instances of mis-staging. Junior doctors rated its staging performance highly, showing strong consensus on language capabilities and moderate on learning assistance. Experts rated ChatGPT-4's treatment strategy: high agreement on subject knowledge (median 86, mean 84.7), logical reasoning (median 83, mean 82), and analytical skills (median 85, mean 82); moderate on ChatGPT-4's usefulness for treatment decision (median 80, mean 77) and its recommendations (median 80, mean 76.8). Junior doctors rated ChatGPT-4 higher in treatment strategy (medians above 85) with limited consensus (subject knowledge: median 88, mean 84.5; logical reasoning: median 90, mean 83.2; analytical skills: median 90, mean 82.5; usefulness: median 85, mean 81.8;

agreements for: median 85, mean 80.4). ChatGPT is proficient in tumor staging but moderately effective in treatment recommendations. Nonetheless, it shows promise as a supportive tool for clinicians, particularly for those with less experience, in making informed treatment decisions.

25COASDEC60

Title: Comparisons of blood, upper respiratory tract and gut viromes from patients with lung cancer and healthy persons

Wang Li et.al.

International Journal of Cancer, Volume157, Issue9

https://doi.org/10.1002/ijc.70075

Abstract: Lung cancer is the leading cause of cancer-related mortality globally. Although some studies have proposed a potential association between viral infections and lung cancer pathogenesis, the evidence remains inconclusive. This study characterized the virome in blood, upper respiratory tract, and gut samples from 200 lung cancer patients and 75 healthy controls, with the goal of identifying potential microbial biomarkers for lung cancer, using viral metagenomics. Significant differences in viral diversity and composition were observed between cancer and healthy groups, with lower similarities in blood, respiratory, and gut viromes. Notably, LUSC and LUAD groups showed high similarity, with LUAD exhibiting the most diverse virome. In blood, *Anelloviridae* dominated in cancer patients, while *Retroviridae* was more abundant in specific subgroups. The upper respiratory tract virome in cancer patients was enriched with *Siphoviridae* and *Myoviridae*, contrasting with *Retroviridae* in healthy individuals. Gut viromes were dominated by *Podoviridae* and *Virgaviridae* in cancer patients, with *Virgaviridae* showing higher abundance compared to healthy controls. Alpha and beta diversity analyses indicated significant differences in blood and respiratory viromes but not in gut viromes. STAMP and LEfSe analyses identified *Anelloviridae* and *Siphoviridae* as potential biomarkers for lung cancer. Additionally, 242 anelloviruses with complete ORF1 were isolated, revealing high genetic diversity. These findings highlight distinct virome profiles in lung cancer patients, offering insights into potential diagnostic and therapeutic targets.

25COASDEC61

Title: Socioeconomic and childhood cancer survival in Germany: A nationwide assessment based on data from the German Childhood Cancer Registry

Maike Wellbrock et.al.

International Journal of Cancer, Volume157, Issue11

https://doi.org/10.1002/ijc.70042

Abstract: Social inequalities in childhood cancer survival have been observed in many countries, including European nations with universal healthcare systems, suggesting that not all children with cancer have benefited equally from diagnostic and therapeutic enhancements. Despite the growing socioeconomic diversity within Germany's large population, little is known about the extent of social inequalities in German childhood cancer survival. Using German Childhood Cancer Registry data, we identified all children with a cancer diagnosis before the age of 15 years in 1997–2016 in Germany ($N = 35{,}443$). Based on individual residential address information (at time of diagnosis) we applied the German Index

of Socioeconomic Deprivation (GISD) to measure area-based socioeconomic status. Using Cox proportional hazards models, we assessed the association between absolute area-based socioeconomic deprivation (AASD) and 10-year overall survival (OS) (end of follow-up: 15 January 2023) to estimate hazard ratios (HR) and corresponding 95% confidence intervals (CI). The multivariable analyses revealed a null association for AASD and 10-year OS for all cancers combined (HR_{adj} = 1.00, 95% CI 0.97; 1.03). Among children diagnosed with acute myeloid leukaemia and germ cell tumors, a higher AASD (higher levels of deprivation) appeared to be associated with worse survival, particularly pronounced in boys. The opposite was observed among children diagnosed with central nervous system tumors. Contrary to reports from other European countries, we found little evidence for social inequalities in childhood cancer survival in Germany when analysing the GISD. Further research assessing individual-level measures of socioeconomic status is warranted.

25COASDEC62

Title: Stage- and histology-specific sensitivity for the detection of lung cancer of the NELSON screening protocol—A modeling study

Koen de Nijs

International Journal of Cancer, Volume157, Issue11
https://doi.org/10.1002/ijc.70045

Abstract: The Dutch–Belgian lung cancer (LC) screening trial (Nederlands–Leuvens Longkanker Screenings Onderzoek [NELSON]) demonstrated low-dose computed tomography (CT) reduces LC mortality by 24% among men. The NELSON protocol differed from previous trials in the eligibility criteria, the use of volume-based nodule management, and increasing screening intervals. The early-stage sensitivity of the protocol is pivotal in determining the optimal screening strategy, such as the interval and age range. The MIcrosimulation SCreening ANalysis-Lung natural history model was used to reproduce LC incidence and mortality by detection method (clinical or screen-detected), sex, histology, and stage in the NELSON trial based on individual-level data. We evaluated screening effectiveness by stage and histology, accounting for population characteristics, trial design, and LC epidemiology. We find stage IA non-small cell LC (NSCLC) sensitivity of 24.6% (other NSCLC) to 41.0% (adenocarcinoma) at baseline screening. At repeat screening rounds, we find this increased to 70.9% for stage IA adenocarcinoma. For stage IB, the sensitivity by histology ranges from 26.4% to 77.1%; for stage II, 39.6%–81.9%. Upon detection, the probability of LC mortality prevention is estimated at 83% for stage IA. The sensitivity for detecting early-stage LC is found to depend on the histology of cancer and is increased for adenocarcinoma at repeat screenings. Despite a low rate of referral to follow-up screening in the NELSON trial, early-stage CT sensitivity and the probability of mortality prevention were similar to previous estimates from the National Lung cancer Screening Trial. Previously demonstrated screening effectiveness may be maintained when implementing new programs, while reducing unnecessary follow-up when considering NELSON evidence.

25COASDEC63

Title: Overdiagnosis in low-dose CT lung cancer screening: A systematic review and meta-analysis of overall magnitude and subgroup variations

Yihui Du et.al.

International Journal of Cancer, Volume157, Issue11
https://doi.org/10.1002/ijc.70049

Abstract: Overdiagnosis is a major concern in low-dose computed tomography (LDCT) lung cancer screening as it can detect indolent or slow-growing cancers. This study aims to quantify overdiagnosis in LDCT screening and explore its variation by several factors. We conducted a systematic review and meta-analysis following PRISMA guidelines. Four databases (PubMed, Web of Science, Scopus, Cochrane Library) were searched up to October 2024 for studies reporting overdiagnosis in LDCT lung cancer screening. Overdiagnosis was quantified using three metrics: percentage in screen-detected cancers, percentage in all cancers in the screening group, and rate per 1000 screened individuals. Pooled estimates were calculated using random-effects models, and subgroup analyses were performed by follow-up time, histology, nodule type, geography, population risk, and gender. Twenty-six studies were included (8 RCTs, 11 cohorts, 7 ecologic studies). Overdiagnosis declined substantially with extended follow-up, with rates decreasing from 37% (95%CI: 14%–60%) to 7% (95%CI: −7% to 22%; $p = .03$) for screen-detected cancers and from 25% (95%CI: 8%–41%) to 2% (95%CI: 4%–8%; $p = .01$) for all screening-group cancers when follow-up exceeded 5 years. This pattern corresponded to overdiagnosis dropping from 12.26 (95%CI: 3.87–20.64) to 1.46 (95%CI: −2.11 to 5.03) per 1000 screened individuals ($p = .02$). Considerable variations emerged across subgroups: bronchioloalveolar carcinoma 82%, adenocarcinoma 28%, non-adenocarcinoma −11%, $p < .001$; non-solid cancers 66%, part-solid cancers 31%, solid cancers 7%, $p = .002$; Asian countries 38%, Western countries 22%, $p = .009$; general population 38%, high-risk population 22%, $p = .010$. These findings demonstrate that accurate overdiagnosis assessment requires sufficient follow-up duration and must account for substantial variability across clinical and demographic factors.

25COASDEC64

Title: Pembrolizumab Plus Chemotherapy Versus Chemotherapy as Perioperative Therapy in Locally Advanced Gastric and Gastroesophageal Junction Cancer: Final Analysis of the Randomized, Phase III KEYNOTE-585 Study.

Kohei Shitara et al.

J Clin Oncol 43, No. 29
https://doi.org/10.1200/JCO-25-00486

Abstract: We report results of the final analysis of overall survival (OS) and patient-reported outcomes from the phase III KEYNOTE-585 (ClinicalTrials.gov identifier: NCT03221426) study. Participants with previously untreated, locally advanced, resectable gastric and gastroesophageal junction (G/GEJ) cancer were enrolled into the main (n = 804) and fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT; n = 203) cohorts, and randomly assigned 1:1 to neoadjuvant and adjuvant pembrolizumab plus chemotherapy or placebo plus chemotherapy. The primary end points were pathologic complete response (pathCR) by central review, event-free survival (EFS) by investigator, OS, and safety. Patient-reported outcomes was an exploratory end point. After a median follow-up of 59.9 months (range, 39-76), median OS was 71.8 versus 55.7 months (hazard ratio [HR], 0.86 [95% CI, 0.71 to 1.06]) with pembrolizumab plus chemotherapy versus placebo plus chemotherapy in the main cohort. The EFS HR was 0.81 (95% CI, 0.67 to 0.98). Grade ≥3 drug-related adverse event rates were 65% versus 63%. Perioperative pembrolizumab plus chemotherapy did not worsen

health-related quality of life versus placebo. Pembrolizumab plus chemotherapy continued to show improved outcomes in pathCR and a trend toward longer EFS versus placebo in the main and main plus FLOT cohorts. Efficacy and safety outcomes with perioperative pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab in participants with untreated, locally advanced resectable G/GEJ cancer were consistent with previous analyses.

25COASDEC65

Title: Arsenic Trioxide and All-Trans Retinoic Acid Combination Therapy for the Treatment of High-Risk Acute Promyelocytic Leukemia: Results From the APOLLO Trial.

Uwe Platzbecker et al.

J Clin Oncol 43, 3160-3169(2025).

https://doi.org/10.1200/JCO-25-00535

Abstract: The phase III APOLLO trial prospectively compared the efficacy of arsenic trioxide (ATO) in combination with all-trans retinoic acid (ATRA) regimen (ATRA and ATO [ATRA-ATO]) plus low-dose idarubicin versus standard ATRA plus anthracycline-based chemotherapy (ATRA-CHT) regimen (ie, ATRA and idarubicin regimen) in patients with high-risk acute promyelocytic leukemia (APL; EudraCT 2015-01151-68; ClinicalTrials.gov identifier: NCT02688140). Methods- Adult patients with newly diagnosed high-risk APL in the ATRA-ATO arm received ATO 0.15 mg/kg once daily and ATRA 45 mg/m^2 twice daily until complete remission (CR), with two doses of idarubicin 12 mg/m^2 on days 1 and 3, followed by consolidation therapy (four ATRA-ATO cycles). Patients in the ATRA-CHT arm received induction with ATRA 45 mg/m^2 twice daily and idarubicin 12 mg/m^2 once daily on days 1, 3, 5, and 7, followed by three cycles of chemotherapy-based consolidation and 2 years of maintenance therapy. The primary study end point was event-free survival (EFS) at 2 years.Results- As of July 2022, 133 eligible patients had received either ATRA-ATO (n = 68) or ATRA-CHT (n = 65). The study was discontinued prematurely because of slow accrual during the COVID-19 pandemic. After a median follow-up of 37 months (range, 1.7-88.6 months), 2-year EFS was 88% in the ATRA-ATO arm and 71% in the ATRA-CHT arm (HR, 0.4 [95% CI, 0.17 to 0.92]; log-rank test P = .02). At a median of 7.8 and 12.1 months from achievement of CR, molecular relapse occurred in one (1.5%) ATRA-ATO patient versus eight (12.3%) ATRA-CHT patients (P = .014). Overall, 32% and 68% of patients receiving ATRA-ATO and ATRA-CHT, respectively, reported serious treatment-emergent adverse events (P < .01). Conclusion-

The results of the APOLLO trial support the use of ATO and ATRA for the treatment of newly diagnosed patients with high-risk APL.

25COASDEC66

Title: Impact of Human Epidermal Growth Factor Receptor 2 in Patients With Metastatic Colorectal Cancer Treated With Chemotherapy Plus Bevacizumab or Anti-EGFRs: Exploratory Analysis of Eight Randomized Trials.

Marco Maria Germani et al.

J Clin Oncol 43, 3184-3197(2025).

https://doi.org/10.1200/JCO-25-01003

Abstract: Purpose -Human epidermal growth factor receptor 2 (HER2) amplification/overexpression (HER2-pos) is detected in 5% of *RAS/BRAF* wild-type metastatic colorectal cancers (mCRCs). Its prognostic/predictive role in terms of benefit from anti-EGFR/bevacizumab (bev) is debated. Similarly, the role of activating *HER2* mutations (mut) is unclear. Methods- We collected individual data of 1,604 patients with proficient mismatch repair (pMMR)/microsatellite stable (MSS) *RAS/BRAF* wild-type untreated mCRC with HER2 amplification/expression status available enrolled in eight randomized clinical trials (RCT; TRIBE2, TRIPLETE, VALENTINO, ATEZOTRIBE, PANDA, PANAMA, PARADIGM, and CALGB/SWOG80405). Objective response rate (ORR), progression-free survival (PFS), and overall survival (OS) were assessed with respect to HER2 amplification/expression and *HER2* mutational status and according to biologics (anti-EGFR/bev). Results- Patients with HER2-pos were 81 (5%). HER2-pos patients experienced shorter PFS (median PFS [mPFS]: 9.8 *v* 12.2 months, hazard ratio [HR], 1.31, $P = .02$) and OS (median OS [mOS]: 28.0 *v* 34.9 months, HR, 1.37, $P = .01$), also after adjustment for covariates (P_{adj}PFS = .02, P_{adj}OS = .048). ORR was similar between HER2-pos and HER2-negative (HER2-neg) tumors (75% *v* 72%, odds ratio [OR], 1.21, $P = .47$). We found no interaction between HER2 amplification/expression status and biologics' effect in terms of PFS ($P_{int} = .76$), OS ($P_{int} = .76$), and ORR ($P_{int} = .64$). In left-sided HER2-pos tumors, outcomes were similar with chemotherapy plus bev/anti-EGFRs in terms of PFS (9.8 *v* 9.3 months, HR, 0.73, $P = .29$), OS (29.8 *v* 28.0 months, HR, 1.29, $P = .40$), and ORR (59% *v* 79%, OR, 0.39, $P = .10$). *HER2*-mutant tumors (2% of patients with HER2-neg tumors) showed shorter OS than *HER2* wild-type ones (mOS: 23.7 *v* 34.4 months, HR, 1.56, $P = .04$) with no differential effect of biologics (P_{int}ORR = .81; P_{int}PFS = .95; P_{int}OS = .92). Conclusion- To our knowledge, this is the largest analysis of HER2 status in patients with untreated mCRC enrolled in RCT. Waiting for targeted approaches, HER2-pos and mut do not predict benefit from bev/anti-EGFRs and should be regarded as negative prognostic factors in pMMR/MSS *RAS/BRAF* wild-type mCRC.

25COASDEC67

Title: Phase II Dose-Randomized Study of Sunvozertinib in Platinum-Pretreated Non–Small Cell Lung Cancer With Epidermal Growth Factor Receptor Exon 20 Insertion Mutations (WU-KONG1B).

James Chih-Hsin Yang et al.

J Clin Oncol 43, 3198-3208(2025).
https://doi.org/10.1200/JCO-25-00788

Abstract: WU-KONG1B (ClinicalTrials.gov identifier: NCT03974022) is a multinational phase II, dose-randomized study to assess the antitumor efficacy of sunvozertinib in pretreated patients with advanced non–small cell lung cancer (NSCLC) with epidermal growth factor receptor (*EGFR*) exon 20 insertion mutations (exon20ins). Methods- Eligible patients with advanced-stage *EGFR* exon20ins NSCLC were randomly assigned by 1:1 ratio to receive sunvozertinib 200 mg or 300 mg once daily (200 and 300 mg-rand cohorts). After predefined interim analysis, additional patients were enrolled and treated with the 300 mg dose once daily. The primary end point was blinded independent review committee (IRC)–assessed confirmed objective response rate (cORR), and the key secondary end point was duration of response (DoR). Results- Among 85, 89, and 107 efficacy-evaluable patients in

200 mg-rand, 300 mg-rand, and 300 mg-all (including randomly assigned and nonrandomized patients) cohorts, the cORRs were 45.9% (97.5% CI, 33.6% to 58.5%), 47.2% (97.5% CI, 35.1% to 59.5%), and 45.8% (97.5% CI, 34.8% to 57.0%), respectively, per IRC assessment. The predefined null hypothesis was rejected with statistical significance ($P < .0001$). Comparing 300 and 200 mg-rand cohorts, higher cORRs were observed in patients with baseline brain metastasis (52.4% *v* 28.6%) and previous amivantamab treatment (41.7% *v* 25%), as well as longer DoR (13.8 *v* 11.1 months). At 200 and 300 mg once daily, the most common treatment-related adverse events with grade ≥3 included diarrhea (2.2% *v* 18%), blood creatine phosphokinase increased (6.6% *v* 12.6%), and anemia (4.4% *v* 6.3%). Conclusion- Sunvozertinib is efficacious at both 200 and 300 mg once daily in treating platinum-pretreated patients with advanced *EGFR* exon20ins NSCLC. The treatment-related adverse events of sunvozertinib were consistent with an EGFR tyrosine kinase inhibitor, with a more favorable safety profile at 200 mg than 300 mg once daily.

25COASDEC68

Title: Xevinapant or Placebo Plus Platinum-Based Chemoradiotherapy in Unresected Locally Advanced Squamous Cell Carcinoma of the Head and Neck (TrilynX): A Randomized, Phase III Study.

Jean Bourhis et al.

J Clin Oncol 43, 3209-3220(2025).
https://doi.org/10.1200/JCO-25-00272

Abstract: Purpose -TrilynX was a randomized, double-blind, phase III study evaluating the addition of xevinapant (an inhibitor of apoptosis proteins inhibitor) or placebo to chemoradiotherapy (CRT) in patients with unresected locally advanced squamous cell carcinoma of the head and neck (LA SCCHN). Methods- Patients with unresected LA SCCHN (oropharynx [p16-negative only], hypopharynx, or larynx) were randomly assigned 1:1 to six cycles of oral xevinapant 200 mg/day or matched placebo (once daily on Days 1-14 of a 21-day cycle) plus CRT for the first three cycles (cisplatin [100 mg/m^2 once on Day 2 of every cycle] plus intensity-modulated radiotherapy [70 Gy; 35 fractions of 2 Gy/day, 5 days/week]). The primary end point was event-free survival (EFS) assessed by the blinded independent review committee. Progression-free survival, overall survival (OS), and safety were secondary end points. Results- Between September 20, 2020, and February 27, 2023, 730 patients were randomly assigned to xevinapant plus CRT (n = 364) or placebo plus CRT (n = 366). The median (95% CI) EFS was 19.4 months (14.5 to not estimable) with xevinapant and 33.1 months (21.0 to not estimable) with placebo (hazard ratio [HR], 1.33 [95% CI, 1.05 to 1.67]; $P = .9919$). OS was worse in the xevinapant arm (HR, 1.39 [95% CI, 1.04 to 1.86]). Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 320 (87.9%; xevinapant) and 286 (80.3%; placebo) patients; anemia (78 [21.4%] *v* 51 [14.3%]) and neutropenia (71 [19.5%] *v* 69 [19.4%]) were the most common. Serious TEAEs occurred in 194 (53.3%; xevinapant) and 129 (36.2%; placebo) patients. TEAEs leading to death occurred in 22 (6.0%; xevinapant) and 13 (3.7%; placebo) patients. Conclusion- Xevinapant plus CRT did not improve EFS (EFS was shorter with xevinapant *v* placebo) and demonstrated an unfavorable safety profile versus placebo plus CRT in patients with unresected LA SCCHN.

25COASDEC69

Title: Single-Agent Divarasib in Patients With *KRAS G12C*–Positive Non–Small Cell Lung Cancer: Long-Term Follow-Up of a Phase I Study.

Adrian G. Sacher et al.

J Clin Oncol 43, 3249-3253(2025).
https://doi.org/10.1200/JCO-25-00040

Abstract: Divarasib (GDC-6036), an oral, highly potent and selective next-generation KRAS G12C inhibitor, has demonstrated a manageable safety profile and promising antitumor activity in patients with advanced *KRAS G12C*–positive non–small cell lung cancer (NSCLC). Here, we report long-term (≥1 year) follow-up of single-agent divarasib from the ongoing, open-label, and multicenter phase I study (ClinicalTrials.gov identifier: NCT04449874). The primary objective was safety, and the other objectives included preliminary antitumor activity. Overall, 65 patients with advanced *KRAS G12C*–positive NSCLC received single-agent oral divarasib 50-400 mg once daily and 31 patients (48%) were treated beyond 1 year. Divarasib continued to be well tolerated, and the safety profile beyond 1 year was consistent with the overall safety profile. In patients with measurable disease at baseline across all dose levels (n = 63), the confirmed objective response rate was 55.6% (95% CI, 42.5 to 68.1), and the median duration of response was 18.0 months (95% CI, 11.1 to 24.9). The median progression-free survival was 13.8 months (95% CI, 9.8 to 25.4) in the overall population (N = 65) and 15.3 months (95% CI, 12.3 to 26.1) among patients assigned to the 400-mg dose level (n = 44). With extended follow-up, divarasib demonstrated long-term safety and antitumor activity in patients with advanced *KRAS G12C*–positive NSCLC.

25COASDEC70

Title: Benefit of Chemoradiotherapy Versus Chemotherapy After Induction Therapy for Conversion of Unresectable Into Resectable Pancreatic Cancer: The Randomized CONKO-007 Trial.

Rainer Fietkau et al.

J Clin Oncol 43, 3266-3278(2025).
https://doi.org/10.1200/JCO-24-01502

Abstract: To determine the benefit, measured as complete removal of a tumor so that no tumor cells are detectable during histopathologic examination of the resection margin (R0 resection rate), of induction chemotherapy plus chemoradiotherapy (CRT) compared with chemotherapy alone for unresectable pancreatic tumors. Patients and Methods- CONKO-007, an investigator-initiated open-label, multicentric, phase III randomized clinical trial, enrolled 525 patients with unresectable tumors, and 495 patients received induction chemotherapy (402 with fluorouracil, irinotecan, and oxaliplatin [FOLFIRINOX] and 93 with gemcitabine). Patients without progression after 3 months of induction chemotherapy (n = 336) were randomly assigned for continuation of the same chemotherapy (n = 167) or CRT (n = 169; 50.4Gy concurrently with gemcitabine). Resectability was centrally reassessed by a panel of surgeons. Surgery was recommended if possible. After an interim analysis, the primary end point was changed from overall survival (OS) to overall R0 resection rate because of slow recruitment. The median follow-up was 76 months. Important planned secondary end points were R0 resection rate in the surgically treated population and OS. Results- The primary end

point (overall R0 resection rate) was not significantly different between treatment arms with 25% (43 of 169) in the CRT arm versus 18% in the chemotherapy arm (30 of 167; *P* = .113). Secondary end point analysis showed that surgery was performed equally often (*P* = .91); R0 resection rate in patients who underwent surgery was higher after CRT, 69.4% (43 of 62) compared with chemotherapy alone: 50.0% (30 of 60 patients, *P* = .04). Other parameters of resection (ratio of R0/R1/R2/no resection) also favored CRT (*P* = .02). No difference in OS was seen between treatment arms (hazard ratio [HR], 0.937 [95% CI, 0.747 to 1.174]; *P* = .57; randomly assigned intention-to-treat patients). Surgery was associated with longer OS (*P* < .001, HR, 0.525 [95% CI, 0.408 to 0.676]). Conclusion- Although not improving overall R0 resection rate or survival, CRT enables a R0 resection in surgically treated patients more often than chemotherapy alone.

25COASDEC71

Title: Modified Fluorouracil, Leucovorin, Irinotecan, and Oxaliplatin or S-1, Irinotecan, and Oxaliplatin Versus Nab-Paclitaxel + Gemcitabine in Metastatic or Recurrent Pancreatic Cancer (GENERATE, JCOG1611): A Randomized, Open-Label, Phase II/III Trial.

Akihiro Ohba et al.

J Clin Oncol 43, 3345-3354(2025).
https://doi.org/10.1200/JCO.24.00936

Abstract: Modified fluorouracil, leucovorin, irinotecan, and oxaliplatin (mFOLFIRINOX) and nab-paclitaxel + gemcitabine are recommended as first-line treatments for metastatic pancreatic cancer. S-1, irinotecan, and oxaliplatin (S-IROX) demonstrated activity in a phase Ib trial in this population. Therefore, these three regimens were directly compared. Methods- This randomized phase II/III trial was performed at 45 centers in Japan. Eligible patients age 20-75 years with an Eastern Cooperative Oncology Group performance status of 0 or 1 and pathologically confirmed metastatic or recurrent pancreatic cancer were randomly assigned (1:1:1) to receive mFOLFIRINOX (oxaliplatin 85 mg/m^2 over 2 hours, irinotecan 150 mg/m^2 over 90 minutes, l-leucovorin 200 mg/m^2 over 2 hours, each once daily on day 1, and fluorouracil 2,400 mg/m^2 over 46 hours on days 1-3, every 2 weeks), S-IROX (oxaliplatin 85 mg/m^2 over 2 hours, irinotecan 150 mg/m^2 over 90 minutes on day 1, and S-1 80 mg/m^2/day administered orally twice daily on days 1-7, every 2 weeks), or nab-paclitaxel (125 mg/m^2) + gemcitabine (1,000 mg/m^2) on days 1, 8, and 15 every 4 weeks. The primary end point was overall survival (OS). Results- A total of 527 patients were enrolled, with 426 included in the planned interim analysis. The median OS was 14.0 months (hazard ratio [HR], 1.31 [95% CI, 0.97 to 1.77]) and 13.6 months (HR, 1.35 [95% CI, 1.00 to 1.82]) in the mFOLFIRINOX and S-IROX groups, respectively, as compared with 17.1 months in the nab-paclitaxel + gemcitabine group. The predictive probability of achieving superiority in the final analysis was <1% in both groups. Thus, the trial was terminated owing to its futility. Grade 3 to 4 anorexia was more frequent in the mFOLFIRINOX (23.3%) and S-IROX (27.5%) groups than in the nab-paclitaxel + gemcitabine group (5.0%). Conclusion- Neither mFOLFIRINOX nor S-IROX appeared to be superior compared with nab-paclitaxel + gemcitabine as the first-line treatment for metastatic or recurrent pancreatic cancer.

25COASDEC72

Title: PASS-01: Randomized Phase II Trial of Modified FOLFIRINOX Versus Gemcitabine/Nab-Paclitaxel and Molecular Correlatives for Previously Untreated Metastatic Pancreatic Cancer.

Jennifer J. Knox et al.

J Clin Oncol 43, 3355-3368(2025).
https://doi.org/10.1200/JCO-25-00436

Abstract: To assess modified folinic acid/leucovorin, fluorouracil, irinotecan, oxaliplatin (FOLFIRINOX [mFFX]) versus gemcitabine/nab-paclitaxel (GnP) in de novo metastatic pancreatic ductal adenocarcinoma (PDAC) and explore predictive biomarkers. Patients and Methods- Patients were randomly assigned 1:1 to mFFX or GnP with exclusion of germline pathogenic variants in *BRCA1/2* or *PALB2*. The primary end point was progression-free survival (PFS) between arms with 0.3 significance. The per-protocol (PP) population included patients who received one dose of chemotherapy. Pretreatment biopsies underwent whole-genome/transcriptome sequencing and patient-derived organoid (PDO) development, providing correlate recommendations at a molecular tumor board and outcomes assessed according to RNA signatures (basal-like *v* classical). Results- Of 160 patients randomly assigned (80 mFFX, 80 GnP), 140 patients were in the PP population (71 mFFX, 69 GnP), with median follow-up of 8.3 months. The median PFS was 4.0 months for mFFX versus 5.3 months for GnP (hazard ratio [HR], 1.37 [95% CI, 0.97 to 1.92]; $P = .069$) in intention-to-treat. Median overall survival (OS) was 8.5 months with mFFX and 9.7 months with GnP (HR, 1.57 [95% CI, 1.08 to 2.28]; $P = .017$). Genomic data were generated in 94%, transcriptomes in 74%, and PDOs in 50%. The median PFS for those with basal-like was 3.0 (mFFX) and 5.5 (GnP) months ($P = .17$), and classical PDAC was 6.3 (mFFX) versus 5.4 (GnP) months ($P = .36$). The median OS in basal-like was 7.5 (mFFX) and 8.9 (GnP) months ($P = .75$) versus in classical OS was 9.7 (mFFX) and 13.9 (GnP) months ($P = .047$). Overall, 75 (54%) of patients received second-line treatment, 33/75 (44%) correlate-guided. The median time on second-line treatment was only 2.1 months with a median OS of 5.4 months for a correlate-guided choice versus 4.4 months on a standard chemotherapy approach ($P = .45$). Conclusion- In the phase II Pancreatic Adenocarcinoma Signature Stratification for Treatment-01 (PASS-01) trial population, PFS was similar between GnP and mFFX; however, OS and safety trends favored GnP. The second-line setting appears inadequate to offer precision choices, given the short survival observed.

25COASDEC73

Title: Primary Results From Blood and Marrow Transplant Clinical Trials Network 1702: Clinical Transplant-Related Long-Term Outcomes of Alternative Donor Allogeneic Transplantation.

Stephanie J. Lee et al.

J Clin Oncol 43, 3369-3380(2025).
https://doi.org/10.1200/JCO-25-00206

Abstract: The likelihood of finding a human leukocyte antigen (HLA)–matched unrelated donor (MUD) for hematopoietic cell transplantation can be predicted using a donor search prognosis score. Patients without a MUD may use alternative donors (haploidentical related, mismatched unrelated, or umbilical cord blood). Methods- This multicenter biological

assignment trial was conducted by the Blood and Marrow Transplant Clinical Trials Network (BMT CTN 1702). Eligibility criteria were broad to mirror clinical practice. The primary end point was 2-year survival from evaluability and compared between those Very Likely (>90%) and Very Unlikely (<10%) to find a MUD. All other patients, Less Likely to find a MUD, were enrolled in an observational arm. Transplant outcomes were compared for all three groups. Results- A total of 1,751 evaluable patients at 47 centers were Very Likely (54.7%), Less Likely (29.5%), and Very Unlikely (15.8%) to identify a MUD. Survival did not differ in univariate (hazard ratio [HR], 1.00 [95% CI, 0.82 to 1.21]; $P = .98$) or multivariate (HR, 1.07 [95% CI, 0.86 to 1.33]; $P = .56$) analyses between the Very Unlikely and Very Likely groups, measured through 2 years from the beginning of a search for a MUD or alternative donor. Of the transplanted patients (n = 1,179), MUD was used for 94% of the Very Likely, 38% of Less Likely, and 9% of Very Unlikely patients. Multivariate analyses showed no differences in relapse, treatment-related mortality, disease-free survival, and acute and chronic graft-versus-host diseases for the three search prognosis groups after transplantation. Conclusion- Using a donor search prognosis strategy to prioritize an alternative donor for patients Very Unlikely to find a MUD resulted in survival and transplant outcomes that were not statistically different compared with those Very Likely to find a MUD.

25COASDEC74

Title: Colorectal-Specific Radiation Dose and Chemotherapy Risk for Subsequent Colorectal Malignancies in Childhood Cancer Survivors: A Childhood Cancer Survivor Study (CCSS) Report.

Constance A. Owens et al.

J Clin Oncol 43, 3403-3421(2025).
https://doi.org/10.1200/JCO-25-00531

Abstract: Among childhood cancer survivors, we evaluated not previously explored relationships between colorectal subsequent malignant neoplasm (SMN) incidence and colorectum-specific radiation dose metrics currently used in radiation therapy (RT) planning and expanded upon previously reported chemotherapy associations. Methods- The Childhood Cancer Survivor Study (CCSS) includes 5-year survivors of childhood cancer diagnosed between 1970 and 1999. RT was assessed as mean colorectal dose (MCD) and the percent volume ($V_{X\ Gy}$) receiving ≥5, 10, 20, 30, and 40 Gy. Chemotherapy was assessed as cumulative doses for procarbazine and platinum agents, cyclophosphamide-equivalent doses for alkylating agents, and doxorubicin-equivalent doses for anthracyclines. Piecewise-exponential models and excess rate ratio (ERR) models evaluated dose-response relationships for the incidence of colorectal SMNs. Reference groups were those not receiving the assessed treatment(s). Results- Among 25,723 survivors (median follow-up = 28.5 years; range = 5.0-48.9), 104 colorectal SMNs were identified. A dose-response relationship was observed between MCD and colorectal SMN rates; incidence rate ratios (IRRs) for 10 to <20 Gy and ≥20 Gy were 3.6 (95% CI, 1.9 to 6.9) and 8.3 (95% CI, 3.9 to 17.8), respectively. When ≥20% of the colorectum volume was irradiated, IRRs increased with increasing volume. The $V_{20\ Gy}$ IRRs were 3.8 (95% CI, 1.9 to 7.6), 4.9 (95% CI, 2.0 to 12.0), and 8.7 (95% CI, 3.5 to 21.6) for irradiated volumes of 20% to <40%, 40% to <80%, and ≥80%, respectively. The IRR was 1.8 (95% CI, 1.0 to 3.0) for doxorubicin-equivalent dose ≥250 mg/m^2, 3.7 (95% CI, 2.2 to 6.4) for cyclophosphamide-equivalent dose ≥6,000 mg/m^2, and 4.5 (95% CI, 2.0 to

10.1) for platinum dose ≥450 mg/m^2. For procarbazine dose, the IRR was 6.3 (95% CI, 3.0 to 13.2) for 4,200 to <7,036 mg/m^2 and 9.0 (95% CI, 4.3 to 18.9) for ≥7,036 mg/m^2. In the absence of RT, colorectal SMN rates increased with exposure to any platinum-based agent (IRR, 3.8 [95% CI, 1.1 to 12.7]), alkylator (IRR, 4.8 [95% CI, 1.6 to 14.4]), or procarbazine (IRR, 16.9 [95% CI, 5.9 to 48.8]). Colorectal SMN rates increased linearly with procarbazine dose (ERR per 1,000 mg/m^2 = 73.0 [95% CI, 26.4% to 119.6%]) and MCD (ERR per 1 Gy = 20.8 [95% CI, 9.0% to 32.5%]). Quadratic ERR models did not improve data fit compared with linear ERR models. Conclusion- These RT and chemotherapy dose-response relationships can better inform contemporary RT planning for pediatric patients and surveillance guidelines for high-risk survivors.

25COASDEC75

Title: Five-Year Follow-Up Analysis of ZUMA-5: Axicabtagene Ciloleucel in Relapsed/Refractory Indolent Non-Hodgkin Lymphoma.

Sattva S. Neelapu et al.

J Clin Oncol 43, 3573-3577(2025).

https://doi.org/10.1200/JCO-25-00668

Abstract: Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved for relapsed/refractory (R/R) follicular lymphoma (FL). Here, we report updated clinical outcomes from ZUMA-5 in 159 enrolled patients with R/R indolent non-Hodgkin lymphoma (iNHL; 127 with FL and 31 with marginal zone lymphoma) after a median follow-up of 64.6 months. Patients underwent leukapheresis and received lymphodepleting chemotherapy and axi-cel (2 × 10^6 CAR T cells/kg). The overall response rate was 90% (75% complete response rate). The median duration of response was 60.4 months, and the median progression-free survival (PFS) was 62.2 months; median time to next treatment and overall survival were not reached (NR). At data cutoff, 55% of patients were alive without requiring subsequent anticancer therapy. Median lymphoma-specific PFS in patients with FL was NR; 34% had progression or death due to lymphoma or study treatment. Notably, after 30 months postinfusion, progression or lymphoma-related deaths were rare. Late-onset toxicities were infrequent and largely unrelated to axi-cel. Durable response and prolonged survival in FL were associated with robust early CAR T-cell expansion and naïve product phenotype. These findings confirm sustained responses and manageable safety with axi-cel in the long term among patients with R/R iNHL and its potential as a curative therapy in FL.

25COASDEC76

Title: Sirolimus and Cyclosporine With Post-Transplant Cyclophosphamide or Mycophenolate Mofetil as Graft-Versus-Host Disease Prophylaxis in Unrelated Donor Hematopoietic Cell Transplantation.

Masumi Ueda Oshima et al.

J Clin Oncol 43, 3600-3609(2025).

https://doi.org/10.1200/JCO-25-01238

Abstract: To determine whether sirolimus (SIR) and cyclosporine (CSP) combined with post-transplantation cyclophosphamide (PTCy), after nonmyeloablative or reduced-intensity conditioning unrelated donor hematopoietic cell transplantation (HCT), would be more

effective than SIR, CSP, and mycophenolate mofetil (MMF) in reducing the risk of chronic graft-versus-host disease (cGVHD) without increasing risk of recurrent malignancy. Methods- In a Phase II trial of HLA-matched or mismatched unrelated donor mobilized blood HCT (ClinicalTrials.gov identifier: NCT03246906), adults with hematologic malignancies ineligible for myeloablative HCT were randomly assigned 1:1 to GVHD prophylaxis with SIR/CSP/PTCy (50 mg/kg once daily on days +3, +4) or SIR/CSP/MMF. The primary end point was 1-year chronic GVHD-free relapse-free survival (CRFS). Results- One hundred forty-five patients were randomly assigned and transplanted. Median follow-up among survivors was 3.0 (range, 0.6-7.0) years. Comparing PTCy-based with non–PTCy-based immunosuppression, estimated 1-year CRFS was 73% (95% CI, 61% to 82%) versus 48% (95% CI, 36% to 59%), translating into a hazard ratio (HR) for CRFS failure of 0.46 (95% CI, 0.26 to 0.79; $P = .005$) for PTCy. Probabilities of acute GVHD (aGVHD) grades II-IV and III-IV, respectively, were 40% versus 42% and 6% versus 10%. One-year estimates for secondary end points were as follows: moderate-to-severe cGVHD, 3% (95% CI, 1% to 9%) versus 33% (95% CI, 22% to 44%); relapse, 15% versus 15%; progression-free survival, 75% versus 78%; survival, 86% versus 86%; and nonrelapse mortality, 10% versus 7%. The HR of ≥grade 3 infections with PTCy versus non-PTCy was 2.65 (95% CI, 1.41 to 4.97; $P = .003$). Conclusion- After HLA-matched or mismatched unrelated donor mobilized blood HCT, replacing MMF with PTCy, when used in combination with SIR and CSP, significantly reduced risk of cGVHD, without increasing risks of aGVHD or relapse. Thus, the combination of PTCy and SIR/CSP may have synergistic cGVHD-protective effects warranting further study.

25COASDEC77

Title: Simultaneous Durvalumab and Platinum-Based Chemoradiotherapy in Unresectable Stage III Non–Small Cell Lung Cancer: The Phase III PACIFIC-2 Study.

Jeffrey D. Bradley et al.

J Clin Oncol 43, 3610-3621(2025).
https://doi.org/10.1200/JCO-25-00036

Abstract: Immunotherapy targeting PD-L1 improves outcomes in patients with unresectable stage III non–small cell lung cancer (NSCLC) and no progression after definitive, concurrent chemoradiotherapy (cCRT). Earlier administration of immunotherapy, simultaneously with cCRT, may improve outcomes further. Methods- Eligible patients were randomly assigned (2:1) to receive either durvalumab or placebo administered from the start of cCRT. Patients without progression after completing cCRT received consolidation durvalumab or placebo (per initial random assignment) until progression. The primary end point was progression-free survival (PFS) by blinded independent central review. Key secondary end points included objective response rate (ORR), overall survival (OS), the proportion of patients alive at 24 months (OS24), and safety. Results- In total, 328 patients were randomly assigned to receive durvalumab (n = 219) or placebo (n = 109). There was no statistically significant difference with durvalumab versus placebo in PFS (hazard ratio [HR], 0.85 [95% CI, 0.65 to 1.12]; $P = .247$) or OS (HR, 1.03 [95% CI, 0.78 to 1.39]; $P = .823$); OS24 was 58.4% versus 59.5%, respectively. Confirmed ORR was 60.7% with durvalumab versus 60.6% with placebo (difference, 0.2% [95% CI, −15.2 to 16.3%]; $P = .976$). With durvalumab versus placebo, respectively, maximum grade 3 or 4 adverse events (AEs) occurred in 53.4% versus

59.3% of patients, pneumonitis or radiation pneumonitis (group term) in 28.8% (grade ≥3: 4.6%) versus 28.7% (grade ≥3: 5.6%), AEs leading to discontinuation of durvalumab or placebo in 25.6% versus 12.0%, and fatal AEs in 13.7% versus 10.2%. Conclusion- Among patients with unresectable stage III NSCLC, durvalumab administered from the start of cCRT failed to demonstrate additional benefit compared with cCRT plus placebo. Consolidation durvalumab following definitive cCRT remains the standard of care in this setting.

25COASDEC78

Title: Remission Assessment by Circulating Tumor DNA in Large B-Cell Lymphoma.

Mark Roschewski et al.

J Clin Oncol 43, 3652-3661(202**5).**

https://doi.org/10.1200/JCO-25-01534

Abstract: Large B-cell lymphomas (LBCLs) are curable, but patients with residual disease after therapy invariably experience progression. Ultrasensitive methods to detect circulating tumor DNA (ctDNA) as minimal residual disease (MRD) may improve the determination of remission. Methods- We integrated data from five prospective studies of frontline anthracycline-based chemotherapy in patients with LBCL. Tumor-specific phased variants were identified from pretreatment samples and monitored at landmark time points. Serial plasma specimens were blindly analyzed for detectable ctDNA as MRD. MRD status was compared with conventional response criteria for prognosis of progression-free survival (PFS). Results- We studied ctDNA-MRD in 137 patients by monitoring 409 plasma specimens over time. Detectable ctDNA rates decreased during therapy with 55% and 78% of patients achieving undetectable ctDNA after two cycles and at the end of therapy, respectively. After a median follow-up of 37 months, the 2-year PFS for patients with detectable versus undetectable ctDNA after two cycles was 67% versus 96% ($P = .0025$; hazard ratio [HR], 6.9) and after therapy was 29% versus 97% ($P < .0001$; HR, 28.7), respectively. Ninety-two (94%) patients with undetectable ctDNA at the end of therapy remained alive without progression, while 19 (68%) patients with detectable ctDNA progressed or died. MRD status at the end of therapy had greater prognostic utility than conventional lymphoma response criteria using positron emission tomography (PET) scans (HR, 3.6 for positive PET and 28.3 for detectable ctDNA).
Conclusion- Ultrasensitive ctDNA detection after frontline LBCL therapy is more prognostic than conventional radiographic response criteria. A refined definition of remission with ctDNA-MRD may improve clinical and psychological outcomes for patients with LBCL.

25COASDEC79

Title: Metformin Active Surveillance Trial in Low-Risk Prostate Cancer.

Neil E. Fleshner et al.

J Clin Oncol 43, 3662-3671(2025).

https://doi.org/10.1200/JCO-25-01070

Abstract: Active surveillance (AS) is a standard management strategy for low-risk prostate cancer (PCa), but a significant proportion of patients ultimately experience disease progression. Metformin, a commonly prescribed antidiabetic agent, has demonstrated antitumor activity in preclinical studies and observational data, prompting investigation into its potential to delay PCa progression. Patients and Methods- The Metformin Active

Surveillance Trial (MAST) was a multicenter, randomized, double-blind, placebo-controlled phase III trial evaluating the efficacy of metformin in men with low-risk, localized PCa managed with AS. Eligible participants were randomly assigned 1:1 to receive either metformin (850 mg twice daily) or placebo and were followed for up to 36 months. The primary end point was time to progression, defined as therapeutic and/or pathologic progression. Progression-free survival (PFS) was assessed using Kaplan-Meier analysis and Cox proportional hazards models. Results- A total of 408 patients were randomly assigned (205 metformin, 203 placebo). After a median follow-up of 36 months, 144 participants experienced progression (70 metformin, 74 placebo), with no significant difference in PFS (hazard ratio [HR], 1.09 [95% CI, 0.79 to 1.52]; $P = .59$). Negative biopsy rates at 36 months were 41.0% (metformin) versus 31.1% (placebo; $P = .181$). In prespecified subgroup analysis, metformin was associated with increased pathologic progression among obese patients (BMI ≥ 30; HR, 2.36 [95% CI, 1.21 to 4.59]; $P = .0092$). Conclusion- Metformin did not reduce progression in men with low-risk PCa on AS. The observed adverse effect in obese patients merits further investigation.

25COASDEC80

Title: Five-Year Outcomes of the POLARIX Study Comparing Pola-R-CHP and R-CHOP in Patients With Diffuse Large B-Cell Lymphoma.

Franck Morschhauser et al.

J Clin Oncol 43, 3698-3705(2025).

https://doi.org/10.1200/JCO-25-00925

Abstract: In the POLARIX study (ClinicalTrials.gov identifier: NCT03274492), polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) showed a significant progression-free survival (PFS) benefit versus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in patients with previously untreated intermediate- or high-risk diffuse large B-cell lymphoma (DLBCL; median follow-up: 28 months). In this 5-year update, sustained PFS benefits favoring Pola-R-CHP were observed. In the global intention-to-treat population (N = 879; median follow-up: 64.1 months), Pola-R-CHP demonstrated a significant PFS benefit over R-CHOP (hazard ratio [HR], 0.77 [95% CI, 0.62 to 0.97]), with 5-year PFS rates of 64.9% (95% CI, 59.8 to 70.0) and 59.1% (95% CI, 53.9 to 64.3), respectively. Although not statistically significant, overall survival analysis showed a HR of 0.85 (95% CI, 0.63 to 1.15) at the 5-year data cut compared with 0.94 (95% CI, 0.67 to 1.33) at the 2-year data cut. In the expanded population, 46 and 62 patients had lymphoma-related deaths in the Pola-R-CHP and R-CHOP arms, respectively. Exploratory analyses showed favorable 5-year survival rates with Pola-R-CHP in high-risk subgroups, including activated B-cell DLBCL and International Prognostic Index score 3-5. Long-term tolerability was similar between treatment arms. Findings confirm Pola-R-CHP represents a standard of care for frontline treatment of DLBCL.

25COASDEC81

Title: Cognitive Impairment and Chemoendocrine vs Endocrine Therapy in Pre- and Postmenopausal Women: A Secondary Analysis of the RxPONDER Randomized Clinical Trial.

Kang IM, Forschmiedt JK, Loch MM, et al.

JAMA Oncol.
https://doi.org/10.1001/jamaoncol.2025.5220

Abstract: Importance Breast cancer treatment is associated with cancer-related cognitive impairment (CRCI). However, the association of endocrine therapy (ET) vs chemotherapy plus endocrine therapy (CET) with CRCI is poorly understood. Objective To compare patient-reported CRCI between women with breast cancer treated with ET vs CET and to consider whether menopausal status may be associated. Design, Settings, and Participants This was a prespecified secondary analysis of RxPONDER (SWOG S1007), a multinational phase 3 randomized clinical trial of more than 5000 women with hormone receptor−positive *ERBB2*-negative (formerly *HER2*-negative) breast cancer with 1 to 3 involved lymph nodes and Oncotype DX (21-gene recurrence score) of 25 or less. Participants were enrolled from February 2011 to September 2017, with results first reported in December 2020. Participants were randomly assigned to CET or ET, with ongoing follow-up. This secondary analysis assessed cognitive function using the Patient-Reported Outcomes Measurement Information System Perceived Cognitive Function Concerns (PCF) questionnaire at baseline, 6, 12, and 36 months. Data were analyzed from July 2022 to August 2025. Intervention Random assignment to CET or ET. Main Outcomes and Measures Mean PCF standardized (T) scores by menopausal status over time using generalized estimating equations analysis for continuous outcomes. Results Of the 568 patients who completed the baseline questionnaire and were included in the analysis, 139 (24%) were premenopausal (median [range] age, 47.8 [28.0-56.3] years) and 429 (76%) were postmenopausal (median [range] age, 62.3 [37.3-87.6] years). Among the 274 (48%) who received CET and the 294 (52%) who received ET alone, CET was determined to have a greater negative association with patient-reported CRCI in both the pre- and postmenopausal participants during the 36-month follow-up. In the ET alone group, PCF scores for premenopausal participants decreased from baseline to 6 and 12 months (53.53, 51.51, and 51.72, respectively) but recovered to baseline (54.36) at 36 months. For postmenopausal participants, mean PCF scores were essentially stable (51.72, 51.13, 51.11, and 51.70, respectively); however, in the CET group, PCF scores for both pre- and postmenopausal participants decreased from baseline to 6 and 12 months (premenopausal, 52.84, 49.27, 48.04; postmenopausal, 50.65, 48.39, 47.13, respectively) and did not return to baseline at 36 months (premenopausal, 49.25; postmenopausal, 48.44). The difference in longitudinal mean PCF scores over time between CET and ET groups was −3.02 (95% CI, −5.33 to −0.72; $P = .01$) for premenopausal and −2.37 (95% CI, −3.92 to −0.82; $P = .003$) for postmenopausal participants. Conclusions and Relevance This secondary analysis of the RxPONDER found that CET had a greater negative association with patient-reported CRCI compared to ET alone in both pre- and postmenopausal participants over a 36-month follow-up period. Interventions to prevent or treat CRCI are needed to improve the long-term quality of life of these patients treated with chemotherapy.

25COASDEC82

Title: Bacterial Decolonization With Mupirocin Ointment for Acute Radiation Oral Mucositis Prevention: A Phase 3 Randomized Clinical Trial.

Liao Z, Xiong X, Zhao L, et al.
JAMA Oncol. 2025;11(10):1141–1149.

https://doi.org/10.1001/jamaoncol.2025.2361

Abstract: Importance Acute radiation oral mucositis (AROM) is a major dose-limiting toxic effect in patients with nasopharyngeal cancer undergoing radiotherapy. Reduction of severe (grade ≥3) AROM by bacterial decolonization (BD) could improve treatment tolerance and quality of life. Objective To evaluate the efficacy of BD with mupirocin nasal ointment in alleviating severe AROM compared with standard of care (SoC) by reducing *Staphylococcus aureus* colonization in nasal and oral mucosal during radiotherapy for nasopharyngeal cancer. Design, Setting, and Participants This was a single-center, open-label, phase 3 randomized clinical trial in China that enrolled patients with nasopharyngeal carcinoma (NPC) undergoing definitive chemoradiotherapy between July 2023 and February 2024. Data were analyzed from June 2024 to September 2024. Interventions The BD group received mupirocin nasal ointment twice daily for 3 days before radiotherapy for 5 consecutive days followed by a 1-week break, which was repeated throughout radiotherapy. Patients in the SoC group received routine nasal and oral care. Main Outcomes and Measures The primary outcome was the incidence of severe (grade ≥3) AROM. Oral mucositis assessments were performed by independent evaluators who were blinded to group assignments. Secondary end points included quality of life assessed using the Quality-of-Life Questionnaire−Head and Neck 43 [QLQ-H&N43]), and the colonization levels of *S aureus* in nasal and oral mucosa. Results A total of 176 patients (mean [SD] age, 52.1 [10.1] years; 42 female [23.9%] individuals) were randomly assigned to the BD intervention group (n = 88) or the SoC control group (n = 88). In the BD group, severe AROM occurred in 20 of 88 patients (22.7%) compared with 42 (47.7%) in the SoC group (relative risk, 0.48; 95% CI, 0.31-0.74; $P < .001$). Multivariable logistic analysis confirmed the effect of BD (odds ratio, 0.27, 95% CI, 0.13-0.54; $P < .001$) on severe AROM risk reduction. The QLQ-H&N43 assessment showed BD significantly reduced symptom severity compared to SoC during radiotherapy, with lower median (IQR) pain scores (25.0 [25.0-50.0] vs 50.0 [25.0-50.0]) and fewer swallowing difficulties (8.3 [8.3-33.3] vs 33.3 [8.3-33.3]). Colonization rates of *S aureus* at the end of radiotherapy were lower in the BD than in the SoC group: nasal, 9.4% (8 of 85) vs 22.9 % (19 of 83) and oral, 5.9% (5 of 85) vs 20.5% (17 of 83). Conclusions and Relevance This phase 3 randomized clinical trial demonstrated that BD with mupirocin nasal ointment effectively reduced severe AROM, improved quality of life by alleviating oral pain and swallowing difficulties, and significantly reduced both nasal and oral *S aureus* colonization during radiotherapy. This approach offers a cost-effective strategy for AROM management, and although further studies are required to validate the findings, these results highlight the potential of microbial management to reduce radiation-related complications in patients with nasopharyngeal carcinoma.

25COASDEC83

Title: Outcomes of Solid Organ Transplant Recipients With Advanced Cancers Receiving Immune Checkpoint Inhibitors: A Systematic Review and Individual Participant Data Meta-Analysis.

Saleem N, Wang J, Rejuso A, et al.

JAMA Oncol. 2025;11(10):1150–1159.
https://doi.org/10.1001/jamaoncol.2025.2374

Abstract: Importance Immune checkpoint inhibitors (ICIs) have improved overall survival in patients with advanced-stage cancers. However, data on their efficacy and safety in solid organ transplant recipients (SOTRs) are limited. Objective To examine cancer-specific and patient survival among SOTRs with advanced-stage cancer receiving ICIs and identify factors associated with patient and graft outcomes. Data Sources Electronic databases and clinical registries, including MEDLINE, Embase, ClinicalTrials.gov, Australia New Zealand clinical trials registry, and the World Health Organization International Clinical Trials Registry Platform, were searched from inception to June 2024 without language restriction. Study Selection Case reports and series, observational studies, and clinical trials that described the treatment of advanced-stage cancers using ICIs in SOTRs were included. Data Extraction and Synthesis Individual participant data were extracted and synthesized using a single-stage random-effect model. Main Outcomes and Measures Time to cancer-related death was the primary outcome. The main secondary outcomes included time from ICI initiation to first rejection and cancer response according to Response Evaluation Criteria in Solid Tumors 1.1 criteria. Adjusted Cox proportional hazards regression models were conducted for time-to-event analyses. Results Of 140 studies, 128 studies involving 343 SOTRs treated with ICI were included. Most participants were male (76.9%), kidney transplant recipients (70.9%), with a median (IQR) age of 63 years (14-88 years), and treated with programmed cell death protein-1 inhibitors (72.9%). Within 3 years of ICI initiation, 52.8% (95% CI, 43.9%-61.6%) died of cancers. Acute rejection occurred in 36.2% (95% CI, 30.7%-41.7%) at 1 year, and 18.4% (95% CI, 13.7%-23.1%) experienced graft loss at 1 year. Objective response at 1 year was 31.6% (95% CI, 25.0%-37.7%), with a higher response observed in patients with cutaneous squamous cell carcinoma (cSCC) (61.0% [95% CI, 45.5%-76.4%]) than melanoma (48.5% [95% CI, 26.8%-70.3%]), and other solid organ cancers (26.9% [95% CI, 14.5%-39.3%]). Transplant recipients with melanoma (hazard ratio [HR], 2.29; 95% CI, 1.31-3.99) and solid organ cancers (HR, 2.84; 95% CI, 1.70-4.74) experienced higher rates of cancer-related deaths than those with cSCC. Recipients with melanoma have a higher risk of acute rejection (HR, 2.88; 95% CI, 1.69-4.90) than cSCC. Maintenance with steroids and mammalian target of rapamycin inhibitors (mTORIs) was associated with a lower risk of rejection compared with other immunosuppressive agents (HR, 0.30; 95% CI, 0.14-0.63). Conclusions and Relevance In this study, cancer outcomes in SOTRs receiving ICIs varied by cancer type, with a higher probability of achieving response among those with cSCC than other cancers. Concurrent use of mTORIs and steroids during ICI therapy may reduce the risk of acute allograft rejection.

25COASDEC84

Title: Integrating Quality of Life and Survival in Systemic Therapy for Advanced Hepatocellular Carcinoma: A Network Meta-Analysis.

Celsa C, Di Maria G, Lombardi P, et al.

JAMA Oncol. 2025;11(10):1160–1168.
https://doi.org/10.1001/jamaoncol.2025.2470

Abstract: Importance Multiple immunotherapy-based combinations and tyrosine kinase inhibitors are approved for first-line treatment of unresectable or advanced hepatocellular carcinoma (HCC). While overall survival remains the primary efficacy end point, health-related quality of life (HR-QoL) represents a crucial complementary outcome that has not

been comprehensively compared across available treatments.Objective To compare the HR-QoL effects associated with different first-line treatments for unresectable or advanced HCC and to integrate treatment-induced survival benefit with impact on patients' HR-QoL.Data Sources The MEDLINE, CENTRAL, and Scopus databases were systematically searched for studies published from inception through November 2024. The search was supplemented with manual reviews of reference lists and abstracts from main oncology conferences from the past 5 years (2020-2024).Study Selection Phase 3 randomized clinical trials comparing tyrosine kinase inhibitor monotherapy to immune checkpoint inhibitor–based therapies in first-line advanced HCC and reporting HR-QoL deterioration were included.Data Extraction and Synthesis Study selection and data extraction were performed by 2 independent reviewers, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The Cochrane Collaboration tool was used to assess risk of bias. A bayesian network meta-analysis was performed using sorafenib as the comparator.Main Outcomes and Measures Time to deterioration of HR-QoL domains were assessed using the European Organization for Research and Treatment of Cancer's Quality-of-Life Questionnaire Core 30 and HCC18. Treatment ranking was calculated using surface under the cumulative ranking (SUCRA) for HR-QoL items.Results Seven HR-QoL items from 9 randomized clinical trials enrolling 6425 patients met inclusion criteria. SUCRA calculations showed that atezolizumab plus bevacizumab had the highest probability of reducing deterioration of global health status and QoL (85%), abdominal swelling (95%), jaundice (89%), and pain (86%). When integrating HR-QoL with overall survival, atezolizumab plus bevacizumab outperformed all other treatments across all items.Conclusions and Relevance This network meta-analysis found that atezolizumab plus bevacizumab provides the best balance between QoL preservation and overall survival benefit compared to other systemic therapy options in unresectable or advanced HCC. This integrated assessment of survival and quality of life outcomes offers a more patient-centered approach for treatment selection in clinical practice.

Surgical Oncology

25COASDEC01:

Title: Risk factors and intraoperative identification of non-lepidic predominant lung adenocarcinoma presenting as subsolid nodule: A multicenter study,

Donglai Chen, Qifeng Ding, Yongzhong Li, Zhangqiang Chen, Jian Shu, Yiming Mao, Shanzhou Duan, Lijie Tan, Yongbing Chen,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110471,
https://doi.org/10.1016/j.ejso.2025.110471.

Abstract: The purpose of this study was to assess the prognostic factors for non-lepidic invasive adenocarcinoma presenting as subsolid nodules. The feasibility of detecting non-lepidic predominant patterns on frozen section (FS) was also evaluated.A multicenter retrospective cohort of 614 patients with clinical T1N0M0 non-lepidic invasive adenocarcinoma presenting as subsolid nodule was included. Two subgroups were divided based on the consolidation-to-tumor ratio (CTR) on lung window: ground glass opacity (GGO)-dominant subgroup (CTR<0.5), solid-dominant subgroup (CTR≥0.5). Kaplan-Meier approach and multivariable Cox models were used to identify risk factors for recurrence-free survival (RFS) and overall survival (OS). FS and final pathology (FP) of 100 specimens were also reviewed by five pathologists for tumor grading synchronously. Multivariate analysis indicated that segmentectomy was a risk factor for shortened RFS and OS in the solid-dominant subgroup rather than in the GGO-dominant one. Subset analysis demonstrated survival disadvantages of segmentectomy for high-grade adenocarcinoma but not for intermediate-grade one in the solid-dominant subgroup. However, segmentectomy exhibited non-inferiority to lobectomy in the GGO-dominant subgroup irrespective of tumor grade. The overall accuracy of identifying non-lepidic patterns was 84 % with a good interobserver agreement. Multivariable logistic analysis identified presence of complex glandular pattern and acinar pattern as independent predictors of the discrepancy between FS and FP. Segmentectomy should be cautiously performed for patients with radiologically solid-dominant non-lepidic invasive adenocarcinoma, especially for those with high-grade patterns. FS had high diagnostic accuracy and satisfactory interobserver agreement for tumor grading, which might aid surgeons in determining the appropriate surgical procedure.

Keywords: Subsolid nodules; Grading system; Surgical procedure; Frozen section

25COASDEC02:

Title: Development of a novel predictive nomogram to prevent 'futile surgery' in gallbladder cancers: A single center analysis of 1196 resected gallbladder cancers,

Gurudutt P. Varty, Shraddha Patkar, Mufaddal Kazi, Karthik Velmurugan, Amita Sekhar Padhy, Baskaran Dhanapal,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110492,
https://doi.org/10.1016/j.ejso.2025.110492.

Abstract: Advancement in technical expertise, perioperative care and chemotherapeutic regimes have led to stretching the limits of surgery for gallbladder cancers (GBCs). Being an inherently aggressive cancer, do all the patients of GBCs really benefit from a surgical procedure? A total of 1196 cases of gallbladder adenocarcinoma who underwent curative resection from January 2010 to December 2023 were analysed. FS was defined as recurrences

or deaths within 6 months of surgery. A multivariate model was built and a preoperative nomogram was created. A total of 133 (11.1 %) patients underwent a FS with a median overall survival of 8.9 months compared to 88.7 months for patients who underwent a non-futile surgery ($p < 0.001$). Predefined 'TMH criteria' was used to differentiate 'borderline resectable' GBC (BR-GBC, n = 344, 28.8 %) from upfront resectable GBC (n = 852, 71.2 %) and were subjected to neoadjuvant chemotherapy. Multivariable analysis revealed log CA 19–9 (OR - 1.12, 95 %CI - 1.02–1.22, $p = 0.014$), borderline resectable GBCs (OR, 1.97, 95 %CI, 1.34–2.88, $p = 0.001$) and extended/multivisceral resection (OR - 2.01, 95 %CI - 1.13–3.45, $p = 0.014$) as key preoperative factors predicting a FS. A predictive nomogram was built based on these preoperative factors which had a classification accuracy of 0.888 and a precision of 0.790 on internal validation. In modern day oncology where tumour biology and patient selection assumes prime importance, incorporating our predictive nomogram in preoperative clinical decision-making pathway may guide the clinicians to avoid FS in patients of GBC.

25COASDEC03:

Title: Postoperative recurrence patterns and prognostic determinants in early-onset early-stage gastric cancer: A multicenter retrospective real-world study,

Chenbin Lv, Linyan Tong, Ju Lu, Binbin Xu, Hongda Pan, Qiuxian Chen, Jie Chen, Yuqin Sun, Rongjie Huang, Fenglin Liu, Lisheng Cai,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110544,
https://doi.org/10.1016/j.ejso.2025.110544.

Abstract: While most studies focus on postoperative recurrence in either early-onset (≤45 years) or early-stage gastric cancer, limited attention has been devoted to recurrence dynamics in early-onset EGC. This study characterized postoperative recurrence patterns and identifies clinicopathological risk factors in early-onset early-stage gastric cancer (EGC). We analyzed 7131 patients undergoing curative gastrectomy for gastric cancer (January 2013–December 2019) at two high-volume centers in China, with focused evaluation of clinicopathological characteristics, recurrence patterns, and survival outcomes in early-onset EGC. Among 252 early-onset EGC patients, 41 (16.3 %) developed recurrence, predominantly hematogenous (56.1 %) and peritoneal (34.1 %). Recurrence risk peaked at 10 months postoperatively, declined by 36 months, then gradually rebounded. The 5-year overall survival (OS) and recurrence-free survival (RFS) rates were 76.6 % and 70.2 %, respectively. Multivariate analysis identified elevated preoperative tumor markers, lymph node metastasis (N+), lymphovascular invasion (LVI+), and poor differentiation as independent predictors of recurrence. Early recurrence (≤2 years) was independently driven by elevated preoperative tumor markers and N+, while late recurrence (>2 years) linked to BMI≥25 kg/m2 and LVI+. Subgroup analysis demonstrated that postoperative adjuvant chemotherapy significantly improved RFS (HR = 0.12) and OS (HR = 0.26) in pN2-3 patients compared with those without adjuvant chemotherapy. Early-onset EGC patients with preoperative elevated tumor markers, N+, LVI+, or poor tumor differentiation demonstrated higher recurrence risk, warranting intensified surveillance within 2 years. Postoperative adjuvant chemotherapy is strongly recommended, particularly for pN2-3 disease. Extended follow-up is advised for patients with BMI≥25 kg/m2 or LVI+.

Keywords: Gastric cancer; Early-stage; Early-onset; Postoperative recurrence; Prognosis

25COASDEC04:

Title: T3 gallbladder cancer: surgical outcomes according to the mode of tumor spread and treatment considerations for oncological resectability,

Yusuke Kawachi, Jun Sakata, Tatsuya Nomura, Kabuto Takano, Takuya Ando, Koji Toge, Yuki Hirose, Kazuyasu Takizawa,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110457,
https://doi.org/10.1016/j.ejso.2025.110457.

Abstract: This study aimed to clarify surgical outcomes for patients with pT3 gallbladder cancer according to the mode of tumor spread. A total of 85 patients with pT3 gallbladder cancer who underwent curative-intent surgery were analyzed. Each tumor was classified according to the mode of spread. Five-year overall survival (OS) in patients with involvement of the liver alone (n = 25), involvement of the extrahepatic bile duct alone (n = 29), involvement of one other organ/structure alone or perforation of the peritoneal side of the serosa alone (n = 9), and involvement of both the liver and one other organ/structure (n = 22) was 36.0%, 29.0%, 22.2%, and 9.1%, respectively. For patients with involvement of the liver alone, 5-year OS was > 30% regardless of type of hepatectomy. Among 29 patients with involvement of the extrahepatic bile duct alone, 8 patients survived ≥ 5 years; 3 underwent extended cholecystectomy and 5 underwent more extensive resection. Despite performing extensive resection, 5-year OS was 12.5% for patients with involvement of both the liver and one other organ/structure. The mode of spread other than involvement of the liver alone or extrahepatic bile duct alone was an independent predictor of worse OS (hazard ratio 1.675; p = 0.046). Surgery is an acceptable option for pT3 gallbladder cancer with involvement of the liver alone or extrahepatic bile duct alone regardless of the type of resection procedure. However, the survival benefit of surgery is limited for this tumor with other modes of spread.

Keywords: Gallbladder neoplasms; pT3 gallbladder cancer; Radical surgery; Surgical indication; Tumor spread; Prognosis

25COASDEC05:

Title: An onco-vascular surgical approach: Internal iliac artery transposition for external iliac artery repair during cytoreductive surgery,

Ezgi Altınsoy, Veysel Cem Özcan, Hikmat Zeynalov, Enes Cebeci, Selim Tamam, Serdar Çulcu, Ali Ekrem Ünal,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110503,
https://doi.org/10.1016/j.ejso.2025.110503.

Abstract: Cytoreductive surgery (CRS) in advanced pelvic malignancies may require resection of major vessels, including the external iliac artery (EIA). The aim of this study was to assess the feasibility and safety of ipsilateral transposition of the internal iliac artery as a reconstructive technique for the management of external iliac artery defects. Between 2015 and 2024, six patients underwent CRS with EIA resection and reconstruction using ipsilateral IIA transposition at an expert center in surgical oncology. Postoperative vascular assessment was performed using Doppler ultrasonography and ankle-brachial index (ABI) measurements in all patients, with the exception of one patient who underwent CT angiography and conventional angiography. The cohort included four female and two male patients with a mean age of 58.5 years. Diagnoses included serous ovarian carcinoma (n = 2), liposarcoma (n = 2), and colorectal carcinoma (n = 2); four patients had recurrent disease. Postoperative

complications occurred in four patients (67 %), including surgical site infection in two patients, urinary leakage in one patient, and enterocutaneous fistula in one patient; however, no vascular complications were observed. There was no 30-day postoperative mortality, and two patients died within the first year; one from enterocutaneous fistula complications and one from metastatic disease. Among the surviving patients, none developed chronic limb ischemia or any other symptoms related to the vascular anastomosis. Internal iliac artery transposition is a safe and effective autologous reconstruction technique for EIA defects during CRS. This approach offers reliable vascular repair without extending operative time and may support complete oncologic resection while minimizing morbidity.

Keywords: Autologous vascular grafts; Cytoreductive procedure; External iliac artery; Internal iliac artery transposition; Vascular reconstruction

25COASDEC06:

Title: Re-evaluating the necessity of removing residual calcifications detected after surgery in HR-/HER2+ breast cancer with pathologic complete response,

Cho Eun Lee, Seok Jin Nam, Seok Won Kim, Jonghan Yu, Byung Joo Chae, Se Kyung Lee, Jai Min Ryu,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110476,
https://doi.org/10.1016/j.ejso.2025.110476.

Abstract: Neoadjuvant chemotherapy(NAC) is now widely used in breast cancer to reduce tumor burden and potentially achieve pathologic complete response (pCR). However, when planning breast conserving surgery (BCS) after NAC, considerable debates remain regarding the appropriate extent of surgery. Therefore, this study was designed to comprehensively analyze residual calcifications in patients undergoing BCS following NAC, particularly regarding residual calcifications. This retrospective observational study included hormone receptor-negative (HR-) and human epidermal growth factor receptor 2-positive (HER2+) breast cancer patients treated with NAC followed by BCS from 2015 to 2020. Patients were grouped by the presence of residual calcifications. Imaging (including mammography and magnetic resonance imaging (MRI)), pathology, and clinical data were reviewed. Survival outcomes were analyzed using Kaplan-Meier curves and statistical tests appropriate to variable types. Among 150 HR-/HER2+ breast cancer patients who achieved pCR after NAC following BCS, 34 patients (22.7 %) showed residual calcifications on postoperative mammography. No statistically significant differences were observed in baseline characteristics or survival outcomes according to the presence of postoperative residual calcifications, including local recurrence free survival, disease free survival, distant metastasis free survival and overall survival. Subgroup analyses by yp T stage showed consistent results. In HR-/HER2+ breast cancer patients achieving pCR after NAC, residual calcifications on postoperative imaging were not associated with worse survival outcomes. Close observation may be a reasonable option compared to additional surgery when negative margins and pCR are confirmed.

Keywords: Neoadjuvant therapy; Pathologic complete response; Breast neoplasm; Calcification; Physiologic

25COASDEC07:

Title: CT-based radiomics deep learning signatures for noninvasive prediction of early recurrence after radical surgery in locally advanced colorectal cancer: A multicenter study,

Yongjie Zhou, Jinhong Zhao, Yongming Tan, Fei Zou, Lei Fang, Pengfei Wei, Wei Zeng, Lianggeng Gong, Lan Liu, Linhua Zhong,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110482,
https://doi.org/10.1016/j.ejso.2025.110482.

Abstract: Preoperative identification of high-risk locally advanced colorectal cancer (LACRC) patients is vital for optimizing treatment and minimizing toxicity. This study aims to develop and validate a combined model of CT-based images and clinical laboratory parameters to noninvasively predict postoperative early recurrence (ER) in LACRC patients. A retrospective cohort of 560 pathologically confirmed LACRC patients collected from three centers between July 2018 and March 2022 and the Gene Expression Omnibus (GEO) dataset was analyzed. We extracted radiomics and deep learning signatures (RDs) using eight machine learning techniques, integrated them with clinical-laboratory parameters to construct a preoperative combined model, and validated it in two external datasets. Its predictive performance was compared with postoperative pathological and TNM staging models. Kaplan-Meier analysis was used to evaluate preoperative risk stratification, and molecular correlations with ER were explored using GEO RNA-sequencing data. The model included five independent prognostic factors: RDs, lymphocyte-to-monocyte ratio, neutrophil-to-lymphocyte ratio, lymphocyte-Albumin, and prognostic nutritional index. It outperformed pathological and TNM models in two external datasets (AUC for test set 1:0.865 vs. 0.766, 0.665; AUC for test set 2: 0.848 vs. 0.754, 0.694). Preoperative risk stratification identified significantly better disease-free survival in low-risk vs. high-risk patients across all subgroups ($p < 0.01$). High enrichment scores were associated with upregulated tumor proliferation pathways (epithelial-mesenchymal transition [EMT] and inflammatory response pathways) and altered immune cell infiltration patterns in the tumor microenvironment. The preoperative model enables treatment strategy optimization and reduces unnecessary drug toxicity by noninvasively predicting ER in LACRC.

Keywords: Computed tomography; Locally advanced colorectal cancer; Radiomics; Deep learning; Early recurrence

25COASDEC08:

Title: AI-assisted precise identification and segmentation of parathyroid glands in multi-approach endoscopic and robotic thyroid surgeries,

Jin-Yuan Liu, Si-Cheng Zhang, Qian Ma, Chao-Ming Zhang, Long-Yue Zhang, Yu-Qiu Zhou,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110506,
https://doi.org/10.1016/j.ejso.2025.110506.

Abstract: With the growing demand for cosmetically appealing, scar-free thyroidectomy procedures driving rapid advances in endoscopic and robotic technology, protecting the parathyroid glands (PGs) during remote-access thyroid surgery is essential to minimize complications and ensure favorable outcomes. However, current methods rely primarily on the surgeon's experience and are limited in complex environments. In this study, we

developed a comprehensive artificial intelligence (AI) model for precise PG identification and segmentation during multi-approach remote-access thyroid surgery. A total of 210 surgical videos from Sichuan Cancer Hospital, encompassing multiple remote-access approaches, were used to develop AI models. We trained and evaluated five AI models and selected the best-performing YOLOv11 model for further development of our intelligent system, SmartThyroid. The differences in performance between SmartThyroid and surgeons in terms of PG recognition rates, time, and duration were analyzed. SmartThyroid demonstrated excellent performance, achieving a mean Dice of 0.873, a mean IoU of 0.804, and an AP50 of 0.974. In the test group, SmartThyroid outperformed all surgeons in initial recognition time. It showed higher PG recognition rates and longer duration compared to junior surgeons, while performing similarly to senior surgeons. Furthermore, SmartThyroid significantly reduced initial recognition time and improved duration for all surgeons. Junior surgeons also showed enhanced PG recognition rates. SmartThyroid is an innovative AI model for precise PG identification and segmentation during multi-approach remote-access thyroid surgeries. It enhances the accuracy and efficiency of PGs identification in testing.

Keywords: Parathyroid glands; Artificial intelligence; Thyroid cancer; Robotic thyroidectomy; Endoscopic

25COASDEC09:

Title: Evaluation of risk-reducing radical fimbriectomy followed by delayed oophorectomy in high-risk Women: A single-center retrospective study,

Sophie Schoenen, Carlos Martinez Gomez, Camille Pasquesoone, Julie Alline, Mathilde Duchatelet, Séverine Risbourg,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110469,
https://doi.org/10.1016/j.ejso.2025.110469.

Abstract: Ovarian carcinoma is a leading cause of cancer-related mortality in women. Approximately 20 % of cases are hereditary, mainly BRCA mutations. Current clinical guidelines recommend bilateral salpingo-oophorectomy between ages 35–45 for high-risk individuals, leading to premature menopause. Given evidence supporting the tubal origin of most ovarian cancers, radical fimbriectomy followed by delayed oophorectomy may offer a menopause-sparing alternative for women refusing early ovariectomy.To evaluate the oncologic safety and clinical outcomes of this two-step risk-reducing strategy. This retrospective single-center study included all high-risk premenopausal women who had completed childbearing, declined BSO and underwent radical fimbriectomy between 2014 and 2022. The primary outcome was the incidence of ovarian or pelvic cancer following radical fimbriectomy, estimated using the Kalbfleisch-Prentice method. Secondary outcomes included surgical complications, tubal lesions, menopause onset, breast cancer incidence and delayed oophorectomy rate. A total of 132 women were included; 62.9 % had BRCA1, 25.8 % BRCA2, and 11.3 % other high-risk mutations (RAD51C, PALB2). No tubal lesions were found in 121 cases (91.7 %), while 11 (8.3 %) had abnormalities: one high-grade serous carcinoma, six serous tubal intraepithelial carcinoma, and four minor lesions. After a median 30.4-month follow-up, no high-grade serous carcinoma was reported. Delayed bilateral oophorectomy was performed in 24 women (18.5 %), and menopause occurred in 27 at a median age of 45. One pregnancy occurred post-fimbriectomy via assisted reproductive technology. Radical fimbriectomy with delayed oophorectomy may be a safe and feasible

option for high-risk women seeking to avoid early menopause. Longer-term prospective studies are needed.

Keywords: Radical fimbriectomy; Delayed bilateral oophorectomy; Risk-reducing surgery; Ovarian cancer prevention; Hereditary breast and ovarian cancers

25COASDEC10:

Title: Local management of second breast cancer event after primary breast conserving therapy: The patient's perspective,

Jean-Michel Hannoun-Levi, Julie Margenthaler, Bethany Anderson, Rosa Di Micco, Douglas Arthur, Marianne Aznar,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110484,
https://doi.org/10.1016/j.ejso.2025.110484.

Abstract: In case of a second ipsilateral breast cancer event (2ndiBCE) after primary breast conserving treatment (BCT), patients are offered salvage mastectomy (SM) or, for selected patients, 2ndBCT. An international survey dedicated to breast cancer survivors investigated patients' preferences and expectations. An international survey was drafted jointly with breast cancer patient advocates from the United States (n = 6) and Europe (n = 2). The survey was validated with 33 questions divided into four themes: demographic data, oncological outcomes, patient views and financial issues. The survey was sent to breast cancer survivors. All information provided was anonymized. From 06/24 to 10/24, 105 patients answered the online survey. The common patient profile was a white (76 %), married (61.5 %), Christian (58.8 %), US-resident (70.2 %) woman aged between 61 and 70 (62.2 %). Long-term outcomes were perceived as being well established for SM (51.5 %) and 2ndBCT (17.1 %). Breast re-irradiation was considered at risk of complications (65.7 %), and 63 % of the patients thought that 2ndBCT provides a more acceptable body self-image. 2ndBCT was expected to give superior cosmetic outcomes than SM with breast reconstruction (55.4 %). Having enough information and ample time to consider the pros and cons of treatment options were very important/important for 99 % and 96.2 %, respectively. Treatment choice was not influenced by financial concerns for 68.3 %. Patient perspective is very important in the decision-making process regarding salvage treatments. Physicians must provide clear, timely information which will enable patients to choose the treatment that best meets their expectations.

Keywords: Breast cancer; Ipsilateral breast cancer recurrence; Mastectomy; 2nd breast conserving treatment; Re-irradiation

25COASDEC11:

Title: Robotic single-port (da Vinci SP) versus multiport (da Vinci Xi) for the treatment of atypical endometrial hyperplasia and endometrial cancer: A multi-institutional comparison of surgical outcomes,

Giuseppe Cucinella, Stefano Restaino, Valentina Bruno, Gabriella Schivardi, Filippo Maria Capomacchia,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110508,
https://doi.org/10.1016/j.ejso.2025.110508.

Abstract: The da Vinci SP robotic platform offers a novel single-port approach for minimally invasive surgery. Despite its potential, data on its safety and performance in

gynecologic oncology remain limited. We aimed to compare surgical outcomes of da Vinci SP versus da Vinci Xi systems in the staging of endometrial cancer (EC). This is a multi-institutional study. Data of consecutive patients with apparent early-stage EC or atypical endometrial hyperplasia who underwent robotic surgery between January 2023–March 2025 were collected. The primary outcome was to compare the surgical outcomes between da Vinci SP and da Vinci Xi. A total of 189 patients were included: 97 (51.3 %) underwent SP surgery and 92 (48.7 %) Xi. The median (range) of operative time, estimated blood loss, and postoperative hospital stay were comparable for SP and Xi groups (140 [70–296] vs. 143 [60–297] min, p = 0.66, 40 [0–250] vs. 64 [0–1300] mL, p = 0.12, 3 [1–11] vs. 3[1–10] days, p = 1). Docking time was significantly shorter in the SP group (10 [4–31] vs. 12 [7–30] min for SP and Xi, respectively, p = 0.004). Intraoperative or post-operative complications rates were comparable (p = 0.30 and p = 0.14,respectively). The patient-reported pain score was significantly lower at 12h and 24h in the Xi group (p = 0.001), while was comparable at 48h after surgery (p = 1). The da Vinci SP system appears to be non-inferior to the multiport da Vinci Xi for surgical staging of early-stage EC. Comparable perioperative outcomes support its clinical use, although patient selection criteria and long-term results require further investigation.

Keywords: Endometrial cancer; Single port; Da vinci SP; Robotic; Minimally invasive

25COASDEC12:

Title: Quality of surgery in oncological trials: the patient's perspective,

J.W. Butterworth, P.R. Boshier, A. Tsai, S. Mavroveli, G.B. Hanna,
European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110451,
https://doi.org/10.1016/j.ejso.2025.110451.

Abstract: There has recently been increased focus on patient involvement in decision making within healthcare research. Although expert opinion regarding quality of surgery in oncological trials has been reported, the patients' perspective has not yet been explored. Two in-depth focus groups were conducted with ten participants representing the oesophageal patient association (OPA). Focus group discussion explored patients' opinion regarding quality of surgery in trials and potential mitigating strategies. Identified themes were utilised to create a semi-structured survey subsequently completed by 41 OPA members. Forty-five themes were identified from thematic analysis of focus group data falling within three categories: quality of surgery (n = 16); challenges to quality of surgery (n = 16) and proposed mitigating strategies (n = 13). Strategies to overcome generic challenges included: further education for non-specialists, and enhancing surgeons' training. Trial specific mitigating strategies included: utilising a structured method of assessing surgeons' competencies, including specialist centres, and monitoring of surgery. The survey revealed key challenges to quality of surgery included insufficient beds (90 %) and a lack of funding (75 %). Key survey strategies to overcome challenges to quality of surgery included: Monitoring to check operative standards are being met within trials (94 %), and; raising awareness/training regarding postoperative complications amongst non-specialist healthcare providers (94 %). This is the first study to explore patient perspective on quality of surgery. Public healthcare planners and members of the surgical oncology community should recognise the importance of patient perceived challenges and consider incorporation of their proposed mitigation strategies to improve the quality of surgery in clinical trials.

25COASDEC13:

Title: Locally advanced cervical cancer and para-aortic lymphadenectomy: impact of the number of removed lymph nodes, a FRANCOGYN group study,

E. Lugan, A. Lacorre, F. Margueritte, L. Ouldamer, Y. Kerbage, X. Carcopino, P.A. Bolze, C. Akladios,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110490,
https://doi.org/10.1016/j.ejso.2025.110490.

Abstract: Cervical cancer is the fourth most common cancer worldwide among women. Surgical staging by para-aortic lymph node dissection (PALND) is performed when the cancer is locally advanced (LACC). There are no recommendations concerning the number of lymph node that must be removed during this surgery which hasn't prove is effectiveness concerning survival. We conducted a retrospective multicenter descriptive and comparative study with data from FRANCOGYN group. We included 578 patients with LACC (IB3-IVA FIGO 2028) who underwent a PALND, 190 with <10 nodes and 388 with at least 10 nodes. The primary outcome was to evaluate the impact of the number of lymph nodes removed on the positivity of the staging. The secondary outcomes were to evaluate the impact of the number of lymph nodes removed on the treatment, the morbidity and the survival of the patients. There was no significant difference concerning the positivity of the staging between the two groups with 17,4 % and 16,2 % of positive staging (p = 0,8). There were no significant differences concerning the peri and post operative complications, the modification of the stage and treatment or the OS and DFS. It would appear that para-aortic staging with at least 10 or more nodes does not confer any advantage in terms of positivity and survival over staging with fewer than 10 nodes.

Keywords: Para-aortic lymphadenectomy; Lymph nodes; Cervical cancer

25COASDEC14:

Title: Impact of COVID-19 on neoadjuvant chemotherapy efficacy in patients with breast cancer: An ambidirectional cohort study and mendelian randomization analysis,

Yali Wang, Jiaqi Zhan, Shunyi Liu, Minyan Chen, Lili Chen, Yuxiang Lin, Jialin Hou, Liuwen Yu, Xiaobin Chen,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110496,
https://doi.org/10.1016/j.ejso.2025.110496.

Abstract: Patients with breast cancer are susceptible to coronavirus disease (COVID-19), which affects cancer treatment efficacy and prognosis. However, its effects on neoadjuvant chemotherapy (NAC) response and its genetic correlation with breast cancer remain unclear. We aimed to clarify these effects and investigate potential genetic associations and shared pathogenic mechanisms. In this ambidirectional (retrospective and prospective) cohort study involving 856 breast cancer patients receiving NAC, with and without COVID-19, we evaluated the impact of COVID-19 on NAC response using multivariable logistic regression and three matching methods: propensity score matching, inverse probability of treatment weighting, and overlap weighting. Using single-cell and bulk transcriptome data from the Gene Expression Omnibus and genetic variants from the Genome-Wide Association Study databases, we conducted Mendelian randomization (MR) analysis to explore the core cellular subsets, shared genes, causal relationships, and common pathogenic mechanisms between COVID-19 and breast cancer. Patients with breast cancer and COVID-19 showed poor NAC

responses, including a low objective response rate and reduced likelihood of achieving RCB class 0-I in the HR+/HER2+ subgroup (OR = 0.46, P = 0.028, P for interaction = 0.024). The consistent findings from the three matching models support these results. Integrating single-cell and bulk transcriptome data with MR analyses revealed genetic correlations between COVID-19 and breast cancer and identified ABLIM1 and GZMM as potential genes linked to NAC resistance. SARS-CoV-2 infection during NAC may compromise therapeutic efficacy in patients with breast cancer. ABLIM1 and GZMM may be causal genes in the genetic correlation between COVID-19 and breast cancer.

Keywords: Coronavirus disease; Breast cancer; Severe acute respiratory syndrome coronavirus 2; Neoadjuvant chemotherapy; Mendelian randomization

25COASDEC15:

Title: T≤2cmN0 non-small cell lung cancer with visible pleural retraction will benefit from lobectomy rather than sublobar resection: An inverse probability of treatment weighting study,

Yikai Xing, Zhenyu Yang, Jian Zhou, Zheng Liu, Ying Zhang, Lunxu Liu, Qiang Pu,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110526,
https://doi.org/10.1016/j.ejso.2025.110526.

Abstract: Lobectomy has long been considered as the gold standard for the treatment of early-stage non-small cell lung cancer (NSCLC). However, the efficacy of sublobar resection has been confirmed in some patients. Pleural retraction was observed intraoperatively in some patients, and there is no evidence whether sublobar resection can achieve similar results to lobectomy in these patients. We therefore conducted this retrospective study to compare the survival of lobectomy and sublobar resection in cT1 (≤2 cm) N0M0 NSCLC with visible pleural retraction. We retrospectively included 987 T ≤ 2cmN0 NSCLC patients who underwent radical surgery for lung cancer with visible pleural retraction. Inverse probability of treatment weighting was used to balance the differences of baseline characteristics. We compared the recurrence-free survival (RFS) and overall survival (OS) between those who underwent lobectomy and sublobar resection. Subgroup analysis was also performed. Sublobar resection has worse RFS compared to lobectomy (HR = 1.97, 95 %CI [1.13–3.42], p = 0.02). Patients with solid nodules who received sublobar resection showed both shorter RFS and OS (HR = 2.73, 95 %CI [1.47–5.05], p < 0.01 and HR = 2.29, 95 %CI [1.08–4.86], p = 0.03, respectively). For T ≤ 2 cm N0 NSCLC with pleural retraction, lobectomy is associated with improved recurrence free survival over sublobar resection.

Keywords: Non-small cell lung cancer; Lobectomy; Sublobar resection; Prognosis; Visible pleural retraction

25COASDEC16:

Title: Clinical efficacy and psychological benefits of ultrasound-guided vacuum-assisted excision in outpatient management of benign breast lesions,

Siyuan Wang, Huan Zhang, Jing Lin, Huimin Meng, Zhe Wang, Mingkun Zhang, Liu Yang, Yuan Qin,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110498,
https://doi.org/10.1016/j.ejso.2025.110498.

Abstract: To comprehensively assess the clinical efficacy, peri-procedure safety, and psychological impact of VAE for benign breast lesions. This retrospective observational study included 1413 patients (2008 benign breast lesions) who underwent outpatient VAE between October 2020 and January 2025. Demographic data, lesion characteristics, histopathology, and procedure duration were extracted from electronic medical records (EMRs). Post-procedural complications, pre-/post-procedural anxiety levels (using SAS), and patient satisfaction were retrieved from clinician-documented follow-up records. Most patients (64.26 %) were aged 31–50 years, and all were female. Among 2008 excised lesions, solitary lesions occurred in 59.45 % of patients, with the upper outer quadrant being the most frequent location (44.42 %). Fibroadenoma was the most common diagnosis (78.14 %). High-risk lesions (sclerosing adenosis, papilloma, papillomatosis, and atypical hyperplasia) accounted for 3.04 %. Additionally, carcinoma in situ and invasive carcinoma were identified in 5 cases (0.25 %). The mean procedure duration was 23.33 ± 9.26 min, with low post-procedure complication rates (hemorrhage: 18.54 %, defined as incisional oozing soaking part of the innermost dressing, all resolving spontaneously without intervention; hematoma: 16.63 %, almost all managed with observation/warm compresses; infection: 0.57 %). Pain was reported by 81.32 % of patients post-procedurally, but only 7.57 % required oral analgesics and 0.36 % were not relieved by oral analgesics. 98.91 % achieved excellent cosmetic outcomes. Patient satisfaction was high (98.94 %). Pre-procedure anxiety scores decreased post-procedurally (mean score: 47.47 ± 8.20 vs. 43.27 ± 7.80, $P < 0.001$), with 72.03 % anxiety remission rate. VAE achieves excellent efficacy and safety with psychological benefits, supporting outpatient adoption. Long-term validation studies are warranted.

Keywords: Breast neoplasms; Benign; Minimally invasive procedures; Vacuum-assisted excision; Post-procedure complications; Patient reported outcome measures

25COASDEC17:

Title: Real-world survival benefit of adding immunotherapy to chemotherapy in esophageal cancer: A large SEER-based analysis,

Jing Chen, Hong-Jun Lin, Chang-Qing Liu,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110504,
https://doi.org/10.1016/j.ejso.2025.110504.

Abstract: The integration of immunotherapy with chemotherapy has shown promise in improving survival for advanced esophageal cancer. However, most supporting evidence comes from prospective trials with small cohorts, and large-scale real-world validation remains limited. Esophageal cancer patients from the SEER database (2000–2021) were reviewed and analyzed. Patients diagnosed after 2021 were categorized into the chemotherapy plus immunotherapy group, while those diagnosed earlier formed the chemotherapy-alone group. The primary endpoint was the long-term survival. Additionally, subgroup analyses were further conducted for adenocarcinoma (AC) and squamous cell carcinoma (SC) to assess histology-specific outcomes. A total of 7793 patients were included (5840 chemotherapy-alone, 1953 chemotherapy plus immunotherapy). After PSM, baseline characteristics between the two groups were well balanced. Chemotherapy plus immunotherapy was identified as an independent protective factor for survival both before (HR = 0.868, 95 % CI: 0.766–0.984, P = 0.027) and after matching (HR = 0.845, 95 % CI:

0.745–0.958, P = 0.009). Subgroup analyses revealed consistent survival benefits of combination therapy in both AC and SC patients. The protective effect remained statistically significant in AC (HR = 0.822, 95 % CI: 0.682–0.990, P = 0.039), and a favorable trend was also observed in SC. In addition, female sex, married status, early T stage, and absence of distant metastasis were independently associated with better outcomes across subgroups. This large, SEER-based real-world study confirms that adding immunotherapy to chemotherapy significantly improves survival in esophageal cancer. The benefit was observed in both adenocarcinoma and squamous cell carcinoma subtypes, supporting its broad clinical utility and the need for further prospective validation.
Keywords: Esophageal cancer; Immunotherapy; Chemotherapy; SEER database; Propensity score matching; Survival analysis

25COASDEC18:
Title: Safety of high-dose mitomycin C vs oxaliplatin HIPEC for peritoneal metastases,
Giancarlo Sticca, Mikael Soucisse, Maria Abou-Khalil, Mai-Kim Gervais, Jean-François Tremblay, Pierre Dubé, Lucas Sideris,
European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110534,
https://doi.org/10.1016/j.ejso.2025.110534.
Abstract: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) improve survival in patients with peritoneal metastases (PM). While mitomycin-C (MMC) and oxaliplatin are the primary HIPEC agents for colorectal and appendiceal PM, previous studies comparing both agents relied on outdated low-dose MMC regimens. This study evaluates the safety of high-dose 35 mg/m2 mitomycin C vs 460 mg/m2 oxaliplatin. This retrospective cohort study analyzed all patients with appendiceal and colorectal PM treated at a tertiary-care hospital from 2014 to 2024. Among 282 patients, 48 (17.0 %) received high-dose MMC and 234 (83.0 %) received oxaliplatin. Patient demographics and oncological characteristics were similar ($p > 0.05$). High-dose MMC had significantly more toxic events (35.4 % vs 14.1 %, $p < 0.001$), greater CTCAE median toxicity grade (2 vs 1, $p < 0.001$), higher hepatic cytolysis (2.1 % vs 0.0 %, $p = 0.027$), increased neutropenia (27.1 % vs 4.3 %, $p < 0.001$), more gastric perforations (4.2 % vs 0 %, $p = 0.002$) as well as one case of HIPEC toxicity-related death due to neutropenic enterocolitis (2.1 % vs 0.0 %, $p = 0.380$). Oxaliplatin resulted in more hematomas (12.0 % vs 2.1 %, $p = 0.040$), higher need for parenteral nutrition (94.0 % vs 83.3 %, $p = 0.012$), and longer duration of nutritional support (12.3d vs 8.6d, $p = 0.020$). High-dose MMC had higher abdominal sepsis rates (6.3 % vs 1.3 %, $p = 0.030$). Severe complications, reintervention, ICU transfers, and 90-day mortality were similar ($p > 0.05$). Length of stay was shorter for high-dose MMC (14.7d vs 17.7d, $p = 0.031$). High-dose MMC was associated with increased HIPEC toxicity, primarily neutropenia-related. Clinicians must balance the benefits and drawbacks of high-dose MMC and oxaliplatin to provide an optimal and individualized treatment.
Keywords: High dose mitomycin C; Oxaliplatin; HIPEC; Peritoneal metastases; Toxicity; Postoperative complications

25COASDEC19:

Title: Improving radiomics-based differentiation of supratentorial malignant brain tumors preoperatively with diffusion-weighted imaging: A three-class machine learning algorithm,

Zeyu Ma, Chaoli Zhang, Yang Guo, Yinhua Li, Zilong Wang, Yanmei Hu, Xueping Zhang, Mengjiao Duan,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110533,
https://doi.org/10.1016/j.ejso.2025.110533.

Abstract: To construct a three-class multiparametric radiomic model for classifying supratentorial brain tumors [high-grade glioma (HGG), brain metastases (BM), and primary lymphomas of the central nervous system (PCNSL)], and investigate whether diffusion-weighted imaging (DWI)-based radiomic features enhance diagnostic performance. 364 subjects of Dataset 1 with supratentorial HGG (n = 150), BM (n = 126), and PCNSL (n = 88) were split into training (n = 222) and validation (n = 142) sets. 109 subjects of Dataset 2 were regarded as external validation set. In training set, a multiparametric radiomic model based on 31 selected features from conventional MRI (T1WI, T1c, T2WI, and FLAIR), apparent diffusion coefficient (ADC) maps, and a conventional radiomic model based on 28 selected features from conventional MRI were built using a three-class random forest method. The diagnostic performance of two models was assessed. The area under the receiver operating characteristic (ROC) curves (AUCs) of the two models were compared using Delong analysis. The AUCs of multiparametric radiomic model were 0.978, 0.918, and 0.914 for HGG, BM, and PCNSL, respectively, in internal validation set. And 0.916, 0.898, 0.883 in external validation set. The multiparametric radiomic model yielded significantly higher performance in classifying BM ($P < 0.001$, $P = 0.001$, internal and external validation sets) and PCNSL ($P = 0.012$, $P = 0.001$, internal and external validation sets). DWI-based radiomic features offered incremental value beyond conventional MRI and improved model performance in discriminating among the three common supratentorial malignant brain tumors (HGG, BM, and PCNSL).

Keywords: Glioma; Brain metastases; Primary lymphoma of the central nervous system; Diffusion-weighted imaging; Radiomics

25COASDEC20:

Title: Management of peripheral-vein leiomyosarcomas, recurrence patterns and individualised treatment strategy,

Jens KH. Strohäker, Dirk C. Strauss, Myles JF. Smith, Khin Thway, Aisha B. Miah, Shane H. Zaidi,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110448,
https://doi.org/10.1016/j.ejso.2025.110448.

Abstract: Peripheral vein leiomyosarcomas (LMS) are rare soft tissue sarcomas with high metastatic potential. While radiotherapy (RT) is commonly used in high-grade soft tissue sarcomas to improve local control, its benefit in peripheral vein LMS remains unclear, particularly due to their anatomical location and low local recurrence rates. A retrospective analysis was conducted on 141 patients who underwent surgery for peripheral vein LMS between 2000 and 2023. Inclusion required histopathological confirmation by sarcoma-specialist pathologists. Clinical, pathological, and treatment-related data were collected,

including use of radiotherapy and recurrence outcomes. Recurrence-free and overall survival were analysed. Median patient age was 68 years. Most tumours were located in the lower extremity, originating from the greater saphenous or femoral veins. Radiotherapy was administered to 24.1 % of patients, with limited radiological or pathological response observed. Local recurrence was rare (7.1 %) and not significantly associated with RT, tumour depth, grade, or margin status. Distant recurrence occurred in 27.8 % of patients with localised disease. On multivariate analysis, deep tumour location (OR 3.1, $p < 0.001$) and high-grade histology (OR 15.9, $p = 0.010$) were the only significant predictors of distant recurrence. Peripheral vein LMS demonstrates a low local recurrence but high metastatic risk. Radiotherapy did not significantly impact local control, and it was typically utilized in higher-grade, deep-seated tumours that carry a greater risk of local relapse. These findings suggest that in peripheral vein LMS, systemic risk outweighs local control benefits from RT, highlighting the need for individualised treatment strategies and further prospective studies.

Keywords: Soft tissue sarcomas; Leiomyosarcomas; Radiotherapy; Local recurrence; Recurrence patterns

25COASDEC21:

Title: Geographic variation in surgery rates among older patients with early (ER positive HER2 negative) breast cancer: Influence of cardiovascular disease and comorbidities: A national registry dataset analysis,

Emma Crewe, Freya Tyrer, John Deanfield, Mark de Belder, Jennifer Lai, Mamas Mamas, David Adlam, Alistair Ring,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110432,
https://doi.org/10.1016/j.ejso.2025.110432.

Abstract: Women over 70 years of age with operable oestrogen receptor positive (ER positive) breast cancer have worse survival outcomes than younger women. Primary surgery is the optimal treatment with primary endocrine therapy reserved for patients who are unfit or who have multiple co-morbidities. Inferior outcomes in this patient population might be explained by underuse of surgery, the rates of which vary considerably between geographical regions in the UK. We determined the rates of surgery versus primary endocrine therapy in a cohort of women aged over 70 in England, with potentially curable ER positive breast cancer, according to the presence of pre-existing cardiovascular disease (CVD), comorbidities, social deprivation, and by geographical location. 33,235 women aged 70 years or older with stage I to III ER positive breast cancer from the 20 regional NHS Cancers Alliances in England were identified from the cancer registry. Linked hospital records were used to identify patient demographics, tumour and treatment characteristics, resection rates, CVD prevalence and other co-morbidities. 25,800 (77.6 %) patients underwent surgery, 6787 (20.4 %) patients received primary endocrine therapy alone, 648 (2 %) patients received no treatment. Both CVD and surgery prevalence varied by geographical location. After adjustment for case mix the differences between Cancer Alliances attenuated and no longer reached statistical significance. We found regional differences in rates of surgery in patients with breast cancer across different centres. After adjustments, the variation is largely attributable to case mix. Under recording of endocrine therapy data in secondary care limits full interpretation.

Keywords: Breast cancer; Cardiovascular disease; Older adults; Surgery

25COASDEC22:

Title: Safety and feasibility of subtotal resection of the remnant stomach for remnant gastric cancer: A propensity score matching analysis compared with completion total gastrectomy,

Lloyd Nario Bordeos, Ki-Yoon Kim, Jawon Hwang, Sung Hyun Park, Minah Cho, Yoo Min Kim, Hyoung-Il Kim, Woo Jin Hyung,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110493,
https://doi.org/10.1016/j.ejso.2025.110493.

Abstract: Completion total gastrectomy (CTG) has mostly been performed despite the lack of standardized surgical treatment for remnant gastric cancer (RGC) in current guidelines. To enhance a patient's postoperative nutritional status and improve their quality of life by preserving the organ, it is necessary to investigate the role of subtotal resection of the remnant stomach (SR) for RGC. This study aimed to evaluate the efficacy of SR by comprehensively comparing its surgical and oncological outcomes with those of CTG for RGC. From January 2001 to December 2022, 229 patients who underwent gastrectomy for RGC, 19 (8.3 %) SR and 210 (91.7 %) CTG, were retrospectively reviewed. Short- and long-term outcomes, including nutritional status, were compared between the two groups after propensity score matching. Fifty-four patients were selected after propensity score matching (SR = 18, CTG = 36). The SR group demonstrated significantly shorter operative time (199.9 ± 47.7 min vs. 250.6 ± 67.9 min; P = 0.003), fewer postoperative complications (22.2 % vs. 61.1 %; P = 0.007), and less body weight loss and vitamin B12 deficiency (P = 0.039 and P = 0.007, respectively) than the CTG group. There was no difference in the 5-year overall and relapse-free survival rates between the SR and CTG groups (77.8 % and 69.9 %, 83.3 % and 75.6 %, respectively; P = 0.799 and P = 0.578, respectively). SR showed better surgical outcomes and postoperative nutritional status than CTG, with oncological outcomes similar to those of CTG. Thus, SR may be a safe and effective treatment option for RGC.

Keywords: Gastric cancer; Remnant gastric cancer; Gastrectomy; Subtotal resection

25COASDEC23:

Title: Association of waiting time from diagnosis to neoadjuvant chemoradiotherapy on interval distant metastases in esophageal cancer patients: A study based on the Netherlands cancer registry,

Jingpu Wang, Zhouqiao Wu, Lucas Goense, Rob H.A. Verhoeven, Jelle P. Ruurda, Richard van Hillegersberg,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110456,
https://doi.org/10.1016/j.ejso.2025.110456.

Abstract: In patients with resectable esophageal cancer, interval distant metastases may be detected following neoadjuvant-intent chemoradiotherapy ((n)CRT). The specific association between the waiting time from diagnosis to the initiation of (n)CRT and interval metastases remains unclear. Patients with esophageal cancer (cT1-4a N0-3 M0) received CRT with or without surgery were extracted from the Netherlands Cancer Registry. Multivariable logistic and cox regression analyses were used to compare different waiting times (≤4, 4–8 and >8weeks) on the risk of interval metastases, post-(n)CRT short-term metastases (detected preoperatively, intraoperatively, or postoperatively within 120 days after CROSS regimen

CRT) and overall survival (OS). Subgroup analysis based on cN stage was performed. Between 2015 and 2021, a total of 4394 patients were included. Compared to the waiting ≤4 weeks, the waiting >8 weeks was associated with higher risk of interval metastases (p-value = 0.045),but the longer waiting times were not associated with higher risk of post-(n)CRT short-term metastases or worse OS. In the cN0 subgroup, compared to the waiting ≤4 weeks, the waiting 4–8weeks (p-value = 0.049; p-value = 0.046) and >8 weeks (p-value = 0.006; p-value = 0.006) was associated with higher risk of interval metastases and post-(n)CRT short-term metastases, but was not associated with worse OS. In the cN + subgroup, the longer waiting times were not associated with interval metastases or post-(n)CRT short-term metastases or OS. A longer waiting time from diagnosis to the initiation of (n)CRT was associated with a higher risk of interval metastases, but not with an increased risk of post-(n)CRT short-term metastases or worse OS.

Keywords: Time interval; Waiting time; Esophageal cancer; Interval metastases; Neoadjuvant chemoradiotherapy

25COASDEC24:

Title: Dual-energy CT radiomics for predicting neoadjuvant chemotherapy response in locally advanced gastric cancer: A dual-vendor validation study,

Jing Li, Xiaoxiao Lin, Hongkun Yin, Tianxia Bei, Xiaoqiang Yao, Xuejun Chen, Shuning Xu, Yi Wang, Jinrong Qu,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110548,
https://doi.org/10.1016/j.ejso.2025.110548.

Abstract: To establish and validate a dual-energy CT (DECT) radiomics model for predicting neoadjuvant chemotherapy (NAC) response in locally advanced gastric cancer (LAGC) across two vendors. This was a secondary analysis drawn from a prospective cohort using DECT data of patients undergoing NAC followed by gastrectomy. Patients were stratified as responders (TRG 0/1) or non-responders (TRG 2/3) based on tumor regression grade (TRG). Radiomics features were extracted from polychromatic images at arterial/venous/delayed phases for building CECT model; Radiomics features extracted from polychromatic images, monochromatic (40 keV, 100 keV) and iodine maps were used to construct DECT model. Predictive features were selected via the least absolute shrinkage and selection operator regression method in the training cohort and tested in the validation cohort. Performances of models were evaluated using areas under the receiver operating characteristic curves (AUCs). In total, 317 patients were recruited: 221 at training dataset (59.9 ± 9.7 years, 37 females, 184 males) and 96 at validation dataset (61.5 ± 8.0 years, 18 females, 78 males). No clinical factors were found to be related with TRG status. The DECT model outperformed CECT model in the training dataset (AUC: 0.806 vs. 0.729, p = 0.041) and showed non-significant superiority in the validation dataset (AUC: 0.752 vs. 0.679, p = 0.225). High-risk patients defined by DECT model had significantly worse overall survival (HR = 1.996, p = 0.012) and disease-free survival (HR = 1.873, p = 0.037) than low-risk counterparts. DECT radiomics demonstrates favorable performance in predicting NAC response and stratifying survival outcomes in LAGC, with cross-vendor generalizability supporting potential clinical utility.

Keywords: Tomography; X-ray computed; Radiomics; Stomach neoplasms; Neoadjuvant therapy

25COASDEC25:

Title: Influence of socioeconomic position on surgical outcomes after resection of colorectal liver metastases,

M.R. de Graaff, N.F.M. Kok, D.J. Grunhagen, M. Nielen, H.A. Marsman, Steven W.M. Olde Damink, K. Bosscha,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110459,
https://doi.org/10.1016/j.ejso.2025.110459.

Abstract: This study investigate the impact of socioeconomic position (SEP) on postoperative outcomes after resection of colorectal liver metastases (CRLM). This retrospective population-based study used data from the Dutch Hepatobiliary Audit, including all patients who underwent liver resection for CRLM, between 2014 and 2018. Neighbourhood SEP (nSEP) characteristics were obtained from Statistics Netherlands, using welfare, education, and labour participation data. The lowest 20 % defines the Low group, the top 20 % the high group. The association of nSEP with short-term postoperative outcomes and overall survival (OS) was assessed. Of 3549 patients who underwent resection, 2579 (72.6 %) were successfully linked between databases. Median (IQR) nSEP scores did not significantly differ from those in the general population. Patients with higher nSEP scores had lower ASA scores ($P < 0.001$). No differences in 30-day mortality (1.4 % vs 1.2 % vs 1.0 %, $p = 0.625$) or major morbidity (10 % vs 9.7 % vs 11 %, $p = 0.809$) were observed between low, medium, or high nSEP. 5-year OS rates were similar: low, 45.7 % (41.4–50.4), medium, 45.9 % (43.3–48.6), high, 50.9 % (46.6–55.7), P-log rank = 0.441. In patients selected for resection of CRLM, nSEP was not associated with postoperative outcomes or survival. Patients should not be withheld from liver resection for CRLM based on SEP.

Keywords: Socio-economic status; Liver resection; Colorectal liver metastasis; Postoperative outcomes; Overall survival

25COASDEC26:

Title: Breast sensation following nipple-sparing mastectomy versus breast-conserving surgery: a mixed-methods study,

Josette Mouawad, James French, Farid Meybodi, Kirsty Stuart, Tim Wang, Jeremy Hsu, Elisabeth Elder,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110477,
https://doi.org/10.1016/j.ejso.2025.110477.

Abstract: Nipple-sparing mastectomy (NSM) and breast-conserving surgery (BCS) allow for preservation of the breast or nipple-areolar complex (NAC). However, this does not guarantee retained sensation in these regions. The prevalence of altered post-operative sensation and its importance to patients remains unclear. This study aims to determine the prevalence of breast and NAC sensation loss in NSM and BCS; to assess its importance to patients; and to compare these outcomes between NSM and BCS. The BREAST-Q Sensation Module and four study-specific questions were sent to NSM or BCS patients at the Westmead Breast Cancer Institute. Comparisons were made between NSM versus BCS, implant-based versus tissue-based NSM reconstruction, BCS with versus without a formal mammaplasty, and treatment with radiotherapy versus without. Semi-structured interviews were also held. 78.8 % and 79.3 % of women experienced breast and/or NAC sensation change, respectively ($n = 174$). 69.9 % and 44.6 % of NSM patients retained varying levels of breast and NAC

sensation, respectively (n = 83). 58.4 % and 60.5 % of BCS patients encountered breast and NAC sensation decrease, respectively (n = 91). Interviews (n = 34) showed that preserved sensation was sometimes of an altered quality and involved neuropathic symptoms. BREAST-Q Sensation scores were worse for NSM than for BCS. NSM reconstruction type did not impact outcomes. NSM patients with radiotherapy had worse BREAST-Q Symptoms scores than those without. BCS mammaplasty status did not influence outcomes, except for patient-reported NAC sensation. Sensation was important to 79.8 % of respondents. NAC sensation was more important to NSM than to BCS patients. Altered sensation is prevalent and significant to both NSM and BCS patients. Future research relating these findings to intraoperative techniques is required.

Keywords: Breast sensation; Nipple-areolar complex sensation; Nipple-sparing mastectomy; Breast-conserving surgery; BREAST-Q

25COASDEC27:

Title: The impact of colorectal cancer diagnosis and treatment on quality of life is increased in young patients,

Van MT. Hoang, Brooke Turner, Rocita Ho, Julie Tucker, April Harrison, Devinder Raju, Karolina Juszczyk, Elizabeth Murphy,

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Abstract: This study aims to assess the Quality of Life (QoL) in Early Onset Colorectal Cancer (EOCRC) patients compared to older CRC (OCRC) patients, addressing unique challenges and concerns and their impacts on QoL. A mixed-method approach was employed, including validated QoL tools (the WHOQOL-BREF, the EORTC QLQ-C30 and QLQ-CR29) and in-depth interviews. All patients completed a one-time survey regardless of cancer stage and treatment journey. Survey data was analysed using descriptive statistics with R version 4.3.1 and interview data was analysed using the Van-Manen method. Ninety-three patients completed the survey, comprising 53 EOCRC and 40 OCRC patients, of whom 10 from each group consented to the interview. EOCRC patients exhibited significantly lower scores in psychological aspects compared to the OCRC cohort (52.3 ± 20.5 vs 66.4 ± 15.8, p = 0.0009, WHOQOL-BREF). They also reported more severe emotional problems (34.6 vs 60.8, p = 0.0002, QLQ-C30), greater embarrassment about their condition (44.7 vs 27.4, p = 0.04), higher levels of anxiety (22.0 vs 49.2, p = 0.00007), more concerns about weight (35.2 vs 51.7, p = 0.04) and body image (41.7 vs 65.6, p = 0.001, QLQ-CR29) compared to their older counterparts. The qualitative interviews identified three primary themes: headspace, physical impacts, and future. The challenges and effects on QoL experienced by younger individuals are clearly reflected in altered body image and psychological distress. EOCRC patients face significant psychological and emotional challenges compared to OCRC patients, emphasizing the need for tailored support and intervention programs across the disease trajectory to address their unique challenges.

Keywords: Colorectal cancer; Early onset colorectal cancer; Quality of life; Cancer care; Bowel cancer

25COASDEC28:

Title: Approaches for esophagectomy for esophageal cancer: a Network Meta-Analysis,

Artur Rebelo, Elisabeth Wadewitz, Yoshiaki Sunami, Juliane Friedrichs, Maurizio Grilli, Johannes A. Vey,
European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110529,
https://doi.org/10.1016/j.ejso.2025.110529.
Abstract: Esophageal cancer remains a leading cause of cancer-related mortality worldwide. Esophagectomy is the cornerstone of curative treatment, but the optimal surgical approach remains debated. Newer techniques such as hybrid esophagectomy, minimally invasive esophagectomy (MIE), and robot-assisted minimally invasive esophagectomy (RAMIE) have been developed to improve perioperative outcomes while maintaining oncologic efficacy. We aim to compare the effects of open, hybrid, minimally invasive, and robot-assisted approaches to esophagectomy on survival and perioperative outcomes in patients with esophageal cancer. A systematic review and network meta-analysis (NMA) were conducted, including 10 reports from 6 randomized controlled trials identified via PubMed, Cochrane Library, Embase, CINAHL, ClinicalTrials.gov, and ICTRP. Comparative analyses between open esophagectomy (OE), hybrid laparoscopy-thoracotomy (HYB LapS-ThoT), MIE, and RAMIE were performed using random-effects NMA models. Hazard ratios (HR), odds ratios (OR), and mean differences (MD) were calculated for outcomes. There were no significant differences in overall survival among OE, HYB LapS-ThoT, MIE, and RAMIE. Pulmonary complications were significantly lower with MIE (OR 0.47, 95 % CI 0.33–0.69, $p < 0.0001$) and RAMIE (OR 0.39, 95 % CI 0.27–0.57, $p < 0.0001$) compared to OE. RAMIE yielded a higher lymph node harvest (MD 1.56, 95 % CI 0.58–2.54, $p = 0.002$) and lower reoperation rates (OR 0.65, 95 % CI 0.45–0.93, $p = 0.020$) than OE. HYB LapS-ThoT was associated with increased anastomotic leakage compared to OE (OR 1.66, 95 % CI 1.02–2.69, $p = 0.041$). MIE and RAMIE significantly reduce pulmonary complications without compromising survival. Hybrid approaches appear to increase the risk of anastomotic leakage. These findings support minimally invasive techniques, especially RAMIE; however, more evidence and further studies are needed to allow for a clearer and more definitive conclusion.

25COASDEC29:

Title: Impact of extensive surgery in a multidisciplinary approach of parameningeal rhabdomyosarcoma in children, adolescent and young adult population,

Olivier Airaudo, Romain Luscan, Jean-François Honart, Sylvie Helfre, Stéphanie Bolle, Daniel Orbach, Salma Moalla,
European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110486,
https://doi.org/10.1016/j.ejso.2025.110486.
Abstract: Parameningeal (PM) site is a well-known unfavorable site for rhabdomyosarcoma (RMS). PM RMS are usually considered unresectable and treated by radiochemotherapy. This study reviews our experience with a multidisciplinary approach, including extensive surgery. We included all patients treated for PM RMS requiring extensive surgery from January 1992 to December 2021. Thirty-one patients were included with a median age of 6 years (range 6 months–17 years). The primary site was the infratemporal fossa in 81 %, nasopharynx in 13 %, and middle ear/paranasal sinus in one case each. At diagnosis, 23 % had lymph node involvement, and 13 % had distant metastases. Twenty-six patients received neoadjuvant chemotherapy before extensive surgery, while five underwent extensive surgery

after radiochemotherapy. Free flap reconstruction was needed for 71 % of patients. Adjuvant radiotherapy (median dose: 50 Gy) was performed in 24 patients, with a median delay of 7.5 weeks post-surgery (range 3-13 weeks). Seven recurrences (23 %) were observed: four local relapses, two leptomeningeal spreads, and one distant metastasis. The median follow-up was 81 months (range 16-223 months). The median time to relapse was 12 months (range 6-36 months). Five-year event-free and overall survival rates were both 73.9 %, with a local failure-free survival of 85.7 %. Our study suggests that incorporating extensive surgery in PM RMS treatment improves long-term local control and survival, even in advanced cases with unfavorable features.

Keywords: Parameningeal; Rhabdomyosarcoma; Head and neck; Surgery; Outcomes; Children

25COASDEC30:

Title: Impact of readmission location on survival after oesophagectomy and gastrectomy,

Ganesh K. Velayudham, Arjan S. Shankar, Sebastian J. Fox, James Bundred, Faiz Ahmed, Paul S. Sundaram,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110470,
https://doi.org/10.1016/j.ejso.2025.110470.

Abstract: Readmissions following oesophagogastric cancer surgery pose a substantial burden on healthcare systems and can adversely impact patient outcomes. While centralisation has improved postoperative mortality, concerns persist about the management of complex complications at peripheral hospitals. This study evaluates 90-day readmission rates following oesophagectomy and gastrectomy, distinguishing between index (hospital where primary surgery was performed) and non-index (peripheral hospital) readmissions. Secondary objectives include identifying risk factors for readmission and assessing the impact of readmission location on long-term survival. A retrospective single-centre analysis was conducted on patients undergoing oesophagectomy or gastrectomy between 2011 and 2024. The primary outcome was unplanned readmission within 90 days of discharge. Multivariable logistic regression identified readmission risk factors. Survival analysis was conducted using Kaplan-Meier and Cox regression models. Of 881 patients (571 oesophagectomy, 310 gastrectomy), readmission rates were 26.1 % and 24.2 %, respectively. Risk factors for readmission included non-severe anastomotic leaks (OR 2.93; $P = 0.004$) and severe complications (OR 2.19; $P = 0.003$) for oesophagectomy, and prolonged hospital stay for gastrectomy (OR 1.04; $P < 0.001$). Protective factors included severe respiratory complications (OR 0.48; $P = 0.024$) and severe complications in gastrectomy patients (OR 0.33; $P = 0.036$). Index readmission was associated with improved survival on univariable analysis only. Complication-readmission patterns vary by procedure type. While the survival benefit of index readmission remains unclear, our results highlight the importance of structured postoperative care to mitigate postoperative morbidity. Further research should identify complications best managed at tertiary centres to guide targeted readmission pathways.

Keywords: Oesophagectomy; Gastrectomy; Readmission; Centralisation

25COASDEC31:

Title: Risk comparison and assessment model of deep vein thrombosis in patients with pituitary adenomas after Surgery:A retrospective cohort study,

Hongyu Wu, Yu Zhang, Xin Ma, Zenghua Mi, Zhijun Yang,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110485,
https://doi.org/10.1016/j.ejso.2025.110485.

Abstract: Deep vein thrombosis (DVT), a major component of venous thromboembolism (VTE), is a common postoperative complication. Its occurrence after pituitary adenoma surgery is influenced by multiple factors. This retrospective study analyzed 1440 pituitary adenoma cases treated at Beijing Tiantan Hospital (2018–2023). The incidence of postoperative DVT was recorded, and logistic regression was used to identify associated risk factors. Differences across pituitary adenoma subtypes were compared. Additionally, Regression and machine learning models were developed to predict DVT. Among 397 patients who underwent postoperative lower limb ultrasound, 104 (7.2 %) developed DVT. Significant risk factors included advanced age, higher body mass index (BMI), intravenous cannulation, prolonged hospital stay, shorter preoperative activated partial thromboplastin time (APTT), longer thrombin time (TT), elevated platelet count, and higher postoperative D-dimer levels. Patients with Cushing's disease exhibited a significantly higher DVT incidence, potentially related to decreased pre- and postoperative APTT and PT/INR values. Conversely, patients with prolactin-secreting adenomas had a lower DVT incidence, possibly due to younger age and higher postoperative PT values. A support vector machine (SVM) model showed strong predictive performance (AUC: 0.82; accuracy: 86.08 %; specificity: 96.72 %). DVT incidence varies by pituitary adenoma subtype. Machine learning enhances predictive models for postoperative DVT in pituitary adenoma patients.

Keywords: Pituitary adenoma; Deep vein thrombosis; Risk factor; Cushing disease; Machine learning

25COASDEC32:

Title: Correlation of supportive proton pump inhibitor use during surgery with outcomes in patients with stage I-III colorectal cancer: A propensity score matching study,

Qianwen Ye, Mingjuan Liu, Mingyue Xu, Meiqi Cui, Bing Yan,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110543,
https://doi.org/10.1016/j.ejso.2025.110543.

Abstract: Proton pump inhibitors (PPIs) are widely used to treat cancer patients in different settings and have been found affect patient outcomes. However, the effect of PPI use during the radical resection of colorectal cancer (CRC) has never been addressed. Data about the use of PPIs, including the cumulative dosage (CD) and dosage per day (DpD), were collected retrospectively. Patients were divided into different subgroups before and after propensity score matching (PSM). The differences in disease-free survival (DFS) and overall survival (OS) between these subgroups were assessed after PSM. Finally, risk factors for survival were validated with a Cox proportional hazard model. Both CD and DpD significantly predicted DFS but not OS. Significant difference in DFS was found between the low- or high-CD subgroups (log rank = 5.78, P = 0.016); whereas similar difference in OS was only found between the low- or high-DpD subgroups (log rank = 4.15, P = 0.042). Finally, only

the DpD was identified as an independent risk factor for both DFS (HR = 1.74, 95 % CI: 1.04–2.91, P = 0.036) and OS (HR = 2.07, 95 % CI: 1.11–3.86, P = 0.023). The use of PPIs during the radical resection of CRC may be correlated with patient outcomes and patients who receive a relatively high DpD tend to have poor outcomes. However, it should be highlighted that the causal relationship between the use of PPIs and survival in these patients is exploratory rather than clinically, which needs to be further validated in future perspective studies.

Keywords: Colorectal cancer; Proton pump inhibitors; Cumulative dosage; Dosage per day; Survival

25COASDEC33:

Title: A novel risk score after neoadjuvant imatinib predicts relapse-free survival in patients with gastrointestinal stromal tumours (GIST),

Javier Pozas, Daniel Lindsay, Alanna Wall, Leonidas Mavroeidis, Khin Thway, Myles Smith, Andrew Hayes,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110473,
https://doi.org/10.1016/j.ejso.2025.110473.

Abstract: Surgery remains the cornerstone of management of localized GIST. Neoadjuvant imatinib facilitates surgery and allows in vivo monitoring of tumour response to therapy. There are no predictive tools to guide the duration of treatment. This study evaluates the impact of clinical and pathological variables on relapse-free survival (RFS) after neoadjuvant imatinib. Single-centre retrospective study of 90 GIST patients who underwent radical surgery after neoadjuvant imatinib. Univariate and multivariate Cox regression analyses were performed to determine the association of clinicopathological variables to RFS. Evaluate Cut-points were used to identify values associated with significantly different outcomes. Between-group differences were assessed with the use of the stratified log-rank test. Univariate Cox regression analyses showed a significant association of RFS with initial tumour size (ITS) (HR 1.11, $p = 0.002$), maximal tumour shrinkage (MTS) (HR 11.7, $p = 0.023$) and residual mitotic count (RMC) (HR 1.09, $p \ll 0.001$). These results were confirmed in a multivariate model (ITS, $p = 0.001$; MTS, $p = 0.003$; RMC, $p \ll 0.001$). Cut-points for ITS, MTS and RMC were established at 9.8 cm, 41 % reduction in size and 2 mitoses, respectively. Patients with large tumours ≥9.8 cm, ≤41 % reduction in size and ≥2 mitoses had shorter RFS. A combined score of these three variables allowed for accurate classification into two risk categories ($p \ll< 0.001$): low (0 or 1 factor) and high-risk (2 or 3 factors). Post-operative imatinib did not influence survival outcomes in either low -risk (HR 1.2, $p = 0.83$) or high-risk patients (HR 1.6, $p = 0.35$). ITS, MTS and RMC are associated with shorter RFS in patients with localized GIST treated with neoadjuvant imatinib. If validated, these findings could guide the design of prospective studies that de-escalate or intensify adjuvant treatment.

Keywords: GIST; Neoadjuvant; Imatinib; Risk score

25COASDEC34:

Title: Risk factors for lymph node metastasis and survival: Toward better endoscopic selection in ulcerative versus nonulcerative early gastric cancer,

Minghan Ren, Yuning Chu, Rongshuang Han, Yunqing Chen, Tao Mao, Xingsi Qi, Shengbo Jin, Zibin Tian,
European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110497,
https://doi.org/10.1016/j.ejso.2025.110497.
Abstract: Lymph node metastasis (LNM) is a major determinant of patient outcomes in early gastric cancer (EGC) patients. This study aimed to identify risk factors for LNM and compare outcomes between patients with ulcerative EGC (UEGC) and with nonulcerative EGC (NUEGC).We retrospectively analyzed the data of 1262 patients with pathologically confirmed EGC who underwent curative gastrectomy. The risk factors for LNM and overall survival (OS) were assessed. OS was estimated with Kaplan–Meier analysis, and prognostic factors were identified via Cox regression analysis.LNM was significantly more common in the UEGC group (16.6 %) than in the NUEGC group (11.6 %) (P = 0.013). According to the multivariable analysis, lymphovascular invasion (LVI) (OR = 17.609, P < 0.001 for NUEGC; OR = 14.587, P < 0.001 for UEGC), superficial submucosal (SM1) invasion (OR = 2.622, P = 0.045 for NUEGC; OR = 2.276, P = 0.022 for UEGC), and deep submucosal (SM2) invasion (OR = 3.276, P = 0.004 for NUEGC; OR = 3.132, P = 0.001 for UEGC) were independent predictors of LNM in both groups, whereas a tumor size>30 mm (OR = 2.644, P = 0.009) was a significant factor only for NUEGC patients. The 5-year OS rate was 89.9 % in the NUEGC group and 87.2 % in the UEGC group (P = 0.028, log-rank test). LNM was an independent predictor of OS in both subtypes of EGC, whereas elevated carcinoembryonic antigen (CEA) levels and SM2 invasion were significant predictors only for UEGC patients.Compared with NUEGC, UEGC presents more aggressive pathological features and is characterized by a significantly higher rate of LNM and worse long-term patient survival, while undifferentiated UEGC <2 cm potentially supports ESD expansion.
Keywords: Early gastric cancer; Lymph node metastasis; Overall survival; Outcomes; Submucosal invasion

25COASDEC35:
Title: Enhancing compliance and decision-making in breast cancer care for older adults: Optimising the NABCOP fitness assessment form,
Kimberly Chong, Iman Azmy, Nour Al-Shurbasi, Ciaran Hollywood, Kathryn Hodgkins, Julia Massey,
European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110475,
https://doi.org/10.1016/j.ejso.2025.110475.
Abstract: The National Audit of Breast Cancer in Older Patients (NABCOP) fitness assessment aims to standardise treatment for breast cancer patients over 70. However, studies have shown that compliance with NABCOP fitness assessment forms is variable. We sought to evaluate the form's usability, to improve compliance and ensure treatment decisions are based on overall patient performance rather than age alone. We conducted two audit cycles involving patients over 70 diagnosed with breast cancer (metastatic or palliative presentations excluded). Cycle 1 (January–December 2021) included 108 patients, while Cycle 2 (January–December 2024) included 93 patients. Between cycles 1 and 2, modifications were made to the fitness assessment forms. These included making the Abbreviated Mental Test Score (AMTS) assessment optional based on clinician-identified cognitive concerns, incorporating Age Gap Decision Tool outcomes, and adding a tick-box for clinicians' overall judgement of

"fitness for surgery". Form compliance improved from 37 % to 87 %. AMTS scores were documented in 11.9 % of cases in the first cycle, with no significant impact on surgical decision-making ($p = 0.26$), supporting reliance on clinical judgment for cognitive assessment. Across both cycles, the mean age for surgical patients was 77 years (SD ± 4.9), compared to 84 years (SD ± 6.2) for conservative management. Frailty scores were strongly associated with treatment decisions ($p < 0.001$), averaging 2.69 for surgical and 4.56 for non-surgical patients. Modifications including simplified cognitive assessment and integration of the Age Gap Tool to the fitness assessment form improved compliance and streamlined decision-making. Frailty assessment remains pivotal in guiding treatment choices.

Keywords: Breast cancer; Older patients; Age bias; NABCOP; Primary endocrine therapy; Surgery treatment; Fitness assessment; Frailty score; Age gap decision tools

25COASDEC36:

Title: Time-varying hazards of recurrence patterns among patients with colorectal liver metastases undergoing liver resection and the role of the modified tumor burden score,

Odysseas P. Chatzipanagiotou, Jun Kawashima, Andrea Baldo, Andrea Ruzzenente, George A. Poultsides,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110527,
https://doi.org/10.1016/j.ejso.2025.110527.

Abstract: Hepatectomy remains the standard treatment for colorectal liver metastases (CRLM), yet over half of patients recur within two years. Optimizing postoperative surveillance is important for timely detection and improved survival. The objective of the current study was to characterize recurrence patterns following CRLM hepatectomy, identify peak time of recurrence based on these patterns, assess the predictive role of the modified Tumor Burden Score (mTBS), and analyze post-recurrence survival by pattern to inform more personalized follow-up. Patients undergoing curative-intent CRLM resection (2000–2023) were identified from a multi-institutional database. Outcomes included recurrence-free survival and recurrence hazard functions for isolated liver, isolated lung, isolated non-liver/lung, intra-/extrahepatic multi-site, and extrahepatic multi-site recurrences. Analyses used flexible parametric modeling, Kaplan-Meier curves, and Cox regression. Among 962 patients, median age was 63.0 years (IQR 55.0–69.0) and most individuals had ASA class>2 ($n = 622$, 64.7 %). Bilateral disease was associated with a higher incidence of R1 resection (20.9 % vs. 14.4 %) and higher mTBS (8.1, IQR 5.9–11.5 vs. 3.4, IQR 2.2–5.1) than unilateral CRLM. Among 511 patients who recurred, isolated liver recurrence was most common (49.7 %), followed by intra-/extrahepatic multi-site (21.7 %), isolated non-liver/lung (11.7 %), isolated lung (11.0 %), and extrahepatic multi-site (5.9 %). Peak recurrence hazards were observed for isolated liver at 5 months (0.025) and intra-/extrahepatic multi-site at 8 months (0.012); smaller, earlier peaks were observed for other patterns of recurrence. Isolated lung recurrence peaked at 14 months. mTBS influenced hazard magnitude, particularly for hepatic recurrences, but not the timing. Distinct time-varying recurrence hazards following CRLM resection highlight the need for early, tailored surveillance, particularly in high burden, bilateral, and liver-involved disease.

Keywords: Colorectal liver metastases; Hepatectomy; Recurrence; Hazards analysis; Post-recurrence survival

25COASDEC37:

Title: Model to predict postoperative complications after hepatectomy based on comprehensive complication index: A retrospective multicenter study,

Mengwen Xue, Yuhe Zhang, Jiarui Li, Yanan Di, Kunyu Han, Ruiping Bai, Rui An, Hui Liu, Xin Shen,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110479,
https://doi.org/10.1016/j.ejso.2025.110479.

Abstract: Postoperative complications following hepatectomy are often complex and involve multiple systems. This study aims to employ the Comprehensive Complication Index (CCI) to thoroughly assess postoperative complications, identify patients at high risk for severe complications, and inform preoperative management and preventive strategies. In this retrospective study, we evaluated all adverse events within 30 days post-hepatectomy. Each complication was individually assessed, and CCI scores were calculated based on the Clavien-Dindo Classification (CDC) system. Short-term outcomes were analyzed for all patients to identify predictors of severe complications. A total of 1350 cases were analyzed, with 21 types of complications recorded, resulting in an overall complication rate of 46.61 %. Patients in the high CCI score group experienced significantly longer postoperative and total hospital stays. Independent risk factors identified included prolonged postoperative hospital stay, increased total intraoperative output, elevated postoperative blood creatinine levels, and preoperative pulmonary comorbidities. Conversely, a higher postoperative neutrophil ratio and red blood cell count were protective factors. Two surgical teams were associated with worse postoperative CCI outcomes. The nomogram model developed in this study demonstrated strong predictive performance, with an area under the ROC curve of 0.844 (95 % CI: 0.814–0.874), a sensitivity of 86.9 %, and a specificity of 65.4 %. The model estimated a 9.36 % risk of severe complications in patients with a total score of 36.

The predictive model developed in this study effectively identifies high-risk patients for severe complications after hepatectomy. This tool can guide perioperative preventive measures and early interventions to improve patient outcomes.

Keywords: Comprehensive complication index; Hepatectomy; Postoperative complications; Predictive model; Retrospective multicenter study

25COASDEC38:

Title: A prediction model of pulmonary metastasis risk in pediatric patients with stage IIB osteosarcoma in the long bone of extremities,

Guodong Zhong, Wanzhen Wang, Aierxiding Aimaiti, Yongqian Wang, Xianbiao Xie, Changye Zou, Junqiang Yin, Jingnan Shen, Gang Huang, Zhiqiang Zhao,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110509,
https://doi.org/10.1016/j.ejso.2025.110509.

Abstract: While epiphyseal plates may resist osteosarcoma invasion, the correlation between epiphyseal involvement (EI) and pulmonary metastasis (PM) or prognosis remains unclear, and no PM prediction models specifically target pediatric patients. This study enrolled 221 patients (≤14 years) with stage IIB osteosarcoma in the long bone of extremities. Using LASSO and multivariate Cox regression analyses, we identified significant risk factors for PM and prognosis, integrating them into a nomogram and nine machine learning (ML) models. After comprehensive performance evaluation, the optimal model was selected to

predict 2-year PM risk, stratifying patients into high- and low-risk groups by median risk score. EI significantly correlated with increased PM risk and poorer prognosis; however, when tumors did not cross the epiphyseal plate, metastasis incidence and prognosis remained comparable irrespective of the tumor-epiphyseal distance. Key risk factors included EI, elevated alkaline phosphatase (ALP), decreased lactate dehydrogenase (LDH), poor chemotherapy response, and elevated LDH ratio. The Random Forest (RF) model showed optimal predictive performance for risk stratification. This study establishes the first pediatric-specific PM risk prediction model for osteosarcoma, enabling personalized management, precise prognosis assessment, and optimized resource allocation, thereby demonstrating artificial intelligence's value in biomedical research.

Keywords: Osteosarcoma; Pediatrics; Patient outcome assessment; Neoplasm metastasis; Predictive learning models

25COASDEC39:

Title: Current status and clinical usefulness of genomic panel testing using PleSSision-160 in resectable esophageal squamous cell carcinoma,

Kazuaki Matsui, Hirofumi Kawakubo, Satoru Matsuda, Eriko Aimono, Kohei Nakamura, Kazumasa Fukuda,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110481,
https://doi.org/10.1016/j.ejso.2025.110481.

Abstract: The clinical importance of treatment approaches based on genomic sequencing has increased in esophageal cancer. This study aimed to clarify the current status and clinical usefulness of genomic panel testing using PleSSision-160 for resectable esophageal squamous cell carcinoma (ESCC). Sixty-six tumor tissue samples from 61 patients with ESCC, including prospectively collected 46 surgical samples and retrospectively collected 20 biopsy samples before neoadjuvant chemotherapy, were tested using the PleSSision-160 panel. The associations of mutation profiles with long-term survival and chemotherapy resistance were investigated. The top five mutations identified in surgical samples using PleSSision-160 were TP53 (80.4 %), KMT2D (13.0 %), NOTCH1 (13.0 %), EP300 (8.7 %), and AMER1 (8.7 %). Although individual mutations did not show significant associations with long-term survival, patients with high copy number alteration (CNA) status (≥30 counts) had poorer 5-year overall survival (OS) and recurrence-free survival (RFS) compared to those with low CNA status ($p = 0.019$ and 0.077 for OS and RFS, respectively). Multivariate analyses identified minimally invasive surgery, pStage ≥ III, and high CNA status as independent factors associated with both 5-year OS and RFS. This study is the first to investigate postoperative survival and chemotherapy resistance based on genomic panel testing using PleSSision-160 for resectable ESCC. The findings suggested that high CNA status was a risk factor for long-term survival. Compared to previous genomic sequencing studies in ESCC, further investigation using PleSSision-160 appears to be a promising approach.

Keywords: Esophageal cancer; Esophagectomy; Genome; DNA; Sequencing; Precision medicine

25COASDEC40:

Title: Impact of neoadjuvant immunotherapy on postoperative complications in oncoplastic breast cancer surgery,

Capucine Barjot, Thomas Gaillard, Romain-David Seban, Lauren Darrigues, Delphine Loirat, Luc Cabel,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110511,
https://doi.org/10.1016/j.ejso.2025.110511.

Abstract: Neoadjuvant pembrolizumab combined with chemotherapy is now standard treatment for stage II and III triple-negative breast cancer (TNBC). However, its impact on postoperative complications remains underexplored especially in oncoplastic or reconstructive procedures. A retrospective before-and-after study was conducted at a single institution from January 2019 to May 2023. Patients with early-stage TNBC treated with chemotherapy alone (CT group) or chemotherapy plus pembrolizumab (CT + P group) were included. Postoperative complications (including delayed wound healing, abscesses, hematomas, infections, implant exposure, and skin necrosis) were compared using univariate and multivariate logistic regression. Among 254 patients (CT: n = 136; CT + P: n = 118), the overall complication rate was 15.7 %. No significant difference was observed between groups (p = 0.061). Delayed wound healing was more frequent in the CT + P group (10 % vs. 3.8 %, p = 0.031). After adjustment, immunotherapy was not independently associated with higher risk (OR 1.27, p = 0.5). Oncoplastic surgeries were associated with higher complication rates in univariate analysis but not in multivariate analysis (OR 1.74, p = 0.2). Complications were more frequent when surgery occurred <14 or >30 days post-treatment (p = 0.029), especially among CT + P patients (interaction p = 0.01). Neoadjuvant pembrolizumab does not significantly increase postoperative complications. Surgical timing appears to be a modifiable factor influencing outcomes.

Keywords: Neoadjuvant pembrolizumab; Postoperative complications; Triple-negative breast cancer; Implant; Oncoplastic surgery

25COASDEC41:

Title: Recurrence patterns following CRS-HIPEC in patients with colorectal peritoneal metastases: Insights from the Dutch CRS-HIPEC registry,

T.B.M. van den Heuvel, F.N. van Erning, P.H.J. Hemmer, E.V.E. Madsen, P.R. de Reuver, R.J. Wiezer, A.J. Witkamp, I.H.J.T. De Hingh,

European Journal of Surgical Oncology,Volume 51, Issue 12,2025,110501,
https://doi.org/10.1016/j.ejso.2025.110501.

Abstract: Cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) is currently the only treatment with curative intent for selected patients with colorectal peritoneal metastases. This population-based study determined the 3-year cumulative incidence of disease recurrence after CRS-HIPEC, identified factors associated with disease recurrence and described how recurrent disease is treated. All patients who underwent complete CRS-HIPEC for non-appendiceal colorectal peritoneal metastases with or without extra-peritoneal metastases in 2019 were selected from the Dutch CRS-HIPEC registry. Follow up data were collected in 2023–2024. Three-year cumulative incidence of recurrence was calculated. Multivariable Cox competing risk regression analysis was used to identify factors associated with recurrence. A total of 157 patients was analysed with a

median follow-up of 31.0 (IQR 17.8–49.5) months. The 3-year cumulative incidence of disease recurrence was 86.3 %. Three-year recurrence-free and overall survival were 13.7 % and 47.8 % respectively. The most common sites of first recurrence were the peritoneum (68.2 %), liver (40.2 %) and lung (37.9 %). Treatment of recurrence was performed in 80.3 % of patients. Treatment mostly entailed systemic therapy (67.9 %). Secondary CRS-HIPEC was performed in 7.6 % of the patients. Factors associated with a higher risk of recurrence were a higher Peritoneal Cancer Index score (HR 1.06, 95 % CI 1.03–1.09) and pN2 (HR 2.07, 95 % CI 1.28–3.36). Most patients that underwent CRS-HIPEC for colorectal peritoneal metastases developed recurrent disease within 3 years. Future research should focus on ongoing developments in both diagnostics and treatment to prevent early recurrence.
Keywords: CRS-HIPEC; Colorectal peritoneal metastases; Recurrence; Population-based

25COASDEC42:
Title: Single center experiences on 38 cases of transoral endoscopic thyroidectomy submental approach (TOETSA): What's new?,
Erwin Danil Yulian, Diani Kartini, I Gusti Ngurah Gunawan Wibisana, Nataniel Jeremy G. Siahaan,
Surgical Oncology,Volume 63,2025,102301,
https://doi.org/10.1016/j.suronc.2025.102301.
Abstract: Currently, endoscopic thyroidectomy techniques continue to evolve in response to the growing demand for better cosmetic outcomes. To date, transoral endoscopic thyroidectomy via the vestibular approach (TOETVA) remains the only technique that leaves no visible external scar. However, this approach has certain limitations. The primary objective of this report is to present our initial experience with an alternative to TOETVA, namely the Transoral Endoscopic Thyroidectomy via Submental approach (TOETSA), in 38 patients at a single center. We performed the TOETSA procedure on 38 patients who met the inclusion criteria between January 2020 and Desember 2023. The procedure was successfully completed in 36 cases, while conversion to open thyroidectomy was required in 2 cases. Unlike conventional TOETSA, in which all instruments are introduced transorally, this approach utilizes two instruments inserted via the vestibular access and one instrument introduced through the submental crease. Among the 38 TOETSA procedures completed successfully, all specimens were extracted intact, with a mean maximum nodule size of 4.01 ± 0.80 cm (range: 2.50–6.40 cm). The mean operative time, which included procedures on large tumors and simultaneous training of novice surgeons, was 186.82 ± 19,46 (range: 147–226 Minutes). No life-threatening or permanent postoperative complications were observed. Cosmetic satisfaction after 6 months of follow-up was also favorable. However, a comprehensive assessment of oncologic safety could not yet be performed, as most patients were only monitored for 8.6 months in average. TOETSA offers favorable therapeutic and cosmetic outcomes with low complication rates, even in larger specimens. Oncological safety should remain the main consideration in technique selection. TOETSA is also feasible as a training platform for novice surgeons.
Keywords: Thyroidectomy; Endoscopy; Transoral; Submental; Minimally invasive

25COASDEC43:

Title: Impact of resected-to-original middle hepatic vein length proportion on posthepatectomy liver failure after right-sided hepatectomy for perihilar cholangiocarcinoma,

Jimin Son, Se Jin Choi, Min Kyu Sung, Woohyung Lee, Ki Byung Song, Dae Wook Hwang, Song Cheol Kim, Jae Hoon Lee,

Surgical Oncology,Volume 63,2025,102302,
https://doi.org/10.1016/j.suronc.2025.102302.

Abstract: Middle hepatic vein (MHV) resection is often required during right-sided hepatectomy for perihilar cholangiocarcinoma (PHCC) to achieve negative margins. However, its resection may compromise hepatic regeneration, potentially increasing the risk of post-hepatectomy liver failure (PHLF). This single-center retrospective cohort study included patients who underwent right-sided hepatectomy for PHCC from 2013 to 2020. Patients who had right trisectionectomy, pancreaticoduodenectomy, or contralateral vascular resection were excluded. The study assessed MHV resection and the proportion of resected-to-original MHV length using CT imaging. The primary outcome was the occurrence of either PHLF (≥ grade B) or 90-day mortality. Among 347 patients, the primary outcome occurred in 9.5 % (33/347). A higher remnant MHV proportion demonstrated a trend toward lower risk of the primary outcome (Odds ratio [OR] 0.989, 95 % confidence interval [CI] 0.978–1.001; p = 0.058). Although any resection of MHV did not remain an independent predictor in multivariable analysis (OR 2.039, 95 % CI 0.883–4.706; p = 0.095), it was significantly associated with the primary outcome in univariable analysis (OR 2.368, 95 % CI 1.115–4.929; p = 0.022). Although not statistically conclusive, MHV resection may increase the risk of PHLF or 90-day mortality in right-sided hepatectomy for PHCC.

Keywords: Perihilar cholangiocarcinoma; Middle hepatic vein; Posthepatectomy liver failure

25COASDEC44:

Title: Postoperative complications and their risk factors in breast cancer patients treated with neoadjuvant chemotherapy,

Olga Kähkönen, Harri Mustonen, Meri Utriainen, Laura Niinikoski, Tuomo Meretoja, Malin Sund,

Surgical Oncology,Volume 63,2025,102303,
https://doi.org/10.1016/j.suronc.2025.102303.

Abstract: Although neoadjuvant chemotherapy (NACT) has become established treatment of breast cancer, its impact on postoperative complications varies across studies. Furthermore, association between known risk factors and different kind of complications is unclear. We aimed to characterize the type, rate and risk factors of postoperative complications in a cohort of breast cancer patients treated with NACT. A retrospective review of breast cancer patients treated with NACT in Helsinki University Hospital between 2020 and 2022 was performed. Complications were graded according to Clavien Dindo classification. Risk factors were identified for overall complications, chronic seroma (defined as a seroma requiring more than five needle aspirations) and hematoma or infection in a multivariable logistic regression model. Out of 4432 patients, 377 met the inclusion criteria. Of these, 216 (57 %) had 314 postoperative complications, commonly seroma (n = 204, 65 %), wound or seroma infection (n = 42, 13 %) and problems with wound healing (n = 19, 6 %). In multivariable analyses,

higher age (OR = 1.03, p = 0.003) and undergoing mastectomy (OR = 6.45, p < 0.001) and/or axillary lymph node dissection (ALND) (OR = 2.54, p < 0.001) were independent risk factors of overall complications. Hypertension increased the odds of chronic seroma (OR = 2.26, p = 0.035) and overweight increased the odds of hematoma or infection (OR = 1.06, p = 0.012). Postoperative complications were common yet in most cases treated in an outpatient setting. Patients with higher age and BMI, and those operated with mastectomy and/or ALND were in greater risk of developing postoperative complications. This study also identified that hypertension could have a role in the development of chronic seroma.

Keywords: Breast cancer; Neoadjuvant chemotherapy; Postoperative complication; Risk factor; Seroma; Hypertension

25COASDEC45:

Title: Mediastinal staging with video-assisted mediastinoscopic lymphadenectomy after endobronchial ultrasound-guided transbronchial needle aspiration: real-world evidence in 228 patients,

Dominik Herrmann, Santiago Ewig, Katharina Greif, Kolja Milobinski, Tugba Bas Kaya, Melanie Oggiano, Thorsten Walles, Stefan Welter, Erich Hecker,

Surgical Oncology,Volume 63,2025,102309,
https://doi.org/10.1016/j.suronc.2025.102309.

Abstract: Accurate staging of mediastinal lymph nodes in patients with non-small-cell lung cancer (NSCLC) is essential to determine further management. Current guidelines recommend confirmatory mediastinoscopy for patients with suspicious mediastinal lymph node metastases in image-based staging but negative findings on endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). In clinical practice, adherence to these recommendations is low and many physicians omit invasive surgical staging. This study aimed to assess the results of subsequent video-assisted mediastinoscopic lymphadenectomy (VAMLA). Retrospective single-center cohort analysis of patients who underwent surgery between 2015 and 2019. All patients were diagnosed with potentially resectable lung cancer or FDG-avid pulmonary nodule suspicious for NSCLC and underwent VAMLA following N0-N2 EBUS-TBNA for mediastinal staging. VAMLA was performed in 228 patients. Nodal upstaging after EBUS-TBNA occurred in 17.5 % of the cases (n = 40). During EBUS-TBNA, 1.72 (±1.06) lymph node stations were sampled, compared to 5.59 (±1.1) resected stations in VAMLA (p < 0.001). Clinical nodal status staged by PET/CT was significantly correlated with the occurrence of nodal upstaging by VAMLA, with an odds ratio of 7.69 in cN2 and 5.88 in patients with cN3, compared to cN0. Complications occurred in 8 patients (3.59 %). VAMLA was false negative in 1 patient (0.4 %). Subsequent VAMLA enables the accurate staging of patients after negative EBUS-TBNA. Overall, 17.5 % of cases had nodal upstaging and would otherwise not have received guideline-compliant treatment for NSCLC. These results underline the role of surgical mediastinal staging after negative EBUS-TBNA in patients with suspicious radiologic findings.

Keywords: NSCLC; VAMLA; EBUS-TBNA; Mediastinal staging; Surgical mediastinal staging

25COASDEC46:

Title: Safety and perioperative outcomes in extraperitoneal versus transperitoneal robot-assisted radical prostatectomy: A propensity score matching study from a single regional center,

Atsushi Igarashi, Riki Obayashi, Akihiro Yamamoto, Akihiko Nagoshi, Tasuku Fujiwara, Naoki Akagi,

Surgical Oncology,Volume 63,2025,102292,
https://doi.org/10.1016/j.suronc.2025.102292.

Abstract: This study aimed to compare perioperative outcomes and complications between the transperitoneal approach (Tp) and extraperitoneal approach (Ep) in robot-assisted radical prostatectomy (RARP) at our institution. We retrospectively reviewed data from 894 patients who underwent RARP between 2014 and 2023, including 539 with Ep and 355 with Tp. Ep was selected for patients who did not require extended lymph node dissection (ELND), whereas Tp was selected for patients who required ELND. Propensity score matching (PSM) was performed, resulting in 326 matched pairs. Primary outcomes included severe complications (Clavien–Dindo grade III or higher). Secondary outcomes included transfusion rates, console time without ELND and postoperative length of stay. Following PSM, severe complications occurred in 0 patients (0 %) in the Ep group and in 14 patients (4.3 %) in the Tp group, with bowel-related complications more frequent in the latter. The transfusion rate was low in both groups (0.6 % [Ep] vs. 0 % [Tp], p = 0.43). Operative parameters showed comparable console time without ELND (185 min [Ep] vs. 179 min [Tp], p = 0.30). Postoperative length of stay was comparable between groups (median, 6 days for both; p = 0.05). Peritoneal injuries occurred in 19 % of patients in the Ep group but did not lead to major complications or conversion to Tp in most cases. This study suggests that both Tp and Ep are feasible approaches for RARP, with Ep potentially associated with fewer bowel complications.

Keywords: Extraperitoneal; Prostate cancer; Robot-assisted surgery

25COASDEC47:

Title: Pressurized intraperitoneal aerosol chemotherapy (PIPAC) in patients with peritoneal malignancies: a monocentric, single-arm open-label phase II clinical trial,

Marco Tonello, Carola Cenzi, Paola Del Bianco, Elisa Pizzolato, Chiara Maria Biatta, Francesca Bergamo,

Surgical Oncology,Volume 63,2025,102293,
https://doi.org/10.1016/j.suronc.2025.102293.

Abstract: Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a promising palliative treatment for patients with peritoneal malignancies who are not candidates for curative surgery. This study aimed to assess the efficacy and feasibility of implementing a PIPAC program at a single cancer center. An open-label, single-arm, phase II study was conducted, enrolling patients with peritoneal tumors of various origins. Participants received bidirectional chemotherapy (intravenous and PIPAC). The primary endpoint was PIPAC efficacy measured as pathological response, while secondary endpoints included safety and feasibility of the technique, quality of life, and clinical outcomes. From March 2021 to March 2024, 32 patients were screened, and 25 were enrolled, resulting in 58 PIPAC procedures. The complication rate was low, with severe surgical complications occurring in 1.7 % of

procedures and CTCAE grade 3 complications in 3.4 %. A major pathological response was observed in 56 % of cases, and seven patients (28.0 %) underwent curative-intent cytoreductive surgery after at least two PIPAC treatments. Both the Peritoneal Cancer Index (PCI) and the Peritoneal Regression Score (PRGS) decreased after repeated PIPAC ($p = 0.016$ and $p = 0.047$, respectively). Ascites volume also decreased significantly after the first PIPAC ($p = 0.001$). The median overall survival (OS) was 9.6 months, with responding patients (PRGS 1–2) showing better clinical outcomes (OS: 21.0 vs. 5.5 months,$p < 0.001$; PFS: 8.2 vs. 2.4 months,$p < 0.001$) and quality of life ($p = 0.003$). PIPAC can be safely combined with systemic chemotherapy in patients with peritoneal malignancies, demonstrating efficacy in controlling ascites and achieving major pathological response. Further studies are necessary to determine its potential survival benefits.

Keywords: Pressurized IntraPeritoneal aerosol chemotherapy; PIPAC; Peritoneal malignancies

25COASDEC48:

Title: Comparison of robotic and natural orifice transluminal endoscopic surgical technique procedures in patients undergoing sentinel lymph node biopsy during endometrial cancer surgery,

Erkan Şimşek, Sema Karakaş, Onur Karaaslan, Özge Akdeniz Yildiz, Sadık Gündüz, Gökhan Demirayak,

Surgical Oncology,Volume 63,2025,102282,
https://doi.org/10.1016/j.suronc.2025.102282.

Abstract: The role of sentinel lymph node dissection in the surgical management of endometrial cancer limited to the uterus is gaining recognition. The safety and applicability of two methods were assessed by examining the results of our patients in the identification of the sentinel lymph node during endometrial cancer surgery. The methods were robotic surgery, a critical component of minimally invasive surgery, and the vNOTES (Natural Orifice Transluminal Endoscopic Surgery Technique), which has recently been introduced for malignant indications. Patients who had endometrial cancer surgery at our center employing robotic and vNOTES technologies between January 2023 and June 2024 were included in this retrospective study. We conducted the dissection of sentinel lymph nodes utilizing a near-infrared technology camera method with indocyanine green (ICG) in both robotic and vNOTES techniques. The patients' records were retrospectively obtained from patient files and hospital records. Among the 76 patients who underwent surgery for endometrial cancer, 24 were treated with vNOTES surgery, whereas 52 received robotic surgery. No statistically significant differences were seen between the two groups for age ($p = 0.447$), body mass index ($p = 0.506$), prior abdominal operations ($p = 0.209$), predicted blood loss ($p = 0.155$), and surgical duration ($p = 0.298$). The detection rates of sentinel lymph nodes (SLN) were similar across the groups: 97 % ($n = 50$) in the robotic group and 96 % ($n = 23$) in the vNOTES group ($p = 0.493$). The only statistically significant difference was observed in postoperative pain scores at the 12th hour, which were lower in the vNOTES group ($p = 0.023$). The vNOTES technique demonstrates comparable sentinel lymph node detection rates to robotic surgery in the management of uterine endometrial cancer. Moreover, it has the advantage of markedly less postoperative discomfort. vNOTES is a

secure and efficacious minimally invasive option, especially for patients with comorbidities or those deemed unsuitable for robotic surgery.

Keywords: Endometrial cancer; Sentinel lymph node biopsy; vNOTES; Robotic surgery; Minimally invasive surgery

25COASDEC49:

Title: The utility of preoperative diagnostics in patients undergoing radical nephroureterectomy for suspected upper tract urothelial carcinoma: Can we justify treatment without prior histologic confirmation?,

Vincent Hoffmann, Martina Dellino, Henning Bahlburg, Moritz Reike, Analena Elisa Handke, Peter Bach,

Surgical Oncology,Volume 63,2025,102291,
https://doi.org/10.1016/j.suronc.2025.102291.

Abstract: The main obstacles to the broad application of neoadjuvant chemotherapy for locally advanced upper tract urothelial cancer(UTUC) are uncertainties regarding the accuracy of preoperative diagnostics. This study aimed to examine the predictive value of preoperative diagnostic results regarding the histopathologic findings at the time of radical nephroureterectomy (RNU). An institutional dataset of patients undergoing RNU for suspected UTUC between 01/2018 and 12/2023 was analyzed. We examined the preoperative utilization of different diagnostic means and their predictive value in detecting locally advanced(i.e., ≥T2) disease. Separate uni-and multivariable logistic regression models were employed to examine the association between preoperative findings and final histology. At the time of RNU, 64.4 %(n = 74) of patients were diagnosed with ≥T2 disease. Out of 115 patients, 41.7 % underwent RNU based on cross-sectional imaging findings alone, thirty of whom had undergone a prior endourologic diagnostic workup without evidence of UTUC(62.5 %). There were no false-positive diagnoses of UTUC. On multivariable logistic regression and consecutive receiver operating characteristic(ROC) analysis, only a tumor size ≥1.9 cm during cross-sectional imaging was associated with advanced disease(OR 2.99, 95 %CI 1.65–5.43, $p < 0.001$). In this cohort of patients undergoing RNU for suspected UTUC, only tumor size during cross-sectional imaging was associated with advanced disease. These results support the notion of tumor size as an independent risk factor, which may, in turn, guide further treatment decisions.

Keywords: Endourology; Neoadjuvant chemotherapy; Nephroureterectomy; Urothelial cancer; UTUC

25COASDEC50:

Title: Beyond traditional risk factors: The identification of preoperative serum ferritin as a novel predictor of anastomotic leakage after colonic surgery,

Mohamed Hassin Mohamed Chairi, Patricia Josefina Madroñal Escribano, Alicia Ron García,

Surgical Oncology,Volume 63,2025,102283,
https://doi.org/10.1016/j.suronc.2025.102283.

Abstract: To identify predictive risk factors associated with anastomotic leakage (AL) following colon resection surgery. Observational and retrospective cohort study of patients undergoing colon resection with colonic/colorectal anastomosis from January 2018 to December 2023. Demographic, patient, surgery, and outcome data were analysed. Risk

factors were identified with both univariate and multivariate analysis. A total of 639 patients who underwent colon resection with anastomosis were included in this study. Among them, 62 patients (9.7 %) developed AL. Univariate analysis identified age, male sex, preoperative serum ferritin levels >51.75 ng/mL, minimally invasive surgical approach, extended resection and preoperative C-reactive protein levels >10 mg/L as factors associated with AL. Multivariate analysis revealed that preoperative serum ferritin (OR 5.55, $p = 0.001$) and preoperative C-reactive protein levels (OR 54.97, $p < 0.001$) were independent and significant predictors of AL. Our study has identified preoperative C-reactive protein as a predictor of AL, consistent with findings reported in the literature, and highlights preoperative serum ferritin as a novel predictor of AL following colonic anastomosis.
Keywords: Anastomosis; Anastomotic leakage; Risk factor; Colon surgery; Ferritin; CRP

25COASDEC51:
Title: Complications of ovarian metastases from well-differentiated small bowel neuroendocrine neoplasms: a focus on bowel and ureteral obstruction,
Sydney J. Wellens, Nicholas J. Skill, Kevin M. Sullivan, Mary A. Maluccio, Kristen E. Limbach,
Surgical Oncology,Volume 63,2025,102300,
https://doi.org/10.1016/j.suronc.2025.102300.
Abstract: Ovarian metastasis from small bowel neuroendocrine neoplasms (SBNENs) was traditionally considered rare, but more recent series have suggested a higher prevalence. This case series seeks to examine the features and outcomes of patients with neuroendocrine ovarian metastases (NOM). Female patients with histologically confirmed well-differentiated SBNENs were identified using a prospectively maintained database (2014–2024). The electronic medical record was reviewed for details of diagnosis, histopathology, biomarkers, and outcomes among patients with and without NOM. 175 patients met inclusion criteria. 35 patients (20 %) had ovarian metastasis; for this group, 31.4 % had small bowel obstruction only, 5.7 % had ureteral obstruction only, and 14.3 % had both SBO and ureteral obstruction. 22 (62.9 %) also had peritoneal metastasis. 13 patients had ovarian metastasis but no peritoneal metastasis; within this group, 38.5 % had SBO, 15.4 % had ureteral obstruction, 76.9 % developed carcinoid syndrome, and 7.69 % died. There were no significant differences in rate of SBO ($p = 0.280$), ureteral obstruction ($p = 0.716$), or death ($p = 0.091$) between those with ovarian metastasis only and those with peritoneal metastasis only. Median overall survival was not reached. This case series of female patients with SBNENs represents one of the largest available in the literature and demonstrates high rates of complications for those with ovarian metastasis, even in the absence of peritoneal metastasis. Prophylactic oophorectomy may be considered for SBNEN patients given the known development of severe complications throughout the progression of this disease where expectation for survival is lengthy.
Keywords: Small bowel neuroendocrine tumor; Neuroendocrine ovarian metastases; Complications; Survival

25COASDEC52:
Title: Rectal cancer surgery timing after neoadjuvant therapy: balancing downstaging and perioperative outcomes,

Giacomo Calini, Alice Gori, Claudio Isopi, Antonino Spinelli, Gianluca Pellino, Matteo Fiore,
Surgical Oncology,Volume 63,2025,102299,ISSN 0960-7404,
https://doi.org/10.1016/j.suronc.2025.102299.

Abstract: Neoadjuvant therapy (NAT) and Total Mesorectal Excision (TME) improves oncological outcomes in locally advanced rectal cancer (LARC). We aimed to define the optimal timing for rectal resection and TME after NAT, balancing pathologic Complete Response (pCR) and downstaging with the fewest complications. Stage I-III rectal cancer surgery preceded by NAT were retrieved from a retrospective collaborative of 81 centers in Italy 2018–2021. Logistic regression (LR) examined the independent association between postoperative outcomes (pCR, downstaging, intra- and postoperative complications, incomplete resection) and NAT protocols: chemoradiotherapy (nCRT) and short-course radiotherapy (S-CRT) stratified for timing (<8w; 8-12w; >12w) between NAT completion and surgery. Overall, 1428 patients were included: 1042 received nCRT, 187 SCRT, 125 long-course RT, and 74 others. Different timing of nCRT were not associated with any of the outcomes. Time interval >12w for S-CRT was significantly and independently associated with pCR (OR 4.99, 95 %CI 1.4–18), but with similar downstaging, intra- and post-operative complications, and incomplete resection. LR predicting for pCR found a significant association with ASA≥3 (OR 0.67, 95 %CI 0.5–0.9) and with S-CRT <8 weeks (OR 0.31, 95 %CI 0.13–0.74), while no variables were found to be associated with downstaging and intraoperative complications. Postoperative complications were associated with male, ASA≥3, and medium-low rectal cancer, while incomplete resection with ASA≥3, and BMI. Unlike previous literature, the timing of nCRT was not associated with pCR, downstaging, intra- and postoperative complications, or incomplete resection. Timing >12 weeks between SCRT completion and TME showed improved pCR with similar downstaging, intra- and post-operative complications, and incomplete resection.

25COASDEC53:

Title: Ten-year outcomes of 3D-conformal accelerated partial vs. whole breast irradiation after breast-conserving surgery: A randomized study from India,

Budhi Singh Yadav, Sofia Loganathan, Divya Dahiya, Arun Singh Oinam,
Surgical Oncology,Volume 63,2025,102305,
https://doi.org/10.1016/j.suronc.2025.102305.

Abstract: To compare long term clinical outcomes after accelerated partial breast irradiation (APBI) versus whole breast irradiation (WBI) using 3-dimensional conformal external beam radiation therapy in women with breast cancer after breast conservation surgery (BCS). Women >35 years of age with invasive or noninvasive breast cancer ≤4 cm treated by BCS were randomized to 3D-CRT APBI (34 Gy/10 fractions/5 days) or WBI (40 Gy/16 fractions/3 weeks ± boost irradiation). The primary outcome was ipsilateral breast tumor recurrence. Important secondary outcomes were late toxicities using Radiation Therapy Oncology Group scores, Late Effects Normal Tissue Task Force and Subjective, Objective, Management, Analytic scales, adverse cosmetic outcome and distant metastases. The secondary endpoints of radiation toxicities and cosmesis were published in an interim analysis. Here we present the primary outcome and the late toxicities data. Patient and tumor characteristics, local recurrence and rates of adverse cosmetic outcomes were compared using

Fisher exact tests. Locoregional recurrence free survival (LRRFS), disease free survival (DFS) and overall survival (OS) was calculated using Kaplan-Meier curves. All statistical tests were 2 sided, with $p < 0.05$ considered statistically significant. Between June 2011 and December 2015, 132 women with breast cancer were randomized to 3D-CRT APBI or WBI. Patient and tumor characteristics were balanced between the two arms. Median follow-up was 10.8 years (range, 3.2–13.6 years). Local recurrence was observed in 3 (4.6 %) and 2 (3 %) patients in APBI and WBI arms ($p = 0.62$), respectively. Distant metastases occurred in 5 (7.6 %) and 3 (4.4 %) patients in APBI and WBI arms ($p = 0.35$), respectively. The HR for locoregional recurrence was 1.62 (95 % CI, 0.27–9.67, $p = 0.60$) for APBI (65 patients, 3 local recurrences) vs. WBI (67 patients, 2 local recurrences). The 10-year LRRFS rates (95 % CIs) were 97 % (88–99 %) and 95 % (86–98 %), respectively. The HR for disease-recurrence (local or distant) was 1.47 (95 % CI, 0.51–4.25, $p = 0.47$) for APBI (65 patients, 8 recurrences) vs. WBI (67 patients, 6 recurrences). The 10-year DFS rates (95 % CIs) were 92 % (83–97 %) and 88 % (77–94 %), respectively. The HR for death was 1.14 (95 % CI, 0.23–5.67, $p = 0.87$) for APBI (65 patients, 3 deaths) vs. WBI (67 patients, 3 deaths). The 10-year OS rates (95 % CIs) were 97 % (87–99 %) and 95 % (85–98 %), respectively. Adverse cosmesis was significantly higher in patients treated with WBI: 18 (30 %) compared with 3 (5 %) with APBI ($p < 0.001$). Late arm edema was observed in 1 (1.5 %) patients in APBI arm as compared to 4 (6 %) in WBI arm ($p = 0.72$). In women with breast cancer after BCS, APBI was comparable to WBI in terms of LRRFS, DFS and OS. Cosmetic outcome was better in APBI arm. Late arm edema was also comparable between the two arms.

Keywords: Accelerated partial breast irradiation; Whole breast irradiation; Local recurrence; Late toxicities

25COASDEC54:

Title: Overall survival improvement with locoregional control in patients with metastatic breast cancer. Single-institution experience,

María Tereza Nieto-Coronel, Nancy Reynoso-Noveron, Ariana Tabares-Yañez, Claudia Haydee Arce- Salinas,

Surgical Oncology,Volume 63,2025,102304,
https://doi.org/10.1016/j.suronc.2025.102304.

Abstract: The benefit of local control on the overall survival of patients with metastatic breast cancer remains controversial. This study aimed to evaluate the impact of locoregional treatment of the primary tumor (surgery and/or radiotherapy) in Mexican patients diagnosed with de novo metastatic breast cancer. This retrospective study evaluated 671 patients with de novo metastatic breast cancer, diagnosed between the years 2007–2015, using data from a local database of breast cancer patients. The decision for locoregional treatment was made by the attending physician. Among 671 patients, the median follow-up was 26.83 months. Patients who underwent locoregional control (surgery and/or radiotherapy) had a median survival of 41.57 months compared to 21.3 months in those without locoregional control ($p < 0.001$). Median survival was 51.5 months in patients treated with surgery versus 25,53 months in those without surgery ($p < 0.001$) and 40.1 months versus 25.23 months in patients receiving chemoradiotherapy ($p < 0.001$). Multivariate analysis confirmed that surgery significantly improved overall survival (HR 0.50; 95 % CI:0.32–0.77; $p = 0.002$). However, after adjusting for potential confounders using propensity score matching, the survival benefit

associated with surgery did not reach statistical significance. Our retrospective analysis shows no survival benefit from locoregional control after adjustment for potential confounders. However, given the observed survival differences, it is important to identify which patient subgroups may derive benefit in prospective studies.
Keywords: Breast cancer; Loco-regional; Surgery; Radiotherapy; Metastasic

25COASDEC55:
Title: Short-term surgical outcomes for colon adenocarcinoma: Racial-Ethnic comparisons in a universal access health system,
Yvonne L. Eaglehouse, Sarah Darmon, Michele M. Gage, Craig D. Shriver, Kangmin Zhu,
Surgical Oncology,Volume 63,2025,102295,
https://doi.org/10.1016/j.suronc.2025.102295.
Abstract: Access to care has been identified as a contributor to racial-ethnic differences in treatment receipt and survival of colon cancer in the U.S. Less is known about racial-ethnic differences in aspects and outcomes of colon cancer surgery and whether access to care plays a role. We aimed to study colon cancer surgery and short-term postoperative outcomes in the Military Health System (MHS), which provides access to care regardless of patient characteristics. We used the MilCanEpi database to identify patients aged 18 or older who were diagnosed with stage I-III colon adenocarcinoma between 2001 and 2014 and received colectomy as treatment. Outcomes included positive surgical margins, inadequate lymphadenectomy (<12 nodes examined), 30-day complications (any; general or gastrointestinal), and 30-day hospital readmissions. Multivariable Poisson regression models estimated the adjusted risk ratios (ARRs) and 95 % confidence intervals (CIs) in association with race-ethnicity for each outcome.The study included 157 Asian or Pacific Islander, 258 non-Hispanic Black, 111 Hispanic, and 1131 non-Hispanic White patients. Overall, the risk of measured outcomes did not differ significantly for racial-ethnic minority groups compared to non-Hispanic White (ARRs and their 95 % CIs included 1.00). By complication type, Hispanic patients had significantly lower risk of bowel obstruction (ARR = 0.55, 95 % CI = 0.32, 0.96) compared to non-Hispanic White patients, with no other statistically significant racial-ethnic differences. In the universal access MHS, there were no overall significant racial-ethnic differences in surgical aspects or experience of 30-day outcomes of colectomy for non-metastatic colon cancer.
Keywords: Colectomy; Complications; Hospital readmission

25COASDEC56:
Title: The efficacy of thoracic duct ligation for post-esophagectomy chylothorax in esophageal cancer: a nationwide inpatient cohort study,
Takashi Shigeno, Keisuke Okuno, Taichi Ogo, Toshiro Tanioka, Kenro Kawada, Hisashi Fujiwara, Hiroyasu Kagawa,
Surgical Oncology,Volume 63,2025,102279,
https://doi.org/10.1016/j.suronc.2025.102279.
Abstract: Recently, thoracic duct embolization (TDE) has been increasingly adopted as a first-line minimally invasive therapy for post-esophagectomy chylothorax instead of thoracoscopic thoracic duct ligation (TTDL). However, the therapeutic efficacy and advantages of TDE over TTDL are still controversial. This study aimed to evaluate and

compare the clinical and financial outcomes of TDE and TTDL for post-operative chylothorax after esophagectomy using a national database. We retrieved data from patients with esophageal cancer who underwent TDE (n = 312) or TTDL (n = 167) for chylothorax after esophagectomy between April 2012 and March 2022 from the Diagnosis Procedure Combination database in Japan. We compared the success rate of the first intervention, length of post-interventional hospital stay, and total hospitalization cost between the TDE and TTDL groups using propensity score matching analysis. The success rate of the first intervention was significantly higher in the TTDL group than in the TDE group (odds ratio, 6.13; 95 % confidence interval [CI], 3.25 to 11.55). The length of post-interventional hospital stay was significantly shorter (regression coefficient, −14.8 days; 95 % CI, −26.7 to −2.9) and the total hospitalization cost was significantly lower in the TTDL group than in the TDE group (regression coefficient, −1,258,212 yen; 95 % CI, −2,082,407 to −434,017). This nationwide cohort study showed that TTDL was associated with a shorter length of post-interventional hospital stay, lower total hospitalization cost, and higher success rate of the first intervention than TDE for post-esophagectomy chylothorax.

25COASDEC57:

Title: A novel technology for margin extension and local control in breast conservation surgery: Saline-coupled intraoperative radiofrequency ablation (SIRA),

Alyssa Bailey, Tyler R. Wanke, Rhea Verma, Thomas Kurth, Conor Shanley, Erin Mohr, Scott Irving,

Surgical Oncology,Volume 63,2025,102280,
https://doi.org/10.1016/j.suronc.2025.102280.

Abstract: Breast-conserving therapy (BCT) results in reoperation in ∼20 % of cases due to positive margins, and a 7–13 % recurrence risk at 5 years persists despite negative margins and radiation. Enhancing margin treatment is critical to reducing local recurrence and improving survival. To optimize and evaluate the performance of a Saline-coupled Intraoperative Radiofrequency Ablation (SIRA) device in producing uniform 1 cm ablations in lumpectomy cavities and compare it to prior-generation RFA technology in previous clinical studies. This case series (2018–2023) included 55 mock lumpectomies performed on prophylactic mastectomy or cadaver breasts under an IRB-approved protocol. Inclusion required disease-free, sufficient-volume breast tissue with patient consent. 55 ablations were performed on breasts from 44 female patients. The SIRA produced an ablation depth of 1.0 ± 0.2 cm (mean, SD), no significant difference between margins ($p = 0.056$). No significant difference in ablation depth across the following: BI-RADS breast composition ($p = 0.212$), age ($p = 0.188$), height ($p = 0.643$), weight ($p = 0.522$), tissue volume removed ($p = 1.000$), breast surgery history ($p = 0.246$), chest chemotherapy/radiation history ($p = 0.477$), or surgeon ($p = 0.579$). Significant difference in depth and variance between the SIRA and previous-generation technology ($p < 0.001$ and $p = 0.016$), with SIRA significantly deeper and more uniform. Lumpectomy followed by SIRA could reduce positive margin rates and treat additional tissue, resulting in reduction in re-excision rates and serve as a potential alternative to radiation therapy.

25COASDEC58:

Title: Minor resection for primary hepatocellular carcinoma promotes curative recurrent treatments,

Mei-Pei Huang, Rey-Heng Hu, Hou-Ying Cheng, Chih-Yang Hsiao, Ming-Chih Ho, Yao-Ming Wu, Po-Huang Lee, Cheng-Maw Ho,

Surgical Oncology,Volume 63,2025,102281,
https://doi.org/10.1016/j.suronc.2025.102281.

Abstract: The extent of primary hepatectomy for hepatocellular carcinoma (HCC) may influence long-term outcomes, especially at recurrence. We investigated whether initial minor or major hepatectomy impacts retreatment options and survival following recurrence. We retrospectively reviewed patients with primary HCC who underwent either initial major or minor hepatectomy. Outcomes analyzed included overall survival (OS), and post-recurrence overall survival (OS-R). Prognostic factors were analyzed using propensity score matching (PSM). Among 1836 patients experienced recurrence, 873 matched cases were analyzed post-PSM. The crude 5-, 10-, and 15-year OS rates were 86.5 %, 73.9 %, and 61.5 %, respectively, in the minor hepatectomy group, and 76.8 %, 67.6 %, and 62.7 %, respectively, in the major hepatectomy group ($p < 0.001$). OS-R was comparable between the two groups among the matched cases. The prognostic factors for OS-R included the initial cancer stage, recurrent albumin–bilirubin score, recurrence with vascular invasion or extrahepatic metastases, and the selected recurrent treatment. More patients after primary minor hepatectomy underwent re-resection or local ablation as recurrent treatment, and were able to achieve better outcomes. While recurrence rates and post-recurrence survival were similar between groups, minor hepatectomy may preserve greater liver volume, enabling more patients to receive further curative treatments upon recurrence. Minor hepatectomy offers better retreatment options and potentially better long-term survival.

Keywords: Major hepatectomy; Minor hepatectomy; Recurrent hepatocellular carcinoma; Rehepatectomy; Local ablation

25COASDEC59:

Title: Surgical treatment of liver metastasis from pancreatic cancer,

José Manuel Ramia, Nuria Blanco-Asensio, Juan Jesús Rubio, Víctor López-López, Ricardo Robles-Campos,

Surgical Oncology,Volume 63,2025,102308,
https://doi.org/10.1016/j.suronc.2025.102308.

Abstract: Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer-related mortality, projected to become the second by 2030. Liver metastases from PDAC (LMPC) are typically deemed inoperable, with dismal prognosis and limited surgical roles. However, emerging evidence suggests that liver resection may benefit selected patients. This study evaluates overall survival (OS), disease-free survival (DFS), and prognostic factors following hepatic resection for synchronous and metachronous LMPC. A retrospective, multicenter cohort study from the REMENOCOR Project included 66 patients who underwent liver resection for LMPC in Spain between 2010 and 2022. Eligible patients were ≥18 years with histologically confirmed PDAC and liver metastases. Survival outcomes, postoperative morbidity (Clavien-Dindo, CCI), and prognostic indicators were analyzed using Kaplan-Meier and univariate and multivariate methods. R0 resection was achieved in 72.7 % of the

patients, and major complications occurred in 19.6 %, with 1.5 % mortality. The 5-year OS and DFS were 26.6 % and 12.7 %, respectively. LMPC were metachronic in 65.2 % of patients. Synchronous resection correlated with significantly poorer OS (5 % vs. 38 %, $p < 0.05$). Synchronous surgery and advanced pancreatic T-stage emerged as independent negative prognostic factors. Liver resection for metachronous LMPC may offer meaningful survival in selected patients, underscoring the importance of individualized surgical strategies and the need for prospective trials.

Keywords: Pancreatic adenocarcinoma; Liver metastasis; Surgery; Overall survival; Disease-free survival

25COASDEC60:

Title: Prognostic relevance of CT-defined body composition in esophageal cancer patients undergoing curative treatment,

Hannah Götze, Stefan Niebisch, Matthias Mehdorn, Daniel Seehofer, Gertraud Stocker, Timm Denecke, Hans-Jonas Meyer,

Surgical Oncology,Volume 63,2025,102278,
https://doi.org/10.1016/j.suronc.2025.102278.

Abstract: Body composition including low skeletal muscle mass (LSMM) defined by skeletal muscle index (SMI) and subcutaneous and visceral adipose tissue (SAT and VAT) can be assessed using cross-sectional imaging techniques. Previous studies have shown promising prognostic value for several tumour entities, including esophageal cancer (EC). The aim of this study was to analyse possible associations of body composition parameters in patients with esophageal cancer undergoing curative treatment. All patients with EC undergoing curative treatment were retrospectively evaluated between 2016 and 2023. A total of 145 patients (17 female, 11.7 %) with a mean age of 65.9 ± 10.2 years were included in the present analysis. For all patients, staging computed tomography (CT) was used to calculate LSMM, VAT, and SAT. The primary study end point was all-cause overall survival. For statistical analysis group differences were calculated using the Mann-Whitney test. Kaplan-Meier curves and multivariable Cox regression analysis was used to test the effect of body composition parameters on mortality. In total, 51 patients (35.2 %) of the patient cohort died within the observation period. According to the sarcopenia threshold of the SMI, 99 patients (68.2 %) were classified as sarcopenic and according to the VAT threshold, 102 patients (70.3 %) were classified as visceral obese. Sarcopenia and visceral obesity were associated with mortality with a hazard ratio (HR) of 2.05 (95%confidence interval (CI) 1.17, 3.57, $p = 0.01$) and 2.47 (95%CI 1.39, 4.37, $p = 0.002$) in univariable analysis, respectively. Only the combination of both, sarcopenic obesity was significantly associated in multivariable analysis (HR 2.47, 95 %CI 1.39; 4.37, $p = 0.002$) The combination of CT-defined sarcopenia and visceral obesity showed a strong prognostic relevance in EC undergoing curative resection. The effect of sarcopenia and visceral obesity considered separately was of lesser prognostic significance. CT-defined body composition may help to better stratify patients with EC at risk of worse outcome in clinical practice.

Keywords: Esophageal cancer; CT; Body composition; Prognosis

25COASDEC61:

Title: Oncological and functional outcomes of salvage surgery for local oropharyngeal cancer recurrence after primary Radiation±Chemotherapy,

Francisco Laxague, Naif Fnais, Dorsa Zabihi, Kevin Fung, Danielle MacNeil, Adrian Mendez, John Yoo,

Surgical Oncology,Volume 63,2025,102276,
https://doi.org/10.1016/j.suronc.2025.102276.

Abstract: We aimed to analyze the role of salvage surgery for local/locoregional OPSCC recurrences after primary radiotherapy ± chemotherapy (CRT). From 1156 patients, we identified 38 patients undergoing salvage surgery for local/locoregional recurrences. We analyzed surgical and survival outcomes based on surgical approach and clinical variables. Thirty-eight patients underwent SS for a local/locoregional OPSCC recurrence. Patients undergoing SS experienced superior overall survival (3-year 62.1 % vs. 13 %; and OS: 5-year 34 % vs. 0 %; $p < 0.01$) and progression-free survival: 3-year 61.1 % vs. 0 %; and PFS: 5-year 28.6 % vs. 0 %; $p < 0.01$) compared with those undergoing non-surgical treatment. One year after the surgery, 12/27 surviving patients (44.4 %) were tracheostomy dependent, and 12/27 feeding tube dependent. Salvage surgery for locoregional OPSCC recurrences after primary CRT is safe and feasible in selected patients. However, patients should be counselled about the possibility of long-term feeding tube and/or tracheostomy dependency post operatively.

Keywords: Oropharyngeal squamous cell carcinoma; Local recurrence; Salvage surgery; Surgical outcomes; Survival outcomes

25COASDEC62:

Title: Impact of Frozen Section Pathology Examination of Surgical Margins in Sublobar Pulmonary Resections for Clinical Stage IA Non-small Cell Lung Cancer,

Belisario A. Ortiz, Sam K. Engrav, Anja C. Roden, Jennifer M. Boland, Marie-Christine Aubry, Farah A. Abdallah,

The Annals of Thoracic Surgery,Volume 120, Issue 6,2025,Pages 1044-1051,
https://doi.org/10.1016/j.athoracsur.2025.04.005.

Abstract: Sublobar resections are a valid surgical option for many patients with clinical stage IA non-small cell lung cancer (NSCLC). However, assessment of planned lines of resection can be limited when done using robotic technology. Further, incomplete resections are associated with worse outcomes. This study evaluated routine frozen section pathology (FSP) evaluation of margins during sublobar resections for clinical IA NSCLC. Patients with clinical stage IA NSCLC who underwent lung resections during 2018 to 2023 were reviewed. Only patients with a preoperative intention to undergo sublobar resection were included. FSP reports were compared with final pathology. Operative notes were reviewed to determine changes in surgical plan based on intraoperative FSP evaluation of margins.Of 1008 patients who underwent surgery, 642 (63.7%) had a preoperative plan to undergo sublobar resection. Median preoperative tumor size was 1.5 cm (interquartile range, 1.1-2.0 cm). A positive margin was identified in 8 patients (1.25%) intraoperatively or postoperatively. FSP successfully identified 7 of 8 patients (87.5%) intraoperatively, all corresponding to the parenchymal margin. In 5 of 7 patients (71.4%), the surgeon could alter the procedure to achieve a final negative margin. The final rate of non-R0 resection was 3 of 642 (0.47%).

Therefore, FSP decreased the potential rate of non-R0 resection from 1.25% to 0.47% (62% reduction). FSP is a valuable tool to assess resection margins during intended sublobar resections of clinical stage IA NSCLC. Intraoperative margin analysis can identify most patients with positive margins, allowing the surgeon to alter the planned procedure, if appropriate, minimizing non-R0 resections.

25COASDEC63:

Title: Synchronous Primary Early-Stage Non-Small Cell Lung Cancer: Trends in Management and Factors Associated With Improved Survival,

Whitney S. Brandt, Nikki E. Rossetti, Daniel B. Eaton, Pamela Samson, Theodore Thomas, Brendan T. Heiden,

The Annals of Thoracic Surgery,Volume 120, Issue 6,2025,Pages 1033-1042,
https://doi.org/10.1016/j.athoracsur.2025.07.058.

Abstract: Outcomes after multimodality curative-intent treatment of patients with synchronous primary early-stage I non-small cell lung cancer (SPELC) are inadequately understood. We performed a retrospective study using the Veterans Health Administration database of patients diagnosed with 2 stage I SPELC tumors who received treatment with either stereotactic body radiotherapy (SBRT) or surgery from 2006 to 2024. We evaluated use of SBRT and surgery as well as factors associated with overall survival (OS) and disease-free survival (DFS) by Cox proportional hazards models. A total of 835 patients were included; 294 (35.2%) underwent SBRT-SBRT, 149 (17.8%) received SBRT-surgery, and 392 (47%) underwent surgery-surgery. Patients treated with SBRT had more comorbidities (P < .0001) and were older (P < .0001). Use of SBRT increased from <20% in 2008 to >60% of cases in 2024. The adjusted 5-year OS was 51.7% (SBRT-SBRT) vs 72% (SBRT-surgery) vs 66.7% (surgery-surgery; P < .0001). Multivariable analysis demonstrated that patients who underwent SBRT-SBRT had worse OS (hazard ratio, 1.71; 95% CI, 1.32-2.22), but those in the SBRT-surgery group and surgery-surgery group had similar OS. Adjusted 5-year DFS was 42.7% (SBRT-SBRT) vs 42.6% (surgery-SBRT) vs 57.26% (surgery-surgery). On multivariable analysis, DFS was inferior in the SBRT-SBRT group (hazard ratio, 1.525; 1.198-1.942; P = .0006) and SBRT-surgery group (hazard ratio, 1.530; 1.011-2.314; P = .04) than in the surgery-surgery group. In veterans with stage I SPELC, there is heterogeneity in outcomes based on treatment modality among other factors. Patients who are selected for surgery for both lesions have the best DFS but similar OS to those who undergo surgery-SBRT.

25COASDEC64:

Title: Neoadjuvant Immunochemotherapy for Stage II-IIIB Non-Small Cell Lung Cancer With Mutations Beyond EGFR 19del, L858R, and ALK Rearrangement,

Hongdou Ding, Bo Tao, Li Xu, Gening Jiang, Haifeng Wang,

The Annals of Thoracic Surgery, Volume 120, Issue 6,2025,Pages 1052-1061,
https://doi.org/10.1016/j.athoracsur.2025.04.016.

Abstract: Neoadjuvant immunochemotherapy (neoICT) is not currently recommended for patients with stage II-IIIB non-small cell lung cancer (NSCLC) harboring oncogenic driver mutations, especially tyrosine kinase inhibitor–sensitizing epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK). This study aimed to compare the pathologic

response and survival outcomes between neoICT and neoadjuvant chemotherapy (neoChT) in patients with stage II-IIIB NSCLC harboring driver mutations beyond EGFR exon 19 deletion (19del), exon 21 L858R, and ALK rearrangement.Patients with stage II-IIIB NSCLC harboring driver mutations (EGFR 20ins/EGFR G719X/KRAS/BRAF/c-MET/HER-2/ROS1/RET/PIK3CA) who underwent neoICT or neoChT followed by curative-intent resection were retrospectively enrolled between November 2019 and August 2023. Kaplan-Meier analysis was performed to evaluate recurrence-free survival (RFS). Multivariable Cox proportional hazards regression was used to identify factors influencing survival outcomes after propensity score matching (2:1).A total of 52 and 24 patients received neoICT and neoChT, respectively. Kirsten rat sarcoma virus (KRAS) mutations were detected in 67.1% (51 of 76) of patients. The major pathologic response (MPR) rates were 53.8% and 4.2%, respectively. NeoICT conferred better RFS than neoChT (2-year RFS rate: 79.5% vs 49.9%; log-rank P = .012). After matching, multivariable Cox proportional hazards regression demonstrated that neoICT was associated with improved RFS compared with neoChT (hazard ratio, 0.33; 95% CI, 0.14-0.80). Similar findings were observed in both the KRAS-mutant and non–KRAS-mutant subgroups. In the neoICT group, nonadenocarcinoma histologic features and elevated programmed cell death ligand 1 levels were correlated with higher MPR rates. NeoICT resulted in superior pathologic response and survival compared with neoChT in both KRAS-mutant and non–KRAS-mutant subgroups.

25COASDEC65:

Title: Predictive value of CT-based arterial enhancement fraction in the preoperative lymphovascular invasion of pancreatic ductal adenocarcinoma,

Wenzheng Lu, Zongbo Li, Yiheng Zhou, Yanqi Zhong, Heng Zhang, Xingbiao Chen, Shudong Hu,

Asian Journal of Surgery,Volume 48, Issue 12,2025,Pages 7292-7298,
https://doi.org/10.1016/j.asjsur.2025.06.249.

Abstract: To investigate whether arterial enhancement fraction (AEF) from computed tomography (CT) can be used to assess lymphovascular invasion (LVI) status in pancreatic ductal adenocarcinoma (PDAC). A total of 92 patients with histopathologically confirmed PDAC who underwent CT were included and assigned to this retrospective study. The CT attenuation values of CT-derived enhancement parameters between the groups positive and negative for LVI were evaluated. The optimal combination of enhancement parameters for predicting LVI status was investigated by employing binary logistic regression models and evaluated via receiver operating characteristic (ROC) curves. Furthermore, the optimal model was developed into a visual nomogram and evaluated for clinical applicability by using decision curve analysis (DCA). A total of 22 patients positive for LVI and 70 patients negative for LVI were included. The CT values of the arterial phase (Ap), absolute contrast enhancement of the Ap (△Ap), and AEF were significantly higher in the LVI-positive group than the LVI-negative group (all $P < 0.05$). LVI (+) had the highest predictive efficiency for AEF, with an area under the curve (AUC), accuracy, sensitivity, and specificity of 0.798, 0.717, 0.714, and 0.727, respectively. The nomogram incorporating these three predictors exhibited the best evaluation efficacy with an AUC of 0.846, accuracy of 0.826, sensitivity of 0.871, and specificity of 0.682. Subsequently, the DCA of the nomogram indicated optimal

clinical value for predicting LVI status. AEF derived from CT and nomogram have the potential for the preoperative evaluation of LVI status in patients with PDAC.

Keywords: Contrast-enhanced computed tomography; Arterial enhancement fraction; Pancreatic ductal adenocarcinoma; Lymphovascular invasion; Nomogram

25COASDEC66:

Title: Tumor sidedness and the usefulness of laparoscopic surgery in obese colorectal cancer patients in Japan,

Hiroshi Miyakita, Seiichiro Yamamoto, Junichiro Hiro, Kiyonori Kanemitsu, Tomonori Akagi, Kentaro Nakajima,

Asian Journal of Surgery,Volume 48, Issue 12,2025,Pages 7331-7336,
https://doi.org/10.1016/j.asjsur.2025.08.301.

Abstract: Numerous reports suggest that there is no difference in treatment outcomes between obese and non-obese patients undergoing laparoscopic surgery for colorectal cancer. However, contrasting findings also suggest that treatment results may be inferior in obese patients. We aimed to retrospectively analyze outcomes of laparoscopic and open surgeries for right- and left-sided colectomies in 1572 obese patients with colorectal cancer. Patients were classified by surgical type (laparoscopic vs. open) and colectomy location (right vs. left). We assessed body mass index, tumor diameter, blood loss, operative time, lymph nodes removed, metastases, recurrence rate, and overall survival. No relationship was found between body mass index and the surgical method. Tumor diameter was significantly larger in open surgeries for both sides ($p < 0.001$). The combined resection rate was also significantly higher in open surgeries ($p < 0.001$). Laparoscopic surgeries resulted in significantly lower blood loss but significantly longer operative times on both sides ($p < 0.001$). No difference in operative times was noted between left and right laparoscopic surgeries, whereas left-sided open colectomies took significantly longer ($p = 0.9086$, $p < 0.001$). Lymph node-positive metastasis rate, recurrence rate, and overall survival showed no differences. Combined resection (T4b) and tumor size are more critical than body mass index in selecting the surgical approach. Open surgeries had longer operative times for left-sided colectomies, whereas laparoscopic surgeries showed no time difference between sides, suggesting potential advantages for left-sided procedures or greater difficulty with right-sided colectomies. Despite longer operative times, laparoscopic surgery's lower blood loss indicates its oncological safety.

Keywords: Colectomy; Colorectal cancer; Laparoscopy; Obesity; Surgery

25COASDEC67:

Title: Comparative study of intracorporeal versus extracorporeal anastomosis in laparoscopic right colectomy for right colon cancer,

Ayman Abdulmohaymen, Sayed R. Abdelbary, Tamer A. Abouelgreed, Ahmed M. Aydarous, Ahmed Embaby,

Asian Journal of Surgery,Volume 48, Issue 12,2025,Pages 7312-7317,
https://doi.org/10.1016/j.asjsur.2025.08.221.

Abstract: There is no standard operating method for anastomosis in laparoscopic right colectomy. Although there is currently inadequate evidence, some published researches demonstrate the superiority of intracorporeal ileocolic anastomosis (IIA).To compare IIA

with extracorporeal ileocolic anastomosis (EIA) in laparoscopic right colectomy.Between January 2021 and October 2024, 120 laparoscopic right colectomy patients participated in this trial. Patients were randomly grouped into two groups, IIA group (n = 60) and EIA group (n = 60). Both groups were compared regarding clinical aspects, intraoperative features, postoperative recovery, oncological outcomes, and short-term complications.There were no statistically significant difference between study arms regarding demographic criteria and preoperative clinical aspects. Patients within IIA group experienced statistically significant less postoperative pain measured by VAS score on day 0 (p = 0.009), day 2 (p = 0.013), and day 4 (p = 0.0007) and more rapid gastrointestinal recovery measured by time to first flatus (p = 0.0004). However, IIA had longer average operative time than EIA. Otherwise, oncological outcome, and short-term complications were comparable between the study arms with no statistically significant differences.IIA is superior to EIA regarding postoperative pain and return of gastrointestinal motility. Longer operative time is explained by the more complex technique of IIA requiring more laparoscopic skills and expertise.

Keywords: Intracorporeal; Extracorporeal; Ileocolic anastomosis; Laparoscopic right colectomy; cancer colon

25COASDEC68:

Title: Clinical Significance and Preoperative Prediction of High-Grade Subtypes in Early-Stage Lung Adenocarcinoma Eligible for Sublobar Resection,

Mikubo, Masashi and Tamagawa, Satoru and Kondo, Yasuto and Sonoda, Dai and Naito, Masahito and Shiomi, Kazu and Ichinoe, Masaaki and Satoh, Yukitoshi

Journal of Surgical Oncology,volume 132, number = 8,pages 1407-1415,
https://doi.org/10.1002/jso.70117,

Abstract: The indication for sublobar resection is determined based on radiologic findings, but some cases exhibit radiology-pathology discordance. This study aimed to examine the impact of histologic subtypes on radiology-pathology discordance and their preoperative predictability. Methods We reviewed 585 patients with clinical stage IA adenocarcinoma and examined the relationship between radiology-pathology discordance and histologic characteristics, focusing on high-grade components: solid (SOL) or micropapillary (MIP). The predictive ability of radiologic or cytopathologic examinations for those subtypes was evaluated. Results Radiology-pathology discordance was found in 148 (25.2\%) patients and was significantly associated with the presence of histologic high-grade components, with 71.9\% and 70.4\% of patients with upstaged lymph node and pleural invasion statuses having high-grade components. The preoperative prediction of high-grade components varied between subtypes, and radiographically pure-solid appearance and high maximum standardized uptake value were independent predictors of the SOL subtype, but not MIP. Among pre- or intraoperative cytopathologic examinations, intraoperative touch imprint cytology exhibited superior detection ability for MIP component. Conclusions Histologic high-grade components are highly associated with radiology-pathology discordance in early-stage lung adenocarcinoma. Radiologic assessment would be beneficial for predicting the SOL subtype, but not MIP. Alternatively, intraoperative cytologic assessment would complement the detection of MIP subtype.

Keywords: early-stage lung cancer, micropapillary subtype, solid subtype, sublobar resection, upstaging

25COASDEC69:

Title: Complete Cytoreduction of Colorectal Liver Metastases: Evolving Systemic Therapy and Liver Transplantation

Le, Viet and Franko, Jan and Fong, Yuman

Journal of Surgical Oncologyvolume = 132 number = 8 pages = 1317-1319
https://doi.org/10.1002/jso.70112

Abstract: Approximately 50\%–60\% of patients with colorectal cancer develop metastases, of which most have unresectable metastatic liver disease. Several recent studies highlight the progress of systemic therapy in converting patients with high burden of colorectal liver metastases (CRLM) from unresectable to resectable disease, resulting in median overall survival improvements. The improvement of systemic therapy and the evolving spectrum of surgical techniques is allowing multidisciplinary treatment teams an increasing ability to achieve complete cytoreduction of CRLM and offering an increasing number of patients a chance for long-term survival.

Keywords: colorectal liver metastases, cytoreductive surgery, liver surgery, liver transplantation

25COASDEC70:

Title: A Seer-Based Analysis of Survival Predictors in Stage I Colorectal Adenocarcinomas

Emile, Sameh Hany and Horesh, Nir and Garoufalia, Zoe and Oosenbrug, Marcus and Boutros, Marylise and Wexner, Steven D.

Journal of Surgical Oncologyvolume = 132number = 8pages = 1320-1330
https://doi.org/10.1002/jso.70111

Abstract: We assessed predictors of overall (OS) and cancer-specific survival (CSS) in stage I colorectal cancer (CRC). Methods Retrospective analysis of patients with stage I colon or rectal adenocarcinomas from the SEER database (2010–2020) Survival was assessed using Kaplan-Meier statistics and multivariable Cox regression analyses. The primary outcomes were 5-year OS and CSS. Results 40,001 patients (51.3\% male; mean age: 65.1 ± 12.6 years) were included. Colon and rectal cancers accounted for 75.8\% and 24.2\%, respectively. Five-year OS and CSS were 83.1\% (95\% CI: 82.6–83.5\%) and 93.2\% (95\% CI: 92.9–93.5\%), respectively. Factors independently associated with worse OS were age (HR: 1.07; $p < 0.001$), male sex (HR:1.48; $p < 0.001$), Black race (HR: 1.25; $p < 0.001$), single, divorced, or widowed status (HR: 1.49, 1.46, and 1.43; $p < 0.001$), tumor size (HR: 1.001; $p = 0.008$), poorly differentiated carcinomas (HR: 1.32; $p < 0.001$), undifferentiated carcinomas (HR:1.44; $p = 0.026$), perineural invasion (HR: 1.84; $p < 0.001$), elevated CEA levels (HR: 1.68; $p < 0.001$), and systemic therapy (neoadjuvant: HR: 1.3; $p = 0.032$, adjuvant: HR: 2.2; $p < 0.001$, both: HR: 1.97; $p < 0.001$). Factors independently associated with worse CSS were age (HR: 1.05; $p < 0.001$), male sex (HR: 1.32; $p < 0.001$), Black race (HR: 1.43; $p < 0.001$), marital status (HR: 1.44, 1.28, and 1.68; $p < 0.001$), tumor size (HR: 1.003; $p < 0.001$), poorly differentiated carcinomas (HR: 1.77; $p < 0.001$), perineural invasion (HR: 2.29; $p < 0.001$), elevated CEA levels (HR: 2.24; $p < 0.001$), and systemic therapy (neoadjuvant: HR: 2.53; $p = 0.032$, adjuvant: HR: 4.22; $p < 0.001$, both: HR: 3.83; $p < 0.001$). Conclusions Although patients with stage I CRC had excellent survival, single, older, Black, male patients with

large, high-grade tumors associated with perineural invasion and elevated CEA levels had a higher mortality risk.
Keywords: Colorectal Cancer, prognosis, SEER, stage I, survival

25COASDEC71:
Title: Non-Colorectal Cancer-Related Deaths in Patients With Early-Onset Colorectal Cancer: A Population-Based Study
Emile, Sameh Hany and Horesh, Nir and Garoufalia, Zoe and Gefen, Rachel and Dourado, Justin and Boutros, Marylise and Wexner, Steven D.
Journal of Surgical Oncology volume = 132number = 8pages = 1356-1365
https://doi.org/10.1002/jso.70118
Abstract: We assessed causes of death in patients with early-onset colorectal cancer (EOCRC) and factors associated with non-CRC-related deaths. Methods SEER database was screened between 2000 and 2020 for patients with EOCRC. Causes of death were classified into CRC-related and non-CRC-related, and stratified by demographics, disease location, and stage. The main study outcome was the cause of death in EOCRC. Results A total of 67 353 patients (53.9\% male) had EOCRC. In total, 13.2\% of 25 441 deaths were unrelated to CRC. The most common cause of non-CRC-related deaths was medical conditions (36.1\%), mainly heart disease (16.6\%). CRC was more often the cause of death in patients aged < 30 years, female, and stages III and IV disease; whereas medical conditions accounted for more deaths in patients aged 40–50 years, males, and Black. Other primary cancers were more often the cause of death in patients aged 45–50 years, female patients, and Asian patients. Death due to causes other than CRC was significantly more likely when surgery for CRC was performed (OR: 2.35; $p = 0.028$) and when CRC was one of multiple primary cancers (OR: 3.7; $p < 0.001$). Conclusions Most common causes of non-CRC-related deaths were medical conditions and other primary cancers accounting for more deaths in patients aged 40–50 years, males, Black and Asian patients, and with early-stage CRC.
Keywords: cause of death, colorectal cancer, early-onset, SEER

25COASDEC72:
Title: Predictive Factors for Failed Sentinel Lymph Node Mapping in Endometrial Cancer: A Retrospective Multicenter Study
Taliento, Cristina and Scutiero, Gennaro and Cucinella, Giuseppe and Chiantera, Vito and Pontrelli, Giovanni and Klaric,
Journal of Surgical Oncology volume = 132 number = 8 pages = 1391-1398
https://doi.org/10.1002/jso.70106
Abstract: This study aims to evaluate the predictive factors associated with failed sentinel lymph node (SLN) mapping in a large, retrospective cohort of patients with early-stage endometrial cancer (EC). Methods We retrospectively evaluated a series of EC patients who underwent laparoscopic SLN mapping with intracervical indocyanine green (ICG) injection in five referred oncological centers from January 2019 to March 2024. We compared the clinical and pathological features of bilateral and failed SLN mapping, which was defined as either unilateral mapping or no SLN mapping. Logistic regression was used to identify predictors of failure. Results Among 623 analyzed patients, 437 (70.14\%) had a successful bilateral procedure. On univariate analysis, age ($p = 0.03$), non-endometrioid histology

(p = 0.02) and previous vaginal delivery (p = 0.015) were significant associated with failed SLN mapping. On multivariable analysis, only increasing age (OR 1.03; 95\% CI, 1.01–1.04, p = 0.03) and non-endometrioid histology (OR 1.81; 95\% CI, 1.01–3.19) were independently associated with unsuccessful procedure. No significant differences were observed for BMI, enlarged lymph nodes, intraoperative lysis of adhesion, LVSI, grade 3, and FIGO stage. Conclusions Increasing age and non-endometrioid histology are independent predictors of bilateral SLN mapping failure in EC patients undergoing SLN mapping with cervical ICG injection.

Keywords: endometrial cancer, failed SLN mapping, ICG injection, predictive factors, sentinel lymph node

25COASDEC73:

Title: Gluteal Flap Reconstruction Following Complex Rectal Cancer Surgery: A Large Consecutive Series of Perineal Wounds Exploring Risk Factors for Complications

Gould, Laura E. and Pring, Edward. T. and Drami, Ioanna and Constantinides, Joannis and Hodges, Nicola and Steele,

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Abstract: To determine whether high complexity pelvic exenterations alter perineal wound morbidity and to assess risk factors for perineal flap complications following complex rectal cancer surgery. Methods A retrospective analysis of consecutive adults undergoing complex rectal cancer resections with immediate gluteal flap perineal reconstruction between January 2013-July 2021 at a tertiary referral centre. Conventional complex cancer resections were compared with “high complexity” exenterations, including en bloc sacrectomy and extended lateral pelvic side wall excision. Primary outcomes were short-term (wound infection, necrosis, dehiscence) and long-term (sinus, fistula, hernia) perineal flap complications. Results We identified 194 patients (median 56 years, 60\% male) with gluteal flap reconstructions; 163 (84\%) for advanced or recurrent rectal cancer. Gluteal artery perforator flaps were predominantly used (176, 92\%). Wound infections were more common in the conventional group (23.2\% vs. 6.3\%, p = 0.001), but no other differences in complications were observed between groups. Obesity (HR 2.70, 95\% CI 1.22–5.97, p = 0.014) and total pelvic exenteration (HR 2.13, 95\% CI 1.07–4.23, p = 0.031) were associated with short-term complications. Age over 65 years predicted readmission/reoperation (HR 2.66, 95\%CI 1.07–6.6, p = 0.040). Ureteric/ileal conduit leaks were associated with long-term complications (HR 3.37, 95\% CI 1.21–9.34, p = 0.024). No flap losses occurred. Conclusion Gluteal fasciocutaneous perforator flaps provide reliable perineal reconstruction after complex rectal cancer surgery. The extent of surgery and resulting defect size did not significantly influence perineal wound complication rates.

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2nd Campus,New Town: Street Number 299, DJ Block, Action Area I,New Town, Kolkata-700160