AACR 2025 Clinical and AI / ML Preview

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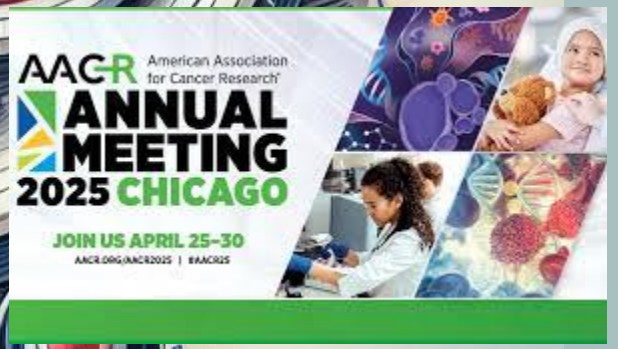

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AACR 2025 Preview – Table of Contents

AACR 2025 – General Overview

- **Global Cancer Research Collaboration:** Leading cancer researchers, clinicians, and industry professionals will converge to discuss the future of cancer treatments and therapies
- **Innovative Therapeutics and Clinical Trials:** A focus on the latest advancements in therapeutic approaches and ongoing clinical trial results
- **Technological Integration in Cancer Care:** Cutting-edge technologies such as AI, big data analytics, and genomics will be explored for their potential to revolutionize cancer treatment
- **Real-World Evidence:** Discussions will highlight the increasing role of real-world data in shaping cancer treatment strategies and improving patient outcomes
- **Comprehensive Educational Offerings:** The conference will provide educational sessions, symposia, and workshops targeting oncology professionals at various stages of their careers
- **Industry and Academia Synergy:** A strong emphasis on fostering collaborations between academia, biotechnology, and pharmaceutical industries to accelerate cancer research and treatment development

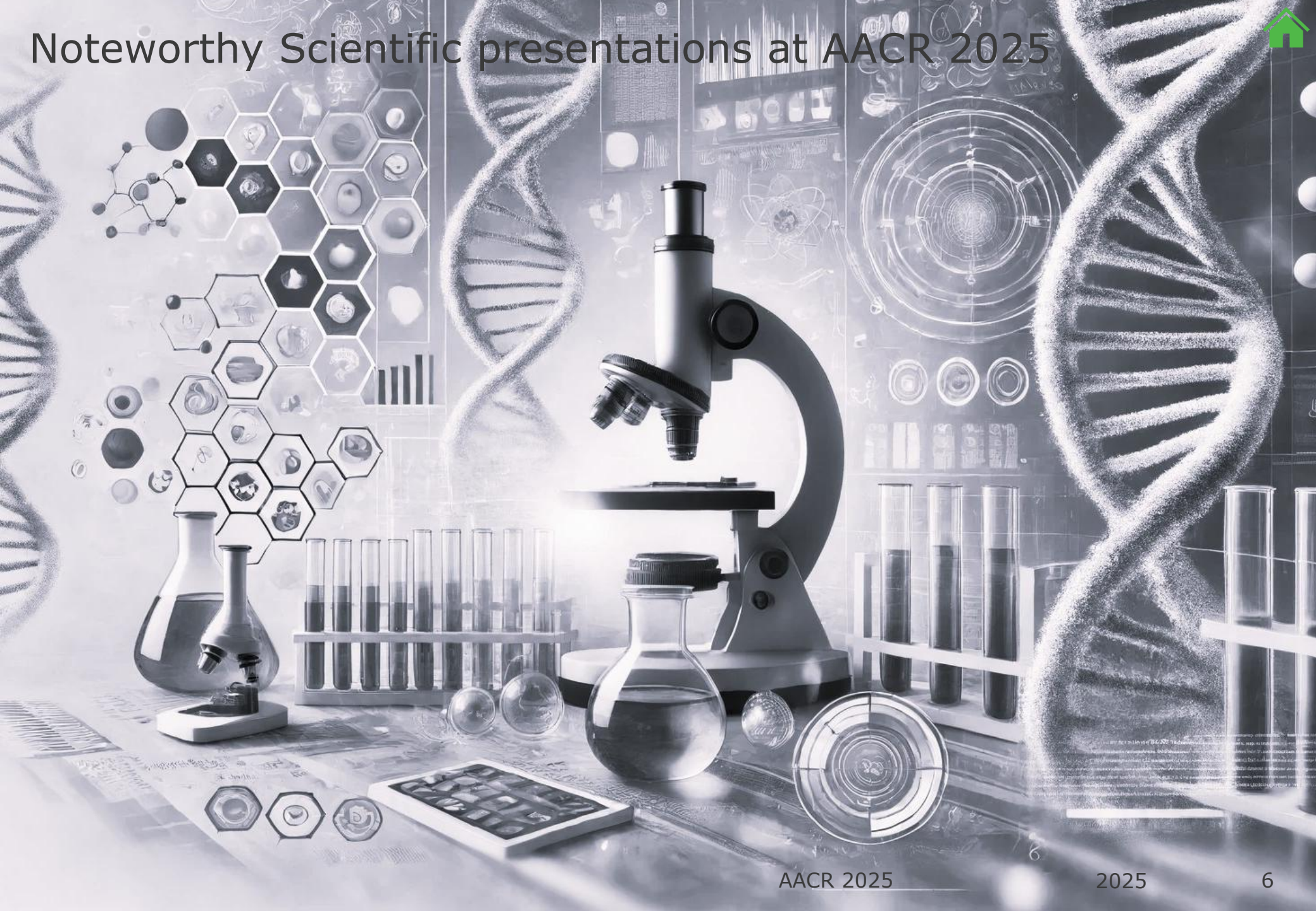
AACR 2025– Conference Themes (1/2)

- **Next-Generation Immunotherapies:** Focus on innovative immune-based treatments like CAR-T, bispecific antibodies, and novel checkpoint inhibitors
- **Precision Oncology:** Emphasis on tailoring cancer therapies based on genetic and molecular profiling of tumors to optimize treatment outcomes
- **Advances in Early Detection:** Exploration of innovative diagnostic tools and biomarkers for the early detection of cancers and monitoring of therapeutic responses
- **Cancer Genomics and Data Integration:** Harnessing large-scale genomic data and AI to identify novel cancer targets and optimize therapeutic strategies
- **Targeted Therapies:** Progress in therapies targeting specific genetic mutations, including small molecules, antibodies, and combination therapies

AACR 2025– Conference Themes (2/2)

- **Overcoming Cancer Resistance:** New approaches to overcoming tumor resistance to therapies, focusing on mechanisms of resistance and combination therapies
- **Cancer Immuno-oncology:** Expanding the role of immunotherapies, including vaccines and cell therapies, to enhance the body's natural immune response to cancer
- **Real-World Evidence in Cancer Treatment:** Utilization of real-world data to evaluate treatment effectiveness, patient outcomes, and strategies for optimizing cancer care
- **Health Disparities in Cancer:** Addressing the inequities in cancer care, including disparities in access to treatments, clinical trials, and outcomes among different populations
- **AI and Machine Learning:** Applying artificial intelligence to drug discovery, patient stratification, and predicting clinical outcomes in cancer therapy

Noteworthy Scientific presentations at AACR 2025



Key Topics From Notable Presentations (1/7)

- **Immunotherapy and Cancer Treatment:** Presentations are set to address immunotherapies like CAR-T, CIMLNK, and bispecific antibody strategies that will show significant potential in overcoming treatment resistance, enhancing survival outcomes in both hematological and solid tumors, with a focus on optimizing safety profiles and targeting precision
  - B-ALL Treatment with CAR-T and Blinatumomab: A retrospective study showed that both CAR-T and Blinatumomab therapies are effective bridging treatments to HSCT in B-ALL, showing similar survival outcomes and enhancing HSCT efficacy
  - CIMLNK + Tafasitamab for B-ALL: The combination of CIMLNK and Tafasitamab demonstrated enhanced cytotoxicity and survival in B-ALL models, offering a novel and potent alternative to CAR-T therapies
  - Immunotherapy in Solid Tumors: BCD-217-2/OCTAVA showed that the nurulimab + prolgolimab combination significantly improved progression-free survival (PFS) in metastatic melanoma compared to monotherapy, while the OriC613 CAR-T targeting MSLN and CLDN18.2 showed potent anti-tumor effects in pancreatic and gastric cancers without gastrointestinal toxicity, highlighting advances in solid tumor immunotherapies

Key Topics From Notable Presentations (2/7)

- **Targeted Therapies and Drug Development:** Sessions will highlight Novel ADCs targeting Claudin 18, EGFR/cMET, and DLL3 that will show significant promise in overcoming resistance and enhancing tumor-specific targeting in gastric, colorectal, and lung cancers, emphasizing the importance of biomarker-driven therapies in clinical development
  - Claudin 18 Testing in Gastric Cancer: Two Claudin 18 IHC tests demonstrated high concordance (100% PPA, NPA, OPA) for diagnosing gastric cancer, offering reliable clinical applications for Zolbetuximab therapy targeting CLDN18.2
  - EGFR x cMET and DLL3 Targeting in Lung Cancer: GQ1033 (EGFR x cMET) and GQ1030 (DLL3) ADCs showed strong preclinical efficacy in NSCLC and SCLC, demonstrating promising therapeutic potential for targeting resistance pathways in these cancers
  - Novel ADCs in Gastrointestinal and Colorectal Cancer: LBL-054 (CDH17-targeted ADC) and AZD9592 (EGFR/cMET bispecific ADC) showed potent anti-tumor activity in gastric and colorectal cancers, with LBL-054 demonstrating strong tumor regression in xenograft models and AZD9592 showing biomarker-predictive efficacy

Key Topics From Notable Presentations (3/7)

- **Preclinical and Early-Stage Research:** Experts will discuss how Preclinical research will be driving the development of novel targeted therapies and combination approaches, enhancing tumor-specific treatment efficacy and highlighting the critical role of biomarkers in optimizing clinical outcomes across various cancer types
  - Innovative Therapeutics and Targeted Approaches: [161Tb]Tb-DOTA-N4MU01 shows promise as a radioligand for Nectin-4+ tumors like TNBC and NSCLC, while AZD9750, an oral AR PROTAC for prostate cancer, demonstrated efficacy in PDX models, providing insights for dose optimization in clinical trials
  - Combination Strategies and Enhanced Tumor Response: Tumor Treating Fields (TTFields) combined with chemotherapy yielded significant tumor regression and synergy in SCLC, while SOT109, an exatecan-based ADC targeting CDH17, demonstrated strong anti-tumor activity with a favorable safety profile, supporting its progression to clinical trials
  - Exploring New Cancer Treatments and Biomarkers: OBI-3424, an AKR1C3-activated prodrug, showed potential in hepatoblastoma models, though AKR1C3 expression as a predictive biomarker needs further validation. These findings emphasize the ongoing development of targeted therapies and the need for biomarker-driven strategies in cancer treatment

Key Topics From Notable Presentations (4/7)

- **Clinical Trials and Phase Studies:** The spotlight will be on Clinical trials across various cancer types, revealing the growing potential of novel agents and combination therapies, emphasizing the importance of biomarkers (such as ctDNA) and patient stratification in optimizing treatment outcomes and guiding future therapy development
  - Efficacy and Safety Across Cancer Types: The DRL_BZ Phase IV study demonstrated consistent efficacy and safety in solid tumors, while the CVL218 Phase Ib/II study showed promising results in advanced TNBC with minimal adverse events, highlighting the potential of novel therapies in treatment-resistant cancers
  - Immunotherapy and Biomarker Insights: The retrospective review on vedolizumab vs infliximab for ICI-induced colitis showed both agents were effective, and the Rucaparib + Nivolumab Phase II trial identified ctDNA as a predictive biomarker for early progression in LMS, underscoring the importance of biomarkers in immunotherapy
  - Innovative Approaches in Neutropenia and ICI Enhancement: The Guard-02 study demonstrated that efbemalenograstim α improved management of chemotherapy-induced neutropenia, while Castalagin's Phase I trial revealed its ability to enhance ICI efficacy in NSCLC and melanoma, emphasizing the role of adjunctive therapies in improving treatment responses

Key Topics From Notable Presentations (5/7)

- **Biomarkers and Predictive Models:** Sessions will highlight that genetic and biomarker-based profiling is crucial in improving treatment outcomes by enabling patient stratification, predicting resistance, and optimizing cancer therapies for more targeted, effective interventions
  - Patient Stratification and Genetic Insights: Studies will highlight that biomarkers such as the I/M score in BTC and PDAC, along with germline protein QTLs from GWAS data, help predict treatment responses and guide the repurposing of therapies, improving efficacy in cancer prevention and treatment
  - Predicting Treatment Outcomes in CRC and NSCLC: Co-mutations in KRAS-mutant CRC (e.g., ARID1A) and liquid biopsy-based CCM-CTCD profiling for EGFR-mutant NSCLC will show potential in predicting therapy efficacy, offering valuable insights for precision care
  - Sacituzumab Govitecan and Multiomics Profiling: SG benefits remain consistent across genetic variations in breast cancer, and multiomics profiling in CCA identifies resistance markers, highlighting the importance of genomic and proteomic data in personalizing treatment strategies

Key Topics From Notable Presentations (6/7)

- **Cancer Microenvironment and Tumor Resistance:** Discussions will focus on targeted therapies and immune modulations, such as STING activation and NOTCH pathway mutations, which show promise in overcoming tumor resistance and enhancing the efficacy of chemotherapy and immunotherapy across various cancers
  - Targeted Therapy Advances: M0674, a trispecific agent, and Disitamab vedotin (DV) are demonstrating enhanced efficacy in overcoming resistance in solid tumors like NSCLC, PDAC, and HER2+ cancers, especially when combined with chemotherapy or ADCs
  - Biomarker Identification and Immune Modulation: Brincidofovir (BCV) shows effectiveness in GBM, independent of MGMT expression, while NOTCH3 mutations in CRC and STING activation in STS highlight the potential of biomarkers for predicting response to immunotherapy and enhancing treatment outcomes
  - Immunotherapy and Tumor Response: Triplet therapy combining PLD, Flt3L, and CD40a significantly enhances immune responses in breast cancer, while STING activation potentiates doxorubicin's efficacy in STS, supporting their integration into future clinical regimens

Key Topics From Notable Presentations (7/7)

- **Miscellaneous Studies and Research:** Innovative therapies, including Trop2-targeting ISACs, STING agonists, and USP1 inhibitors, along with personalized diagnostics like Oncuria-Detect, are advancing cancer treatment and diagnosis will be discussed
  - Liver Health, Diagnostics, and Immunotherapy: Short-chain PFAS were linked to elevated ALT and cirrhosis in the STRIVE study, while Oncuria-Detect showed high sensitivity for detecting bladder cancer. Additionally, KRAS and TP53 mutations were identified as poor predictors of immunotherapy response in GI cancer with liver metastasis
  - Immunotherapy and Targeted Therapies: MCLA-129 demonstrated strong efficacy in NSCLC, while allogeneic NK cells combined with cetuximab enhanced treatment outcomes in HNSCC. Trop2-targeting ISACs showed tumor regression in pancreatic cancer, highlighting the promise of targeted immunotherapy strategies
  - Overcoming Resistance and Enhancing Cancer Care: NXP900, combined with osimertinib, overcame resistance in EGFR-mutant NSCLC, while USP1 inhibitors showed strong anti-cancer activity in ovarian, prostate, and breast cancer models. ACT and CBSM proved effective in improving the quality of life in metastatic breast cancer

Notable Presentations and Late-breaking Sessions at AACR 2025

Notable Presentations at AACR 2025
Immunotherapy and Cancer Treatment (1/5)

Date	Title	Author	Summary
27 April 2025	Efficacy and safety comparison of CAR-T and blinatumomab immunotherapy as bridge-to-transplant strategy in relapsed/refractory B cell acute lymphoblastic leukemia	Wenyue Cao	• **Introduction:** B-cell acute lymphoblastic leukemia (B-ALL) presents significant treatment challenges despite advancements. Hematopoietic stem cell transplantation (HSCT) is a potential cure but faces limitations. Immunotherapies like CAR-T and Blinatumomab show promise as bridging strategies for relapsed/refractory (R/R) B-ALL patients • **Methodology**: A retrospective study at Tongji Hospital analyzed 36 R/R B-ALL patients undergoing HSCT from March 2017 to March 2023. Twenty-seven patients received CAR-T therapy, and nine received Blinatumomab before transplantation. Outcomes assessed included overall survival (OS), progression-free survival (PFS), graft-versus-host disease-free survival (GRFS), non-relapse mortality (NRM), and hematopoietic reconstitution. • **Results:** Median follow-up was 28.07 months. The 2-year OS for the entire cohort was 76.54%. CAR-T and Blinatumomab groups showed similar OS (73.89% vs. 88.89%), PFS (59.03% vs. 44.44%), GRFS (47.86% vs. 13.89%), and NRM (8.52% vs. 11.11%). Safety profiles and transplant complications were similar between groups. • **Conclusions:** CAR-T and blinatumomab therapies show comparable safety and efficacy as bridging treatments to HSCT for R/R B-ALL. Further research is needed to optimize these strategies.
27 April 2025	Cytokine-induced memory-like NK cells with tafasitamab show efficacy against B-cell acute lymphoblastic leukemia	Dimitrios Filioglou	• **Introduction:** Tafasitamab (TAFA), an anti-CD19 monoclonal antibody, enhances tumor activity via antibody-dependent cellular cytotoxicity (ADCC) mediated by NK cells. This study explores combining TAFA with CIMLNK for improved B-ALL responses. • **Methodology**: NK cells were isolated and stimulated with IL-12, IL-15, and IL-18 to generate CIMLNK. Cytotoxicity assays were performed using NALM-6 (B-ALL cell line), assessing degranulation, IFN-γ release, and CD16-mediated ADCC. In vivo, CIMLNK and TAFA were administered to NSG mice with NALM6-luc, and survival was monitored. • **Results:** CIMLNK + TAFA showed significantly higher cytotoxicity against NALM6 compared to CIMLNK or NK cells alone (84.4% vs. 22.7%, p=0.0005). TAFA enhanced degranulation and IFN-γ release, and blocking CD16 abrogated TAFA-induced ADCC. In vivo, survival was significantly longer in the CIMLNK + TAFA group (35 days vs. 28 days for controls, p=0.01). • **Conclusions:** Combining CIMLNK and TAFA shows synergistic effects against B-ALL, enhancing efficacy in vitro and survival in vivo, warranting further clinical exploration.

Notable Presentations at AACR 2025
Immunotherapy and Cancer Treatment (2/5)

Date	Title	Author	Summary
27 April 2025	Proved clinical benefit of low-dose anti-CTLA4 + anti-PD-1 immunotherapy versus mono anti-PD-1 therapy in patients unresectable or metastatic melanoma: Phase III OCTAVA trial	Igor Samoylenko	• **Introduction:** BCD-217-2/OCTAVA (NCT05732805) is a Phase III international, randomized, double-blind, placebo-controlled study evaluating prolgolimab+nurulimab (BCD-217) combination therapy versus prolgolimab monotherapy as first-line treatment for unresectable or metastatic melanoma (un/mM). BCD-217, a combination of nurulimab (CTLA-4) and prolgolimab (PD-1), was recently approved in Russia. This study presents the primary analysis. • **Methodology**: Patients with treatment-naïve, unresectable or metastatic cutaneous melanoma were randomized to receive either combination therapy or prolgolimab monotherapy. The primary endpoint was progression-free survival (PFS). • **Results:** 271 patients were randomized (135 to combination, 136 to monotherapy). After a median follow-up of 15.8 months, median PFS was 15.4 months for combination therapy and 10.8 months for monotherapy (HR 0.68, 95% CI). The combination arm showed superior ORR and DCR. Median overall survival (mOS) was not reached for either group. Grade 3-4 treatment-related AEs were 16.3% in the combination arm and 14.0% in the monotherapy arm. IrAEs were higher in the combination arm (52.6% vs. 32.4%, p=0.0007). • **Conclusions:** The OCTAVA trial showed that nurulimab + prolgolimab combination therapy is more effective than PD-1 monotherapy for metastatic or unresectable cutaneous melanoma with no significant safety concerns.
28 April 2025	Targeting CREB reprograms the tumor immune microenvironment and enhances immunotherapy efficacy in smoking-associated pancreatic cancer	Varunkumar Krishnamoorthy	• **Introduction:** Smoking, a major risk factor for pancreatic cancer, reduces survival benefits from therapies. CREB hyperactivation drives an immunosuppressive TME, limiting ICB efficacy. This study investigates targeting CREB to improve ICB outcomes in smoking-related pancreatic cancer models. • **Methodology**: In vivo models were developed with syngeneic tumors in C57BL/6 mice and Creb-deleted KPC GEMMs. Mice were treated with CREB inhibitor (666-15) and anti-PD-1 therapy. TME and immune cell changes were assessed. • **Results:** CREB inhibition decreased the immunosuppressive TME, enhanced T cell infiltration, and improved anti-tumor effects. • **Conclusions:** Targeting CREB reprograms the TME, enhancing immunotherapy efficacy in smoking-related pancreatic cancer, supporting CREB inhibition in immunotherapy for high-risk smoking populations.

Notable Presentations at AACR 2025
Immunotherapy and Cancer Treatment (3/5)

Date	Title	Author	Summary
28 April 2025	SCR-A0011, a novel bispecific ADC targeting cMET and B7H3, exhibits potent anti-tumor efficacy	Yayuan Fu	• **Introduction:** Abnormal cMET expression is linked to various tumors, making it a clinical target. However, clinical efficacy is limited to cMET-driven or cMET-high tumors. Bispecific antibody-drug conjugates targeting cMET and B7H3 are being explored to expand therapeutic potential. • **Methodology**: SCR-A0011, a bispecific ADC targeting B7H3 and cMET, was developed combining a bispecific antibody with topoisomerase 1 inhibitor (CPT116). SCR-A0011's binding, internalization, and binding capacity were compared to monoclonal ADCs in B7H3/cMET co-expressing cell lines. Tumor lysis and anti-tumor efficacy were evaluated in various cancer types and CDX models. • **Results:** SCR-A0011 showed superior internalization and binding compared to monoclonal ADCs, inducing tumor cell lysis in multiple cancer types. It demonstrated significant anti-tumor activity in CDX models, outperforming parental ADCs in B7H3+cMET+ tumors. SCR-A0011 exhibited excellent stability and developability. • **Conclusions:** SCR-A0011 is a potential First-in-Class bispecific ADC for overcoming resistance in B7H3 and cMET-positive cancers, offering a promising new approach for cancer types.
28 April 2025	GLR1059, next-generation nectin-4-targeted ADC with a novel mechanism-of-action payload, demonstrated significantly potent anti-tumor efficacy and reduced toxicity in preclinical evaluation	Jiao Jiao	• **Introduction:** Nectin-4 is targeted by Enfortumab Vedotin (EV) in urothelial carcinoma, but it causes severe skin toxicities and is not approved for other cancers. GLR1059, a novel nectin-4 ADC, offers enhanced efficacy and reduced toxicity. • **Methodology**: In vitro, GLR1059 was tested for binding affinity, internalization, and cancer cell killing. In vivo, efficacy was evaluated in breast and urothelial carcinoma CDX models, pharmacokinetics in BALB/c and tumor-bearing nude mice, and safety in humanized nectin-4 mice • **Results:** GLR1059 showed superior anti-tumor activity in CDX models, 2-4 times more effective than EV, with a 100-fold higher payload concentration in tumors. It also reduced skin toxicity • **Conclusions:** Preclinical data show that GLR1059 has better efficacy and safety than current nectin-4 ADCs, offering a promising strategy to overcome resistance and reduce toxicity in nectin-4 positive cancers.

Notable Presentations at AACR 2025
Immunotherapy and Cancer Treatment (4/5)

Date	Title	Author	Summary
28 April 2025	Modulating gut microbiota to enhance the efficacy of immunotherapy in triple negative breast cancer	Samarpan Majumder	• **Introduction:** While anti-PD-1 therapy is standard for early TNBC, its efficacy remains limited. This study explores whether modulating the gut microbiota with probiotics can enhance anti-PD-1 therapy efficacy in an obese mouse model of TNBC. • **Methodology**: Two weeks of probiotic supplementation before anti-PD-1 therapy in an obese mouse model of TNBC was developed. Tumor burden was measured after two weeks of treatment. The probiotic blend included 13 human strains (Creative Enzyme, Cat # PRBT-035, NY). Tumor growth, survival, cytokine profiles, and immune cell infiltration were analyzed. • **Results:** Probiotics plus anti-PD-1 therapy significantly improved survival compared to isotype control (p=0.046). Cytokine analysis showed elevated interferon-γ and reduced proinflammatory cytokines in plasma. Immunohistochemistry revealed increased CD8+T and CD4+T cells in tumor tissue of probiotic-treated mice. • **Conclusions:** Probiotic supplementation enhances anti-PD-1 therapy efficacy in early TNBC, providing a basis for larger trials targeting the gut microbiome to improve treatment outcomes.
28 April 2025	Mitochondrial complex I inhibition enhances chemotherapy efficacy in melanoma	Semmer Ali	• **Introduction:** Targeting mitochondrial oxidative phosphorylation (OXPHOS) and TCA metabolism in melanoma remains underexplored. Chemotherapy resistance and metastatic potential are often driven by altered metabolism. • **Methodology**: Metabolomics profiling (LC-MS) and bioenergetics analyses assessed the impact of chemotherapies (Temozolomide, Cisplatin) on metabolism. In vivo studies used YUMM1.7 melanoma allografts in C57BL/6J mice to evaluate tumor growth with chemotherapy and complex I inhibitors (Phenformin, IACS-010759). • **Results:** OXPHOS diversity was noted across melanoma cell lines, with chemotherapy enhancing TCA intermediates, ATP, and complex I activity. Complex I inhibition synergized with chemotherapy, significantly reducing tumor growth in vivo with minimal toxicity. • **Conclusions:** Complex I inhibition combined with chemotherapy enhances chemosensitivity in melanoma with minimal systemic toxicity.

Notable Presentations at AACR 2025
Immunotherapy and Cancer Treatment (5/5)

Date	Title	Author	Summary
29 April 2025	Dual-target CAR-T strategy for MSLN and CLDN18.2: Advancing cancer treatment with superior efficacy and safety	Xiaowen He	• **Introduction:** MSLN and CLDN18.2 are promising CAR-T targets for gastric and pancreatic cancers. Targeting CLDN18.2 alone risks gastrointestinal toxicity. • **Methodology**: OriC613 was designed using an "AND" logic gate, targeting MSLN and CLDN18.2 double-positive tumor cells to reduce GI toxicity. • **Results:** OriC613 showed stronger cytotoxicity against double-positive cells and no toxicity to CLDN18.2-only cells. It improved survival, reduced GI toxicity, and enhanced T-cell expansion and IFN-γ production in pancreatic cancer models. • **Conclusions:** OriC613 shows promising anti-tumor effects and safety, highlighting the need for clinical trials in pancreatic and gastric cancer patients.

Notable Presentations at AACR 2025
Targeted Therapies and Drug Development (1/4)

Date	Title	Author	Summary
27 April 2025	A novel approach of Claudin 18 immunohistochemistry testing demonstrated comparable performance and high concordance compared to Ventana 43-14A in gastric cancer	Changbin Zhu	• **Introduction:** Claudin (CLND)18 is a tight-junction molecule with two isoforms: CLND18.1 and CLND18.2. CLND18.2 is specifically expressed in gastric cancer. Zolbetuximab, the first FDA-approved monoclonal antibody targeting CLDN18.2, is accompanied by the VENTANA® CLND18 (43-14A) IHC test for diagnostic purposes. Validating different Claudin 18 IHC testing approaches can enhance clinical diagnostic convenience. • **Methodology**: Sixty-eight gastric cancer samples were evaluated for Claudin 18 expression using two IHC approaches. AmoyDx CLDN18 (43-14A) was the test reagent, and VENTANA® CLDN18 (43-14A) RxDx served as the reference reagent. Claudin 18 positivity was defined as staining intensity of 2+ or 3+ in ≥75% of tumor cells. • **Results:** The validation showed that 21 positive and 47 negative cases were identified by both reagents. This resulted in 100% positive percent agreement (PPA), 100% negative percent agreement (NPA), and 100% overall percent agreement (OPA). Poisson distribution analysis revealed high consistency in staining intensity between the two methods ($R = 0.99\text{-}1$, $p < 2.26e\text{-}16$). When the positive threshold was adjusted to ≥50% of 2+/3+ cells, high concordance was maintained (PPA 100%, NPA 93.55%, OPA 97.06%). • **Conclusions:** Both Claudin 18 testing approaches showed high concordance, demonstrating potential for versatile clinical application in future gastric cancer diagnostics.
27 April 2025	Novel EGFR x cMET bispecific ADC GQ1033 and DLL3-ADC GQ1030 demonstrated promising therapeutic efficacy in preclinical studies	Sipeng Li	• **Introduction:** Resistance to tyrosine kinase inhibitors (TKIs) in NSCLC leads to relapse, with cMET driving resistance. SCLC has poor survival due to relapse after platinum chemotherapy. DLL3, a validated SCLC target, is explored. • **Methodology**: Using the iGDC™ and iLDC™ platforms, diverse ADC libraries targeting EGFR x cMET and DLL3 were developed and tested in vitro and in vivo, leading to GQ1033 (EGFR x cMET) and GQ1030 (DLL3). • **Results:** GQ1033 showed potent cytotoxicity in HCC827 cells and regression in NCI-H1975 CDX models. In PDX trials, GQ1033 had a 70% ORR. GQ1030 was effective in DLL3-positive cells. • **Conclusions:** GQ1033 and GQ1030, developed using iGDC™ and iLDC™ platforms, showed strong preclinical efficacy, suggesting broader therapeutic potential for lung cancer treatments. These ADCs offer promising new options for both NSCLC and SCLC.

Notable Presentations at AACR 2025
Targeted Therapies and Drug Development (2/4)

Date	Title	Author	Summary
27 April 2025	Fenretinide enhances trastuzumab efficacy in trastuzumab-resistant HER2+ breast cancer cell lines	Debbie O'Reilly	• **Introduction:** BCSCs, resembling embryonic cells, may resist HER2-targeted therapies. This study investigates BCSC markers in HER2+ BC cell lines and evaluates Fen-induced differentiation. • **Methodology**: RNA-Seq data from CCLE were analyzed using RStudio. HER2+ BC cell lines with innate (HCC1569, HCC1954) or acquired (SKBR3-T, BT474-T) trastuzumab (Tras) resistance were studied. Cells were treated with 1 μM Fen for 24 hours, and qPCR analysis was performed. • **Results:** DepMap analysis showed higher CD44 in innate-resistant HCC1569 and HCC1954. qPCR confirmed higher CD44 in HCC1569 ($p = 0.0318$) and lower CD24 in HCC1569 and HCC1954 ($p = 0.008$). Fen reduced colony formation and enhanced Tras efficacy in SKBR3-T but had no effect on BCSC markers. • **Conclusions:** Fen enhances Tras efficacy in acquired Tras-resistant HER2+ BC cell lines but has limited impact on BCSC markers. Further studies are needed to explore Fen's role in overcoming Tras resistance.
27 April 2025	INK4A/B as predictive biomarkers for enhanced efficacy of dual WEE1 and PKMYT1 inhibition in CDK4/6 inhibitor-resistant breast cancer	Mei-Kuang Chen	• **Introduction:** CDK4/6i-R and TNBC show increased replication stress and cell cycle dysregulation, suggesting sensitivity to G2/M transition kinase inhibition (WEE1 and PKMYT1). Inhibiting these kinases may disrupt tumor growth and improve outcomes. • **Methodology**: WEE1 inhibitors (adavosertib, azenosertib) were combined with PKMYT1 inhibitor (lunresertib) in CDK4/6i-R and TNBC models, including PDXs and organoids. RNA sequencing identified treatment response markers, and tumor suppression was assessed in vitro and in vivo. INK4A (p16) and INK4B (p15) were studied as potential biomarkers for dual inhibition. • **Results:** WEE1 and PKMYT1 inhibitors significantly suppressed tumors in CDK4/6i-R and TNBC models. Dual inhibitor SGR-3515 showed similar efficacy. High INK4B expression correlated with better treatment response, while baseline INK4A and INK4B levels predicted sensitivity. INK4B overexpression sensitized cells, while knockdown increased resistance. • **Conclusions:** Dual WEE1 and PKMYT1 inhibition offers a promising strategy for CDK4/6i-R and TNBC. Elevated INK4A and INK4B levels predict treatment response, suggesting their use as biomarkers for therapy selection. Further clinical investigation is needed..

Notable Presentations at AACR 2025
Targeted Therapies and Drug Development (3/4)

Date	Title	Author	Summary
27 April 2025	Developing PDX derived organoid models for efficacy evaluation of anticancer therapies	Weizhong Zhang	• **Introduction:** PDX models are gold standards but are labor-intensive and costly. Cancer organoids (PDXOs) replicate patient tumor profiles, mutations, and therapy responses. This study aims to develop PDXOs for anti-cancer drug evaluation. • **Methodology**: PDXOs were created using the Matrigel embedding method with fresh PDX tumor tissue digests. Models were expanded, cryopreserved, and analyzed. Bright field imaging (BFI) and H&E staining assessed models, while whole exome sequencing (WES) and mRNA sequencing evaluated genetic status. Drug efficacy was tested using CTG and LDH release assays. • **Results:** By October 2024, over 20 PDXOs were established across cancers, including colon, gastric, pancreatic, lung, and liver. PDX and PDXO models showed consistent mutational status and drug response. PDXOs with specific protein expressions were suitable for targeted therapy assessment. Co-culturing with immune cells enabled immune therapy evaluation. • **Conclusions:** PDXO models show promise for evaluating anti-cancer therapies. Their integration with PDX models advances cancer pharmacological research and drug discovery.
28 April 2025	Synergistic efficacy of FGFR4 inhibitor (H3B-6527) and oxaliplatin combination therapy in gastric cancer models	Nadeem Bhat	• **Introduction:** This study evaluates the combination of FGFR4 inhibitor H3B-6527 and Oxaliplatin, focusing on their synergistic effects on tumor suppression and cell death. • **Methodology**: IC50 analyses, colony formation assays, PDX models, IF, IHC, western blotting, and caspase-3/7 luminescence assays assessed the combination's impact on cell proliferation, DNA damage, and apoptosis in MKN28 and HGC27 gastric cancer cell lines. • **Results:** Combination therapy increased sensitivity in MKN28 and HGC27 cells. Colony formation assays showed reduced colony counts. In PDX models, tumor growth was inhibited, and survival was prolonged. IF and IHC showed increased DNA damage (γH2AX), reduced proliferation (Ki67), and elevated apoptosis (cleaved caspase-3). Caspase-3/7 assays confirmed increased apoptosis, with western blot showing elevated cleaved PARP and γH2AX. • **Conclusions:** H3B-6527 and oxaliplatin synergistically enhance apoptosis, DNA damage, and inhibit proliferation in gastric cancer models, supporting their potential in treating chemoresistant gastric cancer.

Notable Presentations at AACR 2025
Targeted Therapies and Drug Development (4/4)

Date	Title	Author	Summary
28 April 2025	Novel hydrophilic CDH17-targeting antibody-drug conjugate exhibits anti-tumor efficacy in preclinical xenograft models	Hong Ling	• **Introduction:** This study develops LBL-054, a CDH17-targeting antibody-drug conjugate (ADC), from a humanized CDH17 IgG1 monoclonal antibody conjugated with a proprietary linker-payload platform. • **Methodology**: The binding affinity of the monoclonal antibody (mAb) to CDH17 was measured via Fortebio and flow cytometry. Internalization was assessed using FACS and anti-Fc-MMAE methods. LBL-054 binding to CDH17 was confirmed in cancer cell lines and cells engineered to overexpress CDH17. Plasma stability was analyzed using LC-MS. Killing activity was tested on CDH17-positive, -negative, and mixed cancer cells. Anti-tumor effects were evaluated in xenograft mouse models. • **Results:** LBL-054 exhibited strong affinity and rapid internalization. It showed greater potency than the LBL-054-Dxd conjugate in killing CDH17-positive cells and was less likely to affect CDH17-negative cells. LBL-054 demonstrated a stronger bystander effect. It also showed high plasma stability and induced significant tumor regression in xenograft models, with better pharmacokinetics compared to LBL-054-Dxd. • **Conclusions:** LBL-054, conjugated with exatecan, showed high stability, strong anti-tumor activity, and good tolerability in preclinical models, supporting its clinical development for CDH17-expressing tumors.
28 April 2025	AZD9592, an EGFR/cMET bispecific antibody-drug conjugate (ADC), demonstrates target-dependent efficacy in colorectal cancer (CRC) patient-derived xenograft (PDX) models	Ying Zheng	• **Introduction:** Despite advances like trastuzumab deruxtecan for HER2-positive CRC, there remains a need for novel therapies, especially for patients with limited treatment options. • **Methodology**: AZD9592's efficacy and biomarker-response relationships were evaluated in CRC PDX models with varying EGFR and cMET expression using IHC-QCS. Responses were defined as ≥30% tumor volume reduction. • **Results:** AZD9592 showed dose-dependent efficacy, with 34.5% response at 8 mg/kg and 14.8% at 4 mg/kg. cMET expression at 8 mg/kg significantly correlated with response ($p<0.02$). An optimized cMET cutoff had an area under the curve of 0.73. No significant differences were seen in KRAS/BRAF-mutant tumors or those with prior irinotecan treatment. • **Conclusions:** AZD9592 demonstrated dose-dependent antitumor activity in CRC PDX models, supporting potential clinical development with biomarker-guided patient selection.

Notable Presentations at AACR 2025
Miscellaneous Studies and Research (1/6)

Date	Title	Author	Summary
29 April 2025	Short chain per- and polyfluoroalkyl substances associate with elevated alanine aminotransferase: cross-sectional analysis results from the STRIVE cohort	Bojung Seo	• **Introduction:** This study investigates associations between short and long-chain PFAS mixtures and elevated ALT or cirrhosis, focusing on baseline factors related to PFAS exposure. • **Methodology**: Data from 349 adults (ages 40-75) in the Southern Liver Health Study (STRIVE) were analyzed. Of the participants, 135 had cirrhosis. Logistic regression assessed associations between individual PFAS serum levels and elevated ALT or cirrhosis. Quantile g-computation examined PFAS mixtures' effects. Linear regression evaluated baseline factors related to PFAS levels. • **Results:** Increasing short-chain PFAS by one quartile was linked to higher odds of elevated ALT (OR: 2.20 [1.32-3.67]), while no association was found for long-chain PFAS mixtures. Perfluoroheptanoate was associated with both elevated ALT and cirrhosis (OR: 1.53 [1.01-2.33] and 1.51 [1.01-2.27]). Long-chain PFAS levels were higher in males and linked to alcohol consumption. Both long- and short-chain PFAS were lower in bottled water users, non-water drinkers, and smokers. • **Conclusions:** Higher short-chain PFAS concentrations were associated with elevated ALT in the STRIVE cohort, with variations based on sex and lifestyle behaviors. These findings suggest further investigation into PFAS mixtures' effects on liver health is needed.
29 April 2025	Performance of the Oncuria-detect bladder cancer test for evaluating patients presenting with hematuria: results from a real-world clinical setting	Hideki Furuya	• **Introduction:** This study evaluated the real-world performance of Oncuria-Detect, a multiplex immunoassay that detects bladder cancer by measuring 10 biomarker proteins in naturally voided urine samples. • **Methodology**: Urine samples from 1,002 patients with hematuria at five USA centers, one European, and one Japanese center were tested. Assay results were compared with clinical data, and a cancer diagnosis was confirmed by biopsy and pathology. The prevalence of bladder cancer in the cohort was 15.9%. • **Results:** In the training set (n=684), Oncuria-Detect identified bladder cancer in 94/109 cases, with sensitivity of 91.8% and specificity of 71.6% (AUC 0.885; 95% CI 0.843-0.927). The assay showed improved performance for high-grade (sensitivity 93.6%) and muscle-invasive (sensitivity 92.1%) bladder cancers. In the test cohort (n=339), the AUC was 0.850 • **Conclusions:** Oncuria-Detect demonstrated high sensitivity and negative predictive value (NPV) for detecting bladder cancer. Its high NPV could rule out 66% of patients from requiring cystoscopy, making it a useful diagnostic tool.

Notable Presentations at AACR 2025
Miscellaneous Studies and Research (2/6)

Date	Title	Author	Summary
29 April 2025	Preclinical investigation of anti-tumor efficacy of allogeneic natural killer cells combined with cetuximab for head and neck squamous cell carcinoma	Chaeyeon Kim	• **Introduction:** This study explores combining allogeneic NK cells with cetuximab to enhance anti-tumor efficacy in HNSCC. • **Methodology**: Allogeneic NK cells from healthy donors were expanded and tested in vitro. NOG xenograft models were used to evaluate efficacy. In vitro assays assessed cytotoxicity against FaDu cells with cetuximab, focusing on antibody-dependent cellular cytotoxicity (ADCC). In vivo, NK cell infusion with cetuximab was tested for tumor growth inhibition and survival improvement. • **Results:** Increasing NK cell dose improved survival and inhibited tumor growth. IL-2 did not enhance responses, but NK cells combined with cetuximab significantly boosted cytotoxicity via ADCC. In vivo, the combination reduced tumor growth and enhanced survival. Flow cytometry and immunohistochemistry confirmed increased NK cell infiltration and ADCC activity. • **Conclusions:** The combination of NK cells and cetuximab improved outcomes in HNSCC, offering a promising strategy for enhancing NK cell-mediated cytotoxicity and supporting future clinical trials.
29 April 2025	Differential clinical outcomes of immune vs non-immune based therapeutics in gastrointestinal malignancies: A retrospective, single center experience of early phase studies	Tarik Demir	• **Introduction:** This study evaluates outcomes in advanced gastrointestinal (GI) cancer patients treated with novel therapeutics and identifies oncogenic pathways predicting poor IO responses in LM patients. • **Methodology**: This retrospective study included patients treated at Northwestern University from 2014 to 2023, enrolled in early-phase trials with CLIA-certified sequencing. Efficacy was measured by progression-free survival (PFS), with responders (PFS ≥ 3 months) and non-responders (PFS < 3 months). Survival analysis was conducted using Kaplan-Meier and logistic regression. • **Results:** 265 patients participated, with 218 (82%) having LM. Of these, 102 (39%) received IO-based therapy. Median PFS was 2.28 months, with 43% achieving PFS ≥ 3 months. Non-IO therapy showed higher PFS (3.48 months vs. 1.8 months for IO, $p<0.0001$). LM did not affect IO outcomes ($p=0.49$). In IO-based LM patients, KRAS and TP53 mutations were linked to non-response. • **Conclusions:** This study found no significant link between LM and survival in IO-treated patients, likely due to varying regimens and small sample size. These findings offer insights for future IO treatment strategies

Notable Presentations at AACR 2025
Miscellaneous Studies and Research (3/6)

Date	Title	Author	Summary
29 April 2025	Discovery of a novel Trop2-targeting immune-stimulating antibody conjugate with efficacy in pancreatic cancer models	Mohan Reddy Mullapudi	• **Introduction:** This study identifies a novel Trop2-targeting ISAC with efficacy in pancreatic cancer models. • **Methodology**: Novel linkers for E104-based ISACs, including glycosylated and deglycosylated versions of sacituzumab (anti-Trop2 antibody), along with a control Trop2_mcValCitPABC_E104 ISAC were synthesised. ISACs were tested for NFκB/IRF-7 activation and IL-6 induction in co-culture models and evaluated for efficacy in xenograft models. • **Results:** Both glycosylated and deglycosylated ISACs had drug-to-antibody ratios (DAR) of 6-8. Next-generation ISACs showed reduced aggregation (<1-2%) compared to controls (30%) and improved pharmacokinetics. In co-culture studies, deglycosylated ISACs triggered more specific NFκB activation. In vivo, a specific ISAC showed efficacy against pancreatic tumors, and a DAR 4 version achieved complete tumor regression in a hTrop2-MC38 model. • **Conclusions:** We developed Trop2-targeting ISACs with reduced aggregation and improved pharmacokinetics. One ISAC achieved complete tumor regression in vivo, demonstrating the importance of linker engineering in improving ISAC efficacy for pancreatic cancer.
29 April 2025	A potent STING agonist induces endothelial PD-L1 and enhances antitumor efficacy of a novel PD-L1/PD-L2 antibody	Ahmad Salameh	• **Introduction:** Combining the STING agonist 8803 (IMGS-203) with the dual anti-PD-L1/PD-L2 monoclonal antibody 27907 showed curative responses in checkpoint-refractory tumor models. This study investigates the underlying mechanisms by analyzing the tumor microenvironment (TME) of treated tumors. • **Methodology**: The efficacy of 8803 and 27907 was tested in murine melanoma (B16F10) and mammary adenocarcinoma (TS/A) models. Mice received intratumor 8803 (10 µg/dose, twice) and systemic 27907 (10 mg/kg, twice weekly for three weeks). Tumors were analyzed after 32 days using H&E, IHC, and FACS. • **Results:** The combination showed strong antitumor activity. IHC and FACS revealed increased myeloid infiltration and reduced M2 macrophages. 8803 upregulated PD-L1 in endothelial cells, which was disrupted by 27907, with increased caspase-3 and CD62p co-expression. PD-L1+/PD-L2+ endothelial cells were selectively eliminated by myeloid cells and PBMCs. • **Conclusions:** The 8803 and 27907 combination induced endothelial damage, correlating with enhanced antitumor responses, myeloid infiltration, and T-cell elevation. These findings support further clinical development.

Notable Presentations at AACR 2025
Miscellaneous Studies and Research (4/6)

Date	Title	Author	Summary
29 April 2025	Overcoming osimertinib resistance in NSCLC with NXP900, a phase 1, highly selective and potent first-in-class total YES1/SRC inhibitor	Neil O. Carragher	• **Introduction:** Src family kinase (SFK) activity has been identified as a key resistance mechanism. NXP900 (eCF506) is a novel, selective SFK inhibitor that locks its target in a "closed" conformation, inhibiting kinase activity and protein complex formation. NXP900 may be an ideal combination partner with osimertinib to overcome resistance in EGFR-mutant lung cancer. • **Methodology**: Cell proliferation assays were conducted with osimertinib and NXP900 across three concentration ratios to calculate synergy using SynergyFinderTM. In vivo, mice with osimertinib-resistant cell line transplants were treated with single agents or combination therapy once tumors reached 100mm³. • **Results:** NXP900 combined with osimertinib showed significant synergy in osimertinib-resistant NSCLC cells in vitro. In vivo, combination treatment prolonged anti-cancer response compared to monotherapy in an EGFR-mutant lung cancer model. • **Conclusions:** Despite osimertinib's effectiveness, acquired resistance is common. NXP900, combined with osimertinib, demonstrates synergy and prolonged tumor inhibition in both in vitro and in vivo models of resistance. These results suggest NXP900's potential in treating EGFR-mutant cancers with osimertinib resistance. A Phase 1 dose escalation study is ongoing.
29 April 2025	In vitro efficacy of novel USP1 inhibitors as a single agent and in combination with SOC in ovarian, prostate, and breast cancer cells independent of BRCA mutational status	Partha Pratim Sarma	• **Introduction:** Ubiquitin-specific protease 1 (USP1) regulates DNA repair and responds to genotoxic stress. Targeting USP1 is a potential cancer therapy. This study investigates the efficacy of novel USP1 inhibitors in ovarian, prostate, and breast cancer cell lines, both as monotherapy and in combination with other agents. • **Methodology**: USP1 inhibitors were tested in ovarian (OVCAR-3), prostate (DU-145), and breast (SUM149) cancer cell lines using cell viability and colony formation assays. Combination treatments with chemotherapy agents were evaluated for synergy using composite scores. • **Results:** USP1 inhibitors alone significantly reduced cell viability and colony formation, regardless of BRCA mutation status. Combined with chemotherapy, they enhanced efficacy, shifting the IC50 and increasing apoptosis compared to monotherapies. • **Conclusions:** USP1 inhibitors showed strong anti-cancer activity both alone and with chemotherapy in ovarian, prostate, and breast cancer cell lines. These results suggest USP1 inhibition may be a promising therapeutic strategy, warranting further preclinical and clinical studies.

Notable Presentations at AACR 2025
Miscellaneous Studies and Research (5/6)

Date	Title	Author	Summary
29 April 2025	Correlation between MET amplification/overexpression status and response to MCLA-129 in advanced non-small-cell lung cancer (NSCLC): biomarker results from a phase 1 trial	Haie Chen	• **Introduction:** This ongoing phase 1b study (NCT04930432), aim to explore the relationship between the MET/EGFR bispecific antibody MCLA-129 and its efficacy in patients with advanced NSCLC, particularly those with MET amplification (METamp) or protein overexpression (OE). • **Methodology**: Eligible patients (≥18 years; ECOG PS 0-1; confirmed metastatic or unresectable NSCLC with EGFR or MET alterations) received MCLA-129 (1500 mg biweekly) intravenously. MET OE was defined as IHC 2+/3+, and METamp was defined based on gene copy number (GCN). A range of GCN cut-offs was used to explore its relationship with efficacy outcomes. • **Results:** As of March 31, 2024, 24 NSCLC patients were evaluable (6 with MET IHC 2+/3+ and 18 with METamp). Four of 6 patients with MET IHC 2+/3+ achieved confirmed PRs (ORR: 66.7%), all with concurrent mutations. Median DOR and PFS were not reached. Eight of 18 patients with METamp achieved confirmed PRs (ORR: 44.4%, PFS: 4.8 months). Among 7 pre-treatment METamp patients, 4 achieved confirmed PRs (ORR: 57.1%) with concurrent mutations. Three of 9 patients progressing on 3rd-generation EGFR-TKIs achieved confirmed PRs. ORR varied across MET GCN cut-offs. • **Conclusions:** MCLA-129 showed significant antitumor activity in advanced NSCLC with MET OE or METamp, particularly in patients with concurrent mutations.
30 April 2025	Feasibility, acceptability, and preliminary efficacy of acceptance and commitment therapy in women living with metastatic breast cancer	Ashley Hatch	• **Introduction:** Metastatic breast cancer (BC) is incurable, but treatment advances extend survival. Women face debilitating symptoms and emotional distress. This study evaluates the acceptability, feasibility, and preliminary efficacy of Acceptance and Commitment Therapy (ACT) for metastatic BC. • **Methodology**: Women with stage IV BC (N=30) were randomized to ACT, usual care, or Cognitive and Behavioral Stress Management (CBSM). Both therapies included 8 weekly 90-minute sessions. Measures were completed at baseline, mid-intervention, post-intervention, and 1-month follow-up. • **Results:** Enrollment was 88.5%, and retention 90%. ACT and CBSM showed strong feasibility and positive outcomes. • **Conclusions:** ACT and CBSM were feasible and acceptable in metastatic BC. A larger randomized trial is needed to confirm effects and determine if ACT improves HRQoL in metastatic BC patients.

Notable Presentations at AACR 2025
Miscellaneous Studies and Research (6/6)

Date	Title	Author	Summary
30 April 2025	Self-reported barriers to healthcare and cancer screening rates: results from the All of Us Research Program	Kevin H. Kensler	• **Introduction:** This study examines how healthcare access barriers affect cancer screening rates for five cancer types in a diverse population, with the goal of informing policies to reduce disparities. • **Methodology**: Participants from the All of Us Research Program (2017-2022) who met USPSTF guidelines for cancer screening were included. They self-reported nine barriers to care. A barrier burden was calculated, and factor analysis identified latent barrier classes. Screening compliance was assessed in health records, and odds ratios (OR) were used to estimate associations. • **Results:** Screening compliance varied: breast (42%), cervical (28%), colorectal (42%), lung (11%), and prostate (36%). Common barriers included cost, provider nervousness, and lack of time off work. Participants with 3+ barriers had lower screening rates, especially for breast (OR 0.66), cervical (OR 0.77), and colorectal (OR 0.77). Three factors—cost concerns, logistical barriers, and competing obligations—were identified. • **Conclusions:** Barriers related to cost, logistics, and competing obligations were associated with lower cancer screening rates, suggesting the need for policies that address multiple access dimensions.

Notable Presentations at AACR 2025
Biomarkers and Predictive Models (1/6)

Date	Title	Author	Summary
27 April 2025	Clinical and biomarker analyses of SHR-1701 combined with famitinib in patients with previously treated advanced biliary tract cancer or pancreatic ductal adenocarcinoma: A phase II trial	Lixia Yi	• **Introduction:** Advanced BTC and PDAC have dismal outcomes with limited therapies. This study investigates SHR-1701 (anti–PD-L1/TGF-β) plus famitinib (RTK inhibitor) in previously treated patients. • **Methodology**: In this open-label, single-arm Phase II trial, 51 patients received SHR-1701 IV Q3W plus famitinib daily. Primary endpoint was ORR; secondary endpoints included DCR, PFS, OS, and safety. Biomarkers were analyzed via RNA-seq, mIHC, and ML. • **Results:** BTC: ORR 28%, OS 16.0 mo; PDAC: ORR 15%, OS 5.3 mo. Grade 3/4 AEs: 29.4%. I/M score identified likely responders. • **Conclusions:** This dual-immunotherapy shows efficacy, manageable safety, and biomarker-based patient stratification potential.
27 April 2025	Leveraging germline genetics to predict the efficacy of repurposing approved cancer therapies for cancer prevention	Chibuzor F. Ogamba	• **Introduction:** Drug development is costly and inefficient. Genetic data may enhance success rates. This study evaluates whether germline protein QTLs can predict preventive efficacy of approved cancer therapies. • **Methodology**: Using 3,081 cis-pQTLs from UK Biobank and Iceland GWAS, Mendelian randomization was applied across 298 therapy-indication pairs using GWAS data for 39 cancers. Genetic results were compared to historical drug approval rates (Phase 1 to approval) using R(G). • **Results:** 49 protein-cancer associations were significant; 36 aligned with drug mechanisms. R(G) for genetic support in prevention was 1.95 (CI: 1.46–2.60), higher in 8/18 cancers and 9/12 pathways. • **Conclusions:** Germline genetics may guide repurposing of cancer therapies for prevention, with high predictive value across cancers and pathways.

Notable Presentations at AACR 2025
Biomarkers and Predictive Models (2/6)

Date	Title	Author	Summary
27 April 2025	Baseline biomarker analyses of patients with chemorefractory KRAS G12C-mutated metastatic colorectal cancer (mCRC) from the phase 3 CodeBreaK 300 study	Marwan Fakih	• **Introduction:** KRAS G12C-mutant CRC has poor prognosis. Soto + pani improved PFS vs T/T or rego in CodeBreaK 300. • **Methodology**: Tumor and plasma ctDNA from 140 and 154 patients, respectively, were sequenced to assess co-mutations and correlate them with clinical outcomes. • **Results:** Common co-alterations included APC, TP53, SMAD4. TGF-β and TP53 mutations linked to shorter TTP. Soto + pani showed benefit across subgroups. ARID1A alterations associated with shorter PFS (2.07 vs 5.78 mo). • **Conclusions:** Soto + pani benefits were consistent across genotypes; ARID1A may predict poor outcomes, though low frequency limits conclusions.
28 April 2025	Circulating tumor cell-based molecular responses stratify EGFR-TKI efficacy in EGFR-mutant lung cancer patients	Seoyoung Lee	• **Introduction:** Liquid biopsy overcomes limitations of tissue sampling. CCM-CTCD enhances CTC detection in EGFR-mutant NSCLC, aiding therapy response monitoring**.** • **Methodology**: In 77 patients on EGFR-TKIs, CTCs were isolated via CCM-CTCD and compared to plasma cfDNA and tissue biopsy. Molecular response was defined by ≥30% CTC count reduction. • **Results:** CCM-CTCD showed higher EGFR mutation sensitivity vs Cobas®. CTC responders had longer PFS (46.3 vs 12.2 mo; HR 0.45) and greater tumor reduction. Discordant mutations revealed tumor heterogeneity. • **Conclusions:** CCM-CTCD CTC profiling is predictive and prognostic, supporting its integration into EGFR-mutant NSCLC precision care pathways.

Notable Presentations at AACR 2025
Biomarkers and Predictive Models (3/6)

Date	Title	Author	Summary
28 April 2025	Circulating tumor DNA (ctDNA) mutation analysis at baseline (BSL) and end of treatment (EOT) with sacituzumab govitecan (SG) and clinical impact on efficacy in patients (pts) with HR+/HER2- metastatic breast cancer (mBC): Biomarker results from TROPiCS-02	Hope S. Rugo	• **Introduction:** Sacituzumab govitecan (SG) improves survival in pretreated HR+/HER2- mBC. Genetic mutations may impact resistance. • **Methodology**: ctDNA from 46% of TROPiCS-02 patients was analyzed at baseline (BSL) and end-of-treatment (EOT) using a 69-gene panel. Mutational associations with PFS and OS were assessed. • **Results:** SG improved PFS/OS regardless of PIK3CA/TP53 status. No TACSTD2 mutations were found. TOP1 mutations were rare. DDR gene variants were frequent but not dynamic. ARID1A showed no resistance link. • **Conclusions:** SG benefit is consistent across genotypes. No clear genomic drivers of resistance emerged; future studies need paired biopsies.
28 April 2025	Immune exclusion signatures identify patients at high risk of relapse despite adjuvant chemotherapy in stage 2 colon cancer in the TOSCA phase 3 trial: PROSIT study	Luca Mazzarella	• **Introduction:** ACT decision-making in stage II CRC is suboptimal. Immune infiltration is prognostic, but transcriptional immune signatures remain unvalidated in trials. • **Methodology**: In TOSCA, 62 relapsed and 62 non-relapsed high-risk stage II CRC patients were matched. RNAseq on 72 FFPE samples assessed 67 immune signatures using Miracle/ssGSEA; outcomes correlated via Cox regression. • **Results:** IES-high patients (~27%) had shorter DFS (41 mo vs not reached; HR 2.5, p = 0.02). IES remained significant post-adjustment. ACT duration showed no DFS benefit. • **Conclusions:** IES identifies poor responders to ACT, guiding intensification strategies in future trials.

Notable Presentations at AACR 2025
Biomarkers and Predictive Models (4/6)

Date	Title	Author	Summary
28 April 2025	Early biomarker dynamics are associated with treatment efficacy in a preclinical model of radiotherapy combined with a DNA damage response agent	Lorraine Mooney	• **Introduction:** Radiotherapy induces both cytotoxic and cytoprotective responses. DDR inhibitors like AZD7648 may enhance therapeutic effects by targeting DNA repair post-irradiation. • **Methodology**: A549 lung cancer cells were treated with radiotherapy, AZD7648, or both in vitro and in vivo. Tumors were irradiated using Xstrahl CIX3. RNA-seq and protein biomarker analysis assessed treatment effects. • **Results:** AZD7648 plus radiotherapy increased cytotoxicity and delayed tumor growth. Biomarker analysis showed altered γH2AX kinetics, indicating DNA-PK target engagement and synergistic action. • **Conclusions:** Combining radiotherapy with DDR inhibition enhances anti-tumor effects. RNA/protein biomarkers validate target engagement, supporting future radiotherapy-combination strategies.
28 April 2025	ESR1 expression as a predictive biomarker for immune checkpoint inhibitor efficacy in estrogen receptor-positive, HER2-negative breast cancer	Jun Arima	• **Introduction:** Late recurrence is common in ER+/HER2– breast cancer, but ICI efficacy is limited. Lower ER-α (ESR1) expression correlates with better ICI response. • **Methodology**: Transcriptomic analysis of 4138 BC patients across 10 cohorts. ESR1-high defined as top two-thirds of expression. Immune features and ICI outcomes were analyzed. • **Results:** High ESR1 linked to fewer TILs, $CD8^+$ T cells, DCs, and lower CD8/Treg ratio. Low ESR1 enriched IL2, TNF-α, and IFN-γ pathways. ESR1 predicted ICI response better than PD-L1 (AUC 0.88 vs. 0.60). • **Conclusions:** High ESR1 expression marks poor ICI response in ER+/HER2– BC. CAF estrogen signaling may offer a therapeutic target to enhance ICI efficacy.

Notable Presentations at AACR 2025
Biomarkers and Predictive Models (5/6)

Date	Title	Author	Summary
28 April 2025	Efficacy of monoclonal antibodies against pathogenic S100A8/9 in myelodysplasia and leukemia models	Rahul Sanawar	• **Introduction:** MDS, CMML, and AML involve differentiation blockade and immunosuppressive MDSCs. S100A8/9 heterodimers drive disease via pro-inflammatory receptor interactions, yet remain untargeted clinically. • **Methodology**: Expression of S100A8/9 and receptors was profiled in patient CD34+ cells (N=183) and CMML scRNA-seq data (N=39). Neutralizing mAbs were generated and functionally validated in receptor binding and human PBMC assays. • **Results:** S100A8/9 and receptor overexpression correlated with severe anemia. Antibodies blocked receptor binding, reduced MDSCs/Tregs, and promoted erythroid colony formation and differentiation in primary patient samples (N=11). • **Conclusions:** S100A8/9 neutralization reverses disease phenotypes, supporting clinical advancement for myeloid malignancy treatment.
29 April 2025	Cancer cell permeability induced by tumor treating fields (TTFields) improves chemotherapy uptake and requires cells to transverse through the G2/M phase under TTFields application	Naama Flint-Brodsly	• **Introduction:** Multidrug resistance limits chemotherapy efficacy. TTFields, known to disrupt cancer cell processes, may enhance drug uptake via increased membrane permeability. • **Methodology**: 4T1 and 4T1-MDR cells were treated with TTFields ± DOX. Drug uptake and cell viability were assessed in vitro. In vivo, mice with 4T1 or LL/2 tumors received TTFields + DOX/PTX, with drug accumulation and tumor growth monitored. • **Results:** TTFields increased permeability during G2/M, equalizing DOX uptake in resistant and sensitive cells. In vivo, TTFields enhanced DOX/PTX accumulation and significantly reduced tumor growth. • **Conclusions:** TTFields reversibly increase permeability and sensitize tumors to chemotherapy, offering a novel strategy to bypass MDR.

Notable Presentations at AACR 2025
Biomarkers and Predictive Models (6/6)

Date	Title	Author	Summary
29 April 2025	B cell subtype is a predictive and pharmacodynamic biomarkers for combination therapy in stage III-IV melanoma: a simon phase II trial	Teruyuki Mizutani	• **Introduction:** irAEs challenge ICI use in melanoma. T and B cells are central to autoimmunity. This study explores B cell subsets as biomarkers in nivolumab, ipilimumab, and tocilizumab-treated patients. • **Methodology**: PBMCs from 70 melanoma patients were analyzed at baseline and week 7 using 35-color spectral flow cytometry. B cell clusters were identified via UMAP and PHATE, with statistical comparisons by logistic regression and Mann-Whitney U. • **Results:** Among 15 B cell clusters, TOX patients had lower baseline naïve B cells ($p = 0.016$). Late memory B cells increased at week 7 ($p = 0.003$), marking pharmacodynamic response. • **Conclusions:** Naïve B cells may predict irAEs, and late memory B cells reflect immune activation, supporting biomarker-guided monitoring in ICI regimens.
30 April 2025	Baseline multiomics and chemotherapy efficacy in preclinical trials using patient-derived xenograft models of cholangiocarcinoma can reveal distinct signatures of chemotherapy response	Amro M. Abdelrahman	• **Introduction:** CCA is typically treated with gemcitabine/cisplatin, yielding modest response rates. This study correlates PDX model responses with baseline multiomics profiles to identify predictive markers. • **Methodology**: 28 CCA PDX tumors underwent transcriptomic, proteomic, and phosphoproteomic profiling. 11 models were treated with gemcitabine/cisplatin, and response quantified via Median Efficacy Index. Pathway enrichment and random forest analysis identified key molecular correlates. • **Results:** Sensitivity to gemcitabine linked to SRPK2, GLK2, RIOK2; resistance to NTRK1, PIP5K1C, CSNK2A2. For cisplatin: response—NTRK1, PRPF4B; resistance—SRPK1, CSNK2A1. Anti-folate and lysine degradation pathways predicted drug response. • **Conclusions:** Multiomics profiling can stratify CCA chemotherapy response. Resistance markers like NTRK1/SRPKs offer new targets for future therapy testing.

Notable Presentations at AACR 2025
Cancer Microenvironment and Tumor Resistance (1/3)

Date	Title	Author	Summary
28 April 2025	The novel trispecific tumor-conditional TRAIL-R agonist M0674 induces tumor cell apoptosis and deepens therapeutic efficacy of systemic and targeted chemotherapies	Christina Esdar	• **Introduction:** TRAIL-R targeting shows limited clinical efficacy due to poor receptor clustering and toxicity. M0674 addresses these via trispecific targeting of TA-MUC1, TRAIL-R1, and R2. • **Methodology**: In vitro/in vivo evaluation of M0674 versus TRAIL-R agonists; apoptosis, viability, and xenograft efficacy tested in monotherapy and combinations. • **Results:** M0674 induces TA-MUC1-dependent apoptosis, spares hepatocytes, and outperforms comparators. Combination with chemo or ADCs yields regressions in NSCLC, PDAC, and gastric models. • **Conclusions:** M0674 safely triggers tumor-selective apoptosis, supporting its development in combo regimens across solid tumors.
28 April 2025	Overcoming resistance in HER2-positive gastric and breast cancers: Efficacy of disitamab vedotin in preclinical models resistant to trastuzumab emtansine and trastuzumab deruxtecan	Negar Pourjamal	• **Introduction:** Resistance to HER2-targeted ADCs T-DM1 and T-DXd limits efficacy. Disitamab vedotin (DV) targets a distinct HER2 epitope and may overcome this resistance. • **Methodology**: DV, T-DM1, and T-DXd were tested alone and in dual combinations in HER2+ gastric/breast cancer cell lines and xenografts, including ADC-resistant models. • **Results:** DV showed potent anti-tumor activity in vitro and in vivo, including in resistant models. Combining DV with T-DM1 or T-DXd enhanced efficacy beyond monotherapy. • **Conclusions:** DV may overcome HER2-ADC resistance, and dual ADC strategies could improve treatment in HER2+ cancers.

Notable Presentations at AACR 2025
Cancer Microenvironment and Tumor Resistance (2/3)

Date	Title	Author	Summary
28 April 2025	Preclinical efficacy assessment of brincidofovir against glioblastoma	Masatoshi Hazama	• **Introduction:** Cidofovir's GBM use is limited by nephrotoxicity. Brincidofovir (BCV), a safer lipid-conjugate, was evaluated for GBM efficacy and predictive biomarkers. • **Methodology**: BCV cytotoxicity was tested in 11 GBM cell lines; transcriptomic profiling identified gene expression differences. MGMT-overexpressing U87MG cells assessed BCV response. In vivo efficacy tested via orthotopic GBM xenografts in mice. • **Results:** Median IC50 was 2.2 μM; sub-micromolar in sensitive lines. GPC6 low and NYAP2 high expression correlated with sensitivity. MGMT overexpression did not impair efficacy. BCV reduced tumor burden and prolonged survival dose-dependently. • **Conclusions:** BCV is active in GBM, independent of MGMT. GPC6 and NYAP2 may predict treatment response.
29 April 2025	Exploring the differences in immunotherapy efficacy and immune microenvironment characteristics among colorectal cancer patients with different notch receptor gene subtypes	Junyi Chen	• **Introduction:** The NOTCH pathway influences tumor progression and immune interactions, but its immunotherapy relevance in CRC remains unclear. • **Methodology**: NGS and mIHC were performed on 249 Chinese CRC samples and 109 MSKCC cohort patients. Immune cell infiltration was quantified in tumor parenchyma and stroma. • **Results:** CRC patients with NOTCH3 mutations had significantly longer OS (11.5 vs 8 mo; P=0.008). NOTCH1–3 mutations correlated with elevated CD8+ T-cell infiltration; NOTCH3/4 mutations showed higher NK cell levels in parenchyma. • **Conclusions:** NOTCH3 mutations may predict improved immunotherapy outcomes via enhanced CD8+ and NK cell infiltration.

Notable Presentations at AACR 2025
Cancer Microenvironment and Tumor Resistance (3/3)

Date	Title	Author	Summary
29 April 2025	Flt3 ligand and CD40 agonist-based therapy in breast cancer promotes myeloid cell CXCL9 secretion and CD8 T cell recruitment but is not dependent on CXCL9 for efficacy	Sangeetha M. Reddy	• **Introduction:** Breast tumors lack antigen-presenting DCs, limiting immunity. Flt3L promotes DC1s; CD40a activates APCs. Combined with chemotherapy, they may enhance immune responses. • **Methodology**: Murine breast cancer models (E0771, AT3, 4T1) received triplet therapy: PLD, Flt3L, and CD40a. Tumors were analyzed via scRNAseq and flow cytometry. $CD8^+$ T cells and CXCL9 were depleted to assess functional roles. • **Results:** Triplet therapy improved tumor control ($p<0.0001$), increased CXCL9 from DCs/macrophages, and enhanced infiltration of stem-like/effector $CD8^+$ T cells. $CD8^+$ depletion abrogated effect; CXCL9 depletion did not. • **Conclusions:** Triplet therapy enhances durable $CD8^+$ T cell responses in breast cancer independent of CXCL9, supporting clinical translation.
29 April 2025	Sting pathway activation potentiates the antitumor efficacy of doxorubicin in soft-tissue sarcoma	Wonyoung Choi	• **Introduction:** STS lacks effective targeted or immunotherapies. Doxorubicin is standard; STING activation may boost its antitumor effect. • **Methodology**: STS cell lines and syngeneic mouse models were treated with doxorubicin ± STING agonist ADU-S100. $CD45^+$ immune cells underwent RNA-seq; gene expression correlated with TCGA-SARC survival data. • **Results:** Doxorubicin triggered STING via cytosolic DNA; effect was lost with Sting1 deletion. Combination with ADU-S100 enhanced tumor suppression. STING-induced immune genes correlated with longer survival in TCGA-SARC patients. • **Conclusions:** STING activation potentiates doxorubicin efficacy in STS and supports clinical evaluation of this combination.

Notable Presentations at AACR 2025
Clinical Trials and Phase Studies (1/3)

Date	Title	Author	Summary
27 April 2025	A prospective, multi-center, phase IV study to evaluate safety and efficacy of Dr. Reddy's bevacizumab (DRL_BZ) in patients with solid tumors	Narendra Maharaj	• **Introduction:** DRL_BZ, a bevacizumab biosimilar, is approved for solid tumors. This Phase IV study assessed its real-world safety and efficacy. • **Methodology**: In a multicenter, single-arm study, 200 patients with mCRC, NSCLC, ovarian, or cervical cancer received DRL_BZ for up to 6 months. • **Results:** 69.5% experienced TEAEs; 12.5% were treatment-related. SAEs in 6%, with 4 drug-related. ORR: 23.1–72.7% across indications; highest in ovarian cancer. • **Conclusions:** DRL_BZ showed a consistent safety profile and clinical efficacy across multiple tumor types, supporting its continued therapeutic use.
27 April 2025	A phase Ib/II study of PARPi Mefuparib Hydrochloride (CVL218) in combination with PD-1 inhibitor plus chemotherapy in metastatic or recurrent triple-negative breast cancer (TNBC)	Steve Shen	• **Introduction:** BRCA-mutated TNBC (~15%) has poor outcomes. CVL218, a next-gen PARPi, crosses the BBB and has low hematologic toxicity. • **Methodology**: Phase Ib/II (NCT06078670) evaluated CVL218 (500 mg BID), toripalimab, and nab-paclitaxel in CPS ≥1 or HRD+ advanced TNBC. • **Results:** Among 11 patients, ORR was 72.7%, DCR 90.9%. Most common ≥G3 TRAE: liver injury (2.6%). No Grade 5 events; all SAEs resolved with treatment. • **Conclusions:** The triplet regimen is well tolerated and shows encouraging efficacy in previously treated TNBC patients.

Notable Presentations at AACR 2025
Clinical Trials and Phase Studies (2/3)

Date	Title	Author	Summary
27 April 2025	Comparing the efficacy of infliximab and vedolizumab in treating steroid-refractory immune checkpoint inhibitor-induced colitis	Irene Li	• **Introduction:** ICI-induced colitis is a severe irAE; biologics like infliximab are used, but data on vedolizumab remain limited. • **Methodology**: Retrospective review (2019–2024) of 17 patients treated with infliximab or vedolizumab for ICI-related colitis at UC San Diego. Excluded non-ICI colitis cases. • **Results:** Steroid taper success: infliximab 66%, vedolizumab 75% (p = 0.70). Vedolizumab group had longer steroid duration (30.2 vs. 18 weeks; p = 0.80). No significant outcome differences by sex or ICI type. • **Conclusions:** Both agents are effective. Infliximab remains a reasonable first-line choice, with no clear superiority of vedolizumab demonstrated.
27 April 2025	Safety and efficacy of same-day administration of novel long-acting G-CSF efbemalenograstim α in breast cancer patients undergoing cytotoxic chemotherapy	Shoubing Zhou	• **Introduction:** Timing of G-CSF post-chemotherapy is debated. Efbemalenograstim α is a novel long-acting G-CSF approved in 2023. Guard-02 assessed its use within 24 hours of chemo. • **Methodology**: In a two-stage study, breast cancer patients received epirubicin/cyclophosphamide and efbemalenograstim α within 24±4 h in cycle 1, then 4±1 h in later cycles. Primary endpoint: grade 3-4 neutropenia (cycles 1–2). • **Results:** Grade 3–4 neutropenia occurred in 25% (cycles 1–2), lower than historical 34.16%. Grade 4 neutropenia: 12.5%. FN: 6.25%. No serious drug-related AEs; most common was mild muscle pain (6.25%). • **Conclusions:** Same-day efbemalenograstim α is safe, effective, and simplifies CIN management for daytime chemotherapy patients.

Notable Presentations at AACR 2025
Clinical Trials and Phase Studies (3/3)

Date	Title	Author	Summary
28 April 2025	Phase II study of rucaparib and nivolumab in patients with leiomyosarcoma	Carmelina Charalambous	• **Introduction:** Rucaparib may enhance nivolumab's immune effect in LMS. This Phase II trial evaluated ctDNA dynamics alongside RECIST imaging. • **Methodology**: 20 LMS patients received rucaparib + nivolumab. ctDNA was measured longitudinally via MSK-ACCESS; tumor sequencing used MSK-IMPACT. Primary endpoint: RECIST-based response by week 24. • **Results:** Baseline ctDNA was detectable in all patients. Rising ctDNA preceded or coincided with progression in 90% of progressing cases, often before RECIST-confirmed changes. Undetectable ctDNA correlated with partial response. • **Conclusions:** ctDNA is a sensitive biomarker for early LMS progression and may outperform RECIST alone in guiding immunotherapy assessment.
28 April 2025	Phase I clinical trial combining camu camu prebiotic enriched with castalagin modulates bile acids and metabolites in combination with cancer immunotherapy in patients with treatment-naïve lung cancer and PD-1 refractory melanoma (NCT05303493)	Jade Maillou	• **Introduction:** Castalagin, a Camu Camu-derived polyphenol, enhances ICI activity via microbiome and bile acid (BA) modulation in preclinical models. • **Methodology**: Phase I trial of 1.5g/day oral CC with ICI in NSCLC (PD-L1 <50%) and ICI-refractory melanoma. Endpoints: safety, DCR. BA/metabolite shifts were analyzed via HPLC; murine models validated findings. • **Results:** No CC-related AEs. NSCLC: 43% DCR (all PR). Melanoma: 35% DCR. CC elevated fecal/serum BA and plasma phenylbutyric acid. BA pathway modulation was essential for antitumor effect in mice • **Conclusions:** CC is safe and enhances ICI efficacy through BA signaling, positioning castalagin as a promising immunotherapy adjunct.

Notable Presentations at AACR 2025
Preclinical and Early-Stage Research (1/3)

Date	Title	Author	Summary
27 April 2025	Preclinical efficacy and safety of [161Tb]Tb-labeled anti-nectin-4 radioimmunoconjugate as theranostic against triple-negative breast cancer (TNBC) and non-small cell lung cancer (NSCLC)	Fabrice Ngoh Njotu	• **Introduction:** Nectin-4 is overexpressed in TNBC/NSCLC; no RLT targets exist. • **Methodology**: [161Tb]Tb-DOTA-N4MU01 was evaluated in Nectin-4+ mouse models for binding, safety, and efficacy. • **Results:** Radioligand showed strong binding, safe pharmacokinetics, and tumor-specific uptake. Repeated 2×5 MBq dosing induced tumor regression and survival benefit across models, including ICBT-resistant TNBC. • **Conclusions:** [161Tb]Tb-DOTA-N4MU01 is a safe, effective RLT option for Nectin-4+ tumors, with potential in ICBT-refractory settings.
29 April 2025	Preclinical mechanistic PK/PD-efficacy modeling for AZD9750, a novel oral androgen receptor degrader (PROTAC), to support dose selection during early clinical development	Pablo Morentin Gutierrez	• **Introduction:** AZD9750 is a novel oral AR PROTAC for prostate cancer entering trials in 2025. • **Methodology**: A mechanistic PK/PD model was developed using hormone-sensitive AR-wt PDX models (MR041, C901), linking AZD9750 plasma levels to AR reduction and tumor response. • **Results:** AZD9750 achieved 50% AR modulation at 0.2–0.7 μM. Tumor regression required 55–80% AR reduction. Model predictions aligned with in vivo tumor dynamics. • **Conclusions:** Modeling defined AR suppression thresholds for efficacy, aiding early clinical dose optimization of AZD9750.

Notable Presentations at AACR 2025
Preclinical and Early-Stage Research (2/3)

Date	Title	Author	Summary
29 April 2025	Preclinical efficacy of tumor treating fields (TTFields) for small cell lung carcinoma (SCLC)	Rotem Engelman	• **Introduction:** SCLC is aggressive with limited treatment options. This study assessed TTFields alone and combined with standard chemotherapies. • **Methodology**: SCLC cell lines and a murine orthotopic model were treated with TTFields ± cisplatin or etoposide. Efficacy was measured via cell count, colony formation, apoptosis, and MRI. • **Results:** TTFields reduced cell viability and induced apoptosis. Combined treatment showed additive/synergistic effects, particularly with etoposide. TTFields significantly reduced tumor growth in vivo. • **Conclusions:** TTFields enhance anti-tumor effects in SCLC and may complement chemotherapy. Further studies with immunotherapy are planned.
29 April 2025	Preclinical safety and efficacy of SOT109, an antibody-drug conjugate targeting cadherin 17 (CDH17) for the treatment of colorectal and other gastrointestinal tract tumors	Amy Jensen-Smith	• **Introduction:** CDH17 is overexpressed in colorectal and other GI cancers. SOT109 is a novel exatecan-based ADC targeting CDH17. • **Methodology**: SOT109 candidates were selected for binding, internalization, and cytotoxicity. Evaluations included in vitro assays and in vivo tumor models (cell- and patient-derived xenografts). • **Results:** SOT109 showed strong tumor-specific binding and induced durable regressions without dose-limiting toxicities. Safety and PK were favorable in non-human primates. • **Conclusions:** SOT109 combines potent anti-tumor activity with a favorable safety profile, supporting advancement into clinical trials for GI cancers.

Notable Presentations at AACR 2025
Preclinical and Early-Stage Research (3/3)

Date	Title	Author	Summary
30 April 2025	Preclinical evaluation of the AKR1C3-activated alkylator OBI-3424 in hepatoblastoma: A report from the Pediatric Preclinical In Vivo Testing Consortium (PIVOT)	Filemon Dela Cruz	• **Introduction:** OBI-3424 is an AKR1C3-activated DNA alkylating prodrug. AKR1C3 is highly expressed in hepatoblastoma and T-ALL. • **Methodology**: Eight hepatoblastoma PDX models were treated with OBI-3424 (2.5 mg/kg weekly ×3). AKR1C3 levels were assessed via IHC (H-scores); efficacy was evaluated via EFS T/C and objective response. • **Results:** OBI-3424 was well tolerated. Partial responses occurred in 3 models; EFS T/C ranged from 2.34–5.62. AKR1C3 expression did not consistently predict response. • **Conclusions:** OBI-3424 demonstrates antitumor activity in hepatoblastoma. AKR1C3's predictive value needs further study to guide clinical development.

Late-Breaking Sessions Information At AACR 2025 (1/10)

Date	Title
27 April 2025	Inferring single-cell spatial gene expression with tissue morphology via explainable deep learning
27 April 2025	MS-CETSA deep functional proteomics uncovers a new induced DNA-repair programs leading to resistance to DNA-damaging drugs
27 April 2025	Exploring androgen receptor alterations (ARa) and their potential association with efficacy of first-line (1L) talazoparib (TALA) + enzalutamide (ENZA) in metastatic castration-resistant prostate cancer (mCRPC): A post hoc analysis of TALAPRO-2
27 April 2025	T cell targeted lentiviral gene delivery using the PACK-IT Platform generates CAR-T cells with superior potency compared to conventional lentivirus and enables in vivo generation of CD19-CAR T cells capable of controlling leukemia in preclinical models
27 April 2025	Decoding tumor cell dynamics driven by mutant TP53 gain-of-function activity in squamous cell carcinoma metastasis
27 April 2025	Circadian misalignment between cancer cells and immune cells drives immune escape

Late-Breaking Sessions Information At AACR 2025 (2/10)

Date	Title
27 April 2025	LINC00152-regulated PDE4D mediates drug resistance and metastasis in highly aggressive breast cancer
27 April 2025	Role of acetylcholine in glioblastoma pathophysiology: Emerging insights
27 April 2025	TJ102: A promising bispecific dual-payload ADC targeting CDH6 and folate receptor alpha (FRα) for the treatment of ovarian and kidney cancers
27 April 2025	CAR-adapted PIK3CD base editing enhances T cell anti-tumor potency
27 April 2025	Spatiotemporally regulated expression of membrane-bound interleukin 12 (mbIL12) for armored adoptive cell therapy (ACT) shows strong antitumor activity in syngeneic solid tumor models without overt toxicity
27 April 2025	Adoptive cell therapy with genetically engineered T cells for epithelial ovarian cancer
27 April 2025	A Man9xPS CAR T cell immunotherapy demonstrates robust preclinical safety and efficacy in an orthotopic pancreatic cancer model

Late-Breaking Sessions Information At AACR 2025 (3/10)

Date	Title
27 April 2025	TIGIT deletion rescues the antitumor activity of low avidity T cells by increasing TCR signal strength
27 April 2025	Efficient feeder cell-free in vitro expansion of NK cells for CAR-NK therapies using human platelet lysate
27 April 2025	A modular framework for cell and gene therapy assessment in preclinical mouse models
27 April 2025	Preclinical evaluation of GPC3 targeting antibody-TCR T cells in HCC models with tumor rechallenging
27 April 2025	Targeting autophagy in neuroblastoma: Inhibiting VPS34 to enhance anti-GD2 immunotherapy
27 April 2025	Combination immunotherapy promotes integrated anti-tumor immunity in fibrolamellar carcinoma
27 April 2025	BTN1A1 and YAP1 crosstalk: A key mechanism in tumor immune evasion and therapeutic targeting

Late-Breaking Sessions Information At AACR 2025 (4/10)

Date	Title
27 April 2025	Extracellular enolase-1 drives cancer-associated fibroblast differentiation in the tumor microenvironment to enhance tumor growth of multiple myeloma: Development of the therapeutic antibody, HuL001
27 April 2025	An agrin mechanotransduction for EGFR-addicted cancers
27 April 2025	Trefoil factor I (TFF1) as a modulator of intrinsic and stroma induced chemoresistance in pancreatic ductal adenocarcinoma
27 April 2025	Modulating TREM1 to boost NK cell activity and overcome MDSC-induced immunosuppression in neuroblastoma
27 April 2025	Characterizing the ovarian cancer immune microenvironment in a syngeneic murine model
27 April 2025	Targeting chromatin remodeling disrupts immune suppression by pathologically activated neutrophils in cancer
27 April 2025	VEGF-C remodels the tumor microenvironment during immunotherapy response in melanoma and promotes T cell memory

Late-Breaking Sessions Information At AACR 2025 (5/10)

Date	Title
28 April 2025	Identification of potent DIAPH3 variants as a powerful biomarker for targeting Native Hawaiian colorectal cancer population
28 April 2025	Elevated autoantibody response to enolase-1 is associated with poor overall survival in African American patients with prostate cancer
28 April 2025	Cultural and social determinants of trust in clinical trials and genomic research among Black and Hispanic cancer patients treated in a safety-net hospital
28 April 2025	Perspectives of clinical trial staff on recruitment barriers to a multicenter randomized controlled colorectal polyp prevention trial
28 April 2025	Predicted gut microbial metabolites and chemotherapy induced toxicity among breast cancer patients
28 April 2025	Metagenomics and metabolomics identify differential biomarkers in MASLD and hepatocellular carcinoma in South Texas Hispanics
28 April 2025	Ultra-processed food intake and colorectal cancer risk in the US NIH-AARP cohort

Late-Breaking Sessions Information At AACR 2025 (6/10)

Date	Title
28 April 2025	Electrochemical biosensor in the detection of pancreatic cancer biomarkers: AI driven model & patient cohort study
28 April 2025	Bioprinting 3D spatially resolved tumor avatars to mimic the native tumor microenvironment
28 April 2025	Clinically relevant humanized mouse models of metastatic prostate cancer facilitate therapeutic evaluation
28 April 2025	Novel multiplex immunoassay for simultaneous profiling of human and mouse immunomodulatory proteins in humanized models
28 April 2025	Development of a novel lung cancer orthotopic transplantation model for preclinical evaluation of anticancer agents
28 April 2025	Evaluating U5 snRNP200-targeting CAR-T therapy for acute myeloid leukemia: A novel multiplex immunoassay for analyte discrimination in mouse models
28 April 2025	OP-3136, a selective KAT6 inhibitor, demonstrates anti-tumor activity in prostate, ovarian, and non-small cell lung cancer preclinical models

Late-Breaking Sessions Information At AACR 2025 (7/10)

Date	Title
28 April 2025	Discovery and characterization of BRSD-143, an orally bioavailable panKRAS inhibitor
28 April 2025	Secreted PTEN-long downregulates PI3K signaling and PD-L1 and promotes anti-tumor antigen-presenting cell functions to cause regressions of mouse tumors
28 April 2025	Novel performance quantification of MCED testing to aid clinical decisions: Analysis of a sequential reflex blood-based methylated ctDNA test
28 April 2025	Utilizing serum-derived lipidomics with protein biomarkers and machine learning for early detection of ovarian cancer in the symptomatic population
28 April 2025	Sharpening the signal: Enhancing liquid biopsy specificity through intra-individual methylation analysis
28 April 2025	MCTarg: A plasma-based metabolic biomarker model for multi-cancer early detection
28 April 2025	Circulating methylated GCM2 and TMEM240 as novel biomarkers for dynamic monitoring of breast cancer progression and treatment response

Late-Breaking Sessions Information At AACR 2025 (8/10)

Date	Title
29 April 2025	SDP01873, a novel HER3×c-Met bispecific antibody-drug conjugate (ADC) targeting EGFR tyrosine kinase inhibitor (TKI)-resistant non-small cell lung cancer (NSCLC), colorectal cancer (CRC) and beyond
29 April 2025	Resistance to trastuzumab deruxtecan (T-DXd) in breast cancer via loss of HER2 expression and binding
29 April 2025	Mechanisms of resistance to the RAS(ON) multi-selective inhibitor daraxonrasib (RMC-6236) in RAS mutant PDAC and potential resolution with RAS(ON) combination therapies
29 April 2025	Overcoming chemotherapy resistance in pancreatic cancer: The impact of novel RAS inhibitors and tumor microenvironment modulation
29 April 2025	Reactivation of Drp1S616 phosphorylation by c-MYC-CDK4/6 signaling axis plays a functional role in resistance to MEK inhibition in pancreatic cancer cells
29 April 2025	VRN101099: A novel treatment option for HER2-driven cancer patients, overcoming T-DXd resistance and brain metastases
29 April 2025	CT1113, a dual USP25/28 inhibitor, promotes antitumor immunity by preventing YTHDF2-mediated complement activation and potentiates anti-PD-1 therapy

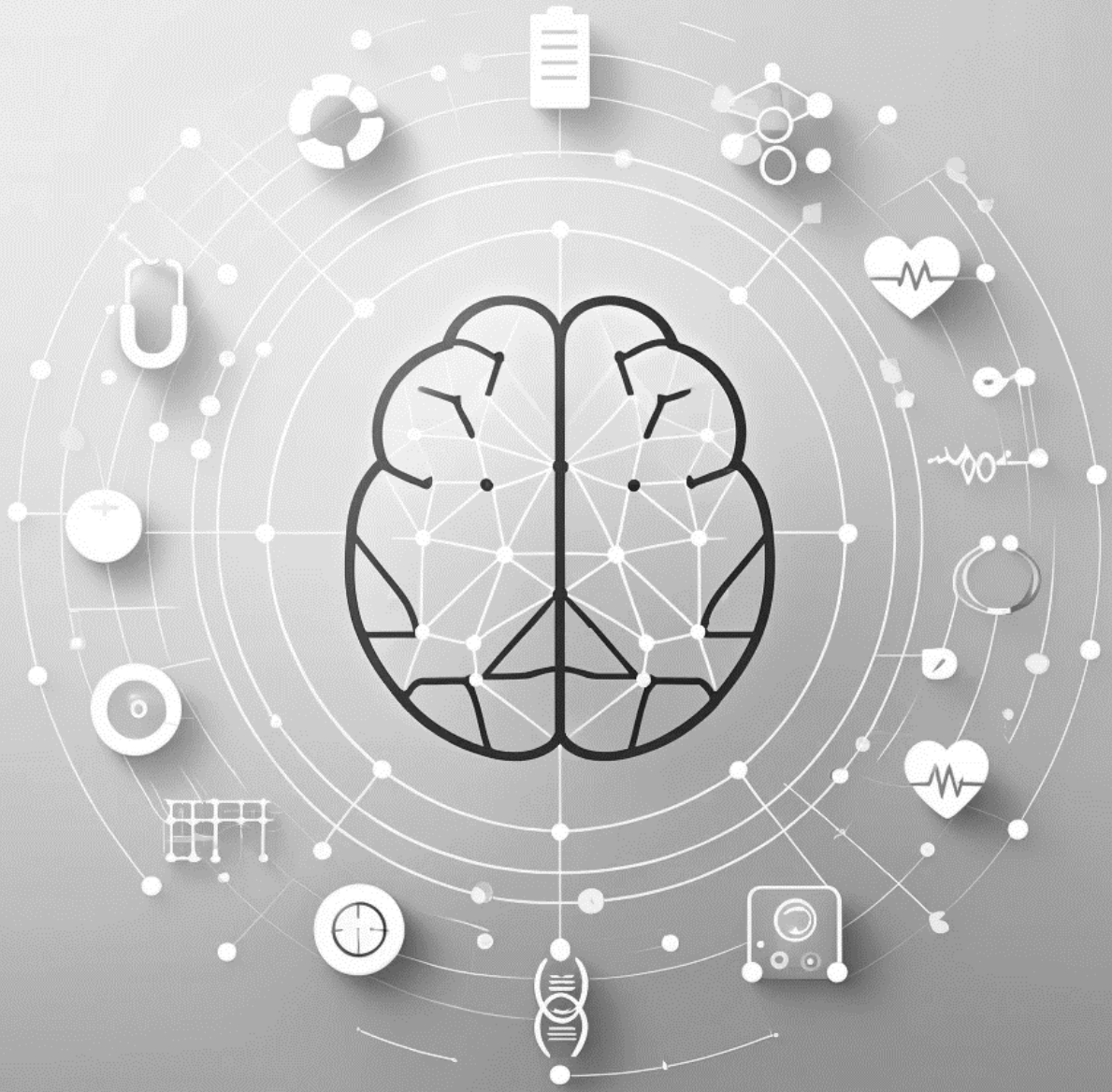
Late-Breaking Sessions Information At AACR 2025 (9/10)

Date	Title
29 April 2025	Broad and synergistic anti-tumor effects of small-molecule dual HIF-1/2 inhibitors in combination with immune checkpoint inhibitors
29 April 2025	ACTL6A (SWI/SNF complex subunit) cooperates with EZH2 and maintains a repressive chromatin state to modulate a immune COLD phenotype in squamous cancers
29 April 2025	Investigating the role of Nfe2l2 in early Alk-dependent lung adenocarcinoma tumorigenesis
29 April 2025	Thioredoxin interacting protein (TXNIP), a regulator of oxidative stress, mediates the RAPGEF3/4 (EPAC1/2) signaling required for melanoma progression
29 April 2025	Inflammatory proteomic signatures of metabolically unhealthy obesity in association with colorectal cancer and adenoma
29 April 2025	Smoking and subsequent primary cancer in breast cancer survivors: A case-cohort study
29 April 2025	Pathway-based analysis of genomic alterations in infant ALL

Late-Breaking Sessions Information At AACR 2025 (10/10)

Date	Title
29 April 2025	Telomere-to-telomere long read whole genome sequencing provides novel insights into ovarian cancer genomics
29 April 2025	ProMiSE: Probabilistic multi-stain estimator for color separation in multiplexed brightfield histopathology images
29 April 2025	Mechanisms of resistance to PD-L1/PARP1-targeted therapy in metastatic castration-resistant prostate cancer inferred by liquid biopsy
29 April 2025	True live single circulating tumor cell capture with no leukocytecontaminant assay for multiomics in large cancer patient population
29 April 2025	AXIN2 promotes WNT-target gene expression via cross-feedback between WNT and retinoic acid signaling pathways based on transcriptionally co-regulated components
29 April 2025	Unraveling the nanomechanical characteristics of invasive lobular carcinoma (ILC)
29 April 2025	Single cell RNA sequencing of cerebrospinal fluid lymphocytes in CARv3 TEAM E treated glioblastoma patients

Noteworthy AI / ML presentations at AACR 2025



Themes from key AI / ML presentations at AACR 2025 (1/5)

- **AACR 2025 will demonstrate the transformative impact of AI/ML in oncology, delivering high-precision, scalable, and inclusive solutions for prediction, patient stratification, imaging, and therapeutic response, driving forward the promise of precision medicine at both individual and population levels**
- Check out the key AI / ML themes at AACR 2025 below:
- **AI-based Ensemble Model for CVD Mortality Prediction:**
  - Study utilized SEER-17 data to develop an ensemble AI model for predicting CVD mortality in Black cancer patients. The model demonstrated high performance with 98% accuracy and an AUC of 0.99, identifying early risk factors such as early diagnosis, age, treatment history, and specific cancer types
- **ML Models for Dietary Risk in GI Cancer:**
  - Using a South Korean cohort of 7,862 adults, a study developed ML models to predict GI cancer risk based on dietary intake. Despite initial failures, customized ML approaches overcame class imbalances, achieving precision of 0.78 and an F1 score of 0.75 for cancer prediction

Themes from key AI / ML presentations at AACR 2025 (2/5)

- **AI-driven SCLC Subtype Classifier:**
  - One study presented a ML-based transcriptional classifier that accurately predicted SCLC subtypes (A, N, P, I). Using 167 RNA-seq samples, the classifier achieved 86% sensitivity and 95% specificity, successfully aligning subtypes with their tumor microenvironment types, such as immune-enriched and immune-desert phenotypes
- **Multiomics-based Classifier for Cholangiocarcinoma:**
  - Multiomics data classify cholangiocarcinoma into subtypes using 60,000 features from 241 tumors. The final model, developed using gradient-boosted trees, achieved 89% accuracy and AUC of 0.98, with a focus on pathways like insulin signaling and amino acid metabolism
- **SerialCTRS for Early NSCLC OS Prediction:**
  - The SerialCTRS deep learning model predicted 1-year OS in NSCLC patients, outperforming RECIST and tumor volume change in a real-world validation. The model significantly stratified OS in different treatment response groups, showing a HR of 2.68 in favor of high response patients
- **ACR-2316 WEE1/PKMYT1 Inhibition Analysis:**
  - ACR-2316, a dual WEE1/PKMYT1 inhibitor, was developed using Acrivon's AP3 platform for tumor regression. Phosphoproteomics and ML validation confirmed its potency in activating CDK1/2 pathways, leading to DNA damage, premature mitosis, and cell death, with Phase 1 trials expected in 2025

Themes from key AI / ML presentations at AACR 2025 (3/5)

- **Machine Learning for Drug Resistance in Breast Cancer:**
  - Study used TCGA-based data to predict drug resistance in breast cancer. An ML pipeline achieved 90% accuracy in identifying gene-treatment interactions, predicting resistance to chemotherapy and hormone therapies, and supporting clinical application for drug resistance predictions
- **PM-AI for Integrative Cancer Analysis:**
  - PM-AI, a conversational AI tool, integrated clinical, genomic, and SDoH data to predict FOLFOX response in colorectal cancer. The tool identified KRAS mutations as predictive of poorer response, making AI-driven precision oncology more accessible and promoting health equity
- **Dietary Pattern Prediction in Gastric Cancer Risk:**
  - The study applied deep learning to identify dietary patterns in a large cohort, linking patterns like 'Noodles' and 'Salty' to higher gastric cancer risks. The model identified HR 4.34 for the salty pattern in younger women, suggesting targeted dietary interventions for cancer prevention
- **AI for Immune Phenotype Classification in Gallbladder Cancer:**
  - Using Lunit SCOPE IO and AI, this study classified immune phenotypes in gallbladder cancer patients. The immune-inflamed (IIP) pattern correlated with better DFS/OS (HR=0.28), suggesting that AI-defined immune profiling can be an important prognostic marker for advanced-stage cancer

Themes from key AI / ML presentations at AACR 2025 (4/5)

- **C the Signs AI Tool for Cancer Triage:**
  - The C the Signs AI tool analyzed 235,662 assessments to triage cancer referrals during the COVID-19 pandemic. By reducing 61,099 unnecessary referrals, the AI tool demonstrated 7.3% conversion rate, surpassing the NHS average and improving efficiency in cancer diagnosis.
- **RAG-enhanced ML for Synergistic Cancer Drug Combinations:**
  - Using RAG-enhanced Mistral v0.2, this study predicted synergistic drug combinations for cancer treatment, achieving an F1 score of 0.80. The model highlighted ADC-based combinations as the best-performing therapies, providing mechanistic explanations for drug synergies
- **DeepSynBa for Cancer Drug Synergy Prediction:**
  - DeepSynBa, a deep learning framework, predicted synergy in drug combinations using NCI-ALMANAC data. It outperformed traditional models, reducing RMSE by 65% and showing strong performance across 9 tissue types and various drug settings
- **TeloPred for Screening Telomerase Inhibitors:**
  - TeloPred, an ML classifier, was developed to predict telomerase inhibitors in cancer research. The model achieved 87.2% accuracy and identified 10 lead candidates, offering a scalable approach for drug discovery in cancer therapy

Themes from key AI / ML presentations at AACR 2025 (5/5)

- **AI-Enhanced Neoantigen Vaccine Optimization:**
  - AI-guided epitope optimization for neoantigen vaccines enhanced MHC-I presentation and T-cell activation. Modified peptides, including those from TP53, improved HLA binding and induced strong $CD8^+$ T-cell responses, demonstrating the potential for next-gen cancer vaccines
- **Multimodal Deep Learning for LCINS Survival Prediction:**
  - A multimodal deep learning model predicted survival in Lung Cancer in Never Smokers (LCINS), achieving C-index of 0.86. The model outperformed gene-specific models, supporting personalized treatment strategies in early-stage disease
- **Perineural Invasion Prediction in Hepatobiliary Cancers:**
  - ML models accurately predicted perineural invasion (PNI) in hepatobiliary cancers, achieving AUC of 0.892. This model helps in preoperative risk stratification, highlighting aggressive tumor features to aid personalized care
- **AI-based Cancer Detection in Frozen Sections:**
  - Study applied AI-based MIL model to detect cancer in frozen section histology (FS) with AUC of 0.9241–0.9536. The approach reduced annotation requirements and improved cancer detection in pathology workflows

Noteworthy AI / ML presentations at AACR 2025

Notable Presentations at AACR 2025
AI / ML (1/20)

Date	Title	Author	Summary
27 April 2025	Predicting stroke as a cause of death in Black cancer patients using ensemble machine learning models	Raghad Wesamah Alrawashdeh	• **Introduction**: CVD-related mortality in Black cancer patients is underexplored. This study applies AI to identify predictive risk factors for CVD death in this underserved population. • **Methodology**: SEER-17 data (2000–2020) on 292,680 Black cancer patients was analyzed using ML models (Random Forest, Logistic Regression, XGBoost, LightGBM, Gradient Boosting). Models were ensembled; performance was assessed via AUC, F1, precision, and recall. • **Results:** CVD mortality occurred in 2.01% of patients. The ensemble model showed strong performance (accuracy: 0.98; AUC micro: 0.99). Key risk factors: early diagnosis year, older age, no treatment, and specific cancer types. • **Conclusions:** Ensemble AI models enable accurate CVD mortality prediction, identifying critical intervention points in Black cancer patients.
27 April 2025	Addressing challenges in integrating dietary factors into machine learning models for gastrointestinal cancer prediction in South Korean cohort	Jeongseon Kim	• **Introduction**: Dietary intake is crucial in GI cancer risk but is rarely used in ML models due to inconsistent data. This study addresses data limitations using a South Korean cohort. • **Methodology**: Data from 7,862 adults (158 GI cancer cases) over 16 years were analyzed. FFQ dietary data, biomarkers, and body metrics informed ML models (Logistic Regression, RF, GBM, SVM). Class imbalance was mitigated using customized sampling/training. • **Results:** Baseline models failed for cancer case prediction (precision = 0). The tailored strategy improved case precision to 0.78 and overall F1 to 0.75. • **Conclusions:** Customized ML approaches can overcome class imbalance, enabling dietary data integration into GI cancer risk prediction.

Notable Presentations at AACR 2025
AI / ML (2/20)

Date	Title	Author	Summary
27 April 2025	A novel machine learning classifier for SCLC transcriptional subtypes	Carl M. Gay	• **Introduction**: SCLC's heterogeneity impedes treatment precision. Existing subtype classifiers lack clinical usability. A new ML-based transcriptional classifier was developed to refine subtype assignment (A, N, P, I). • **Methodology**: Using 167 labeled RNA-seq samples, three hierarchical gradient boosting models predicted subtype probabilities. Performance was validated on a 271-sample metacohort and compared with TME profiles. • **Results:** The classifier showed high sensitivity (0.86) and specificity (0.95). Subtypes aligned with TME types: SCLC-I with immune-enriched TMEs; A/N with immune deserts ($p < 0.005$). • **Conclusions:** This robust classifier enhances SCLC stratification and will guide patient allocation in future trials.
27 April 2025	Feature selection and machine learning strategies optimize an affordable molecular assay for cholangiocarcinoma subtype	Ellen Larson	• **Introduction**: Most cholangiocarcinomas lack targetable mutations. Multiomics can reveal non-mutated, targetable pathways, but clinically feasible classifiers are needed • **Methodology**: 60,000 features (RNA, protein, phosphoprotein) from 241 tumors (US/China) were clustered via Multiomics Factor Analysis. Six feature selection methods and four ML algorithms were tested with 10x10-fold cross-validation. • **Results:** A stable 50-feature set enriched for insulin signaling and amino acid metabolism pathways enabled accurate subtype classification. Gradient-boosted trees + RFE achieved top performance (accuracy: 89%, AUC: 0.98). • **Conclusions:** A cost-efficient, high-accuracy 50-feature multiomics classifier offers scalable subtyping for cholangiocarcinoma and other complex cancers.

Notable Presentations at AACR 2025
AI / ML (3/20)

Date	Title	Author	Summary
27 April 2025	Deep learning response score using baseline and 12-week RECIST chest CTs enhances overall survival (OS) prediction in advanced NSCLC: external validation in a trial with dostarlimab	Brenda F. Kurland	• **Introduction**: Accurate early prediction of ICI benefit in advanced NSCLC is essential. SerialCTRS, a deep learning model, was developed to predict 1-year OS from pre- and 12-week CT scans. • **Methodology**: SerialCTRS was trained on real-world datasets and externally validated in 67 patients from the GARNET trial. It was benchmarked against RECIST 1.1 and tumor volume change using OS hazard ratios and concordance indices. • **Results:** SerialCTRS outperformed RECIST and tumor volume change (concordance: 0.717 vs 0.686 and 0.610). It significantly stratified OS in SD/medium vs CR/PR/high groups (HR 2.68, p=0.03). • **Conclusions:** SerialCTRS enables superior, annotation-free OS prediction in NSCLC, enhancing early treatment response assessment.
27 April 2025	Detailed mechanistic understanding of ACR-2316, a novel, clinical-stage WEE1/PKMYT1 inhibitor, rationally designed for superior single-agent activity through potent activation of CDK1, CDK2, and PLK1 using Acrivon's machine learning-driven AP3 platform	Lei Shi	• **Introduction**: ACR-2316, a dual WEE1/PKMYT1 inhibitor, was rapidly developed using Acrivon's AP3 platform to activate CDK1/2 and PLK1, inducing tumor regression. • **Methodology**: AP3-guided phosphoproteomics and machine learning assessed kinase activity in ACR-2316–treated cancer cells, with validation via flow cytometry, CellTiter-Glo, live imaging, ChIP-seq, and immunofluorescence. • **Results:** ACR-2316 robustly activated CDK1/2 and downstream pathways, causing DNA damage, premature mitosis, and cell death. CDK1/2 inhibition partially rescued effects, confirming on-target action. Unique chromatin regions showed ACR-2316-induced breaks. • **Conclusions:** AP3 enabled rapid design and mechanistic profiling of ACR-2316, supporting its potent, selective anticancer activity; Phase 1 data expected H2 2025.

Notable Presentations at AACR 2025
AI / ML (4/20)

Date	Title	Author	Summary
27 April 2025	A comparative analysis of statistical and machine learning approaches to predict drug resistance based on synergistic genetic alterations	Rishi Nair	• **Introduction**: This study explored machine learning (ML) vs. automated statistical methods for predicting drug resistance in breast cancer (BC) using TCGA-based cBioPortal data. • **Methodology**: 491 genes were assessed for synergistic alterations affecting 5-year OS across six treatment types. A brute-force statistical model identified significant gene-treatment interactions ($p<0.05$; $HR \geq 1$), while an ML pipeline computed treatment relevancy and predicted survival (classification accuracy ~90%, MSE <0.02). • **Results:** 570 gene pairs predicted resistance to chemotherapy, 392 to hormone therapy. ML rankings aligned with statistical outputs (e.g., hormone therapy: 48% high-risk pairs; chemotherapy: 86% poor OS). • **Conclusions:** ML models show promise for predicting gene-driven drug resistance in BC, with potential for refinement and clinical application.
27 April 2025	PM-AI agent: A conversational artificial intelligence system for precision medicine and advancing health equity through integrative clinical, genomic and social determinants of health data analysis	Enrique I. Velazquez-Villarreal	• **Introduction**: PM-AI, a conversational AI system, was developed to simplify integrative cancer analyses involving clinical, genomic, and SDoH data, addressing disparities and workflow complexity. • **Methodology**: PM-AI uses LLMs to translate natural language queries into executable code, automating analyses (e.g., survival, odds ratios) on datasets like TCGA and AACR GENIE. Validation focused on FOLFOX response in colorectal cancer by RAS status, integrating race/ethnicity per NASEM guidelines. • **Results:** PM-AI identified KRAS mutations as predictive of poorer FOLFOX response and higher recurrence risk, confirming literature findings. • **Conclusions:** PM-AI enables scalable, equitable, and expert-independent precision oncology analysis, promoting broader access and health equity.

Notable Presentations at AACR 2025
AI / ML (5/20)

Date	Title	Author	Summary
27 April 2025	Deep learning-derived dietary patterns and gastric cancer risk in women: A large-scale prospective cohort study	Hyobin Lee	• **Introduction**: This study used deep learning and clustering to refine dietary pattern analysis, aiming to link patterns to gastric cancer risk in a large Korean cohort. • **Methodology**: In 84,725 women from the HEXA-G study, baseline dietary data were analyzed using an autoencoder and k-means clustering. Cox models estimated gastric cancer risk (median follow-up: 9.4 years). • **Results:** Ten dietary patterns emerged. 'Noodles' (HR 1.97), 'Low calorie' (HR 1.91), and 'Salty' (HR 4.34 in ages 40–49) patterns had elevated gastric cancer risks versus 'High calorie'. • **Conclusions:** Deep learning-based analysis identified high-risk diets; targeted dietary interventions could reduce gastric cancer incidence.
27 April 2025	A novel single-cell level approach integrating artificial intelligence (AI)-powered histomorphology labeling and spatial transcriptomics enables biomarker identification of treatment-resistance in salivary gland cancer (SGC)	Jin Woo Oh	• **Introduction**: This study combined H&E-AI and spatial transcriptomics (ST) to dissect the TME in rare salivary gland carcinomas (SGC), focusing on resistance mechanisms. • **Methodology**: An integrated pipeline aligned AI-predicted cell morphologies with ST-derived gene expression from 28 tumors (12 validation, 16 SGC test samples), including neoadjuvant-treated SDCs. • **Results:** ST and H&E-AI synergistically identified 20 cell types and 10 tumor subtypes. In matched SDCs, recurrence was linked to EMT/immune evasion gene upregulation (e.g., MYC ↑174%) and low $CXCL9^{+}$ TILs (19.7% vs. 67.0%). • **Conclusions:** This integrative approach revealed actionable insights into therapy resistance, highlighting EMT, immune evasion, and TIL suppression as recurrence drivers.

Notable Presentations at AACR 2025
AI / ML (6/20)

Date	Title	Author	Summary
28 April 2025	Deep learning enables automated detection of circulating tumor cell-immune cell interactions with prognostic insights in cancer	Yuanfei Sun	• **Introduction**: Multicellular circulating tumor cell (CTC) clusters have high metastatic potential, yet manual detection limits clinical utility. AI-driven solutions are needed to improve prognostic precision. • **Methodology**: CTCpose, an AI-powered platform, was developed using CellSearch and single-cell sequencing data from 2,853 blood samples across 1,358 patients. Over 270 morphological and biomarker features were extracted via deep learning. • **Results:** CTCpose automated detection of CTCs, CTC-WBC clusters, and immune cell interactions. Spatial and biomarker features correlated with survival, disease progression, and therapy response. • **Conclusions:** CTCpose enables scalable, high-resolution CTC analysis, advancing predictive modeling and personalized therapy in breast and other cancers.
28 April 2025	Artificial intelligence for predicting spatial proteomics using high-plex digital spatial profiling in carcinomas	Yasin Shokrollahi	• **Introduction**: Manual ROI selection limits spatial proteomics. This study applies deep learning to predict immune and proliferation protein expression directly from mIF images across full carcinoma sections. • **Methodology**: In 62 carcinoma cases (721 ROIs), YOLOv8 detected panCK^{+}/CD45^{+} cells; a Swin Transformer-based multi-instance learning model predicted DSP protein expression using ~120,000 image patches. • **Results:** Strong correlations between predicted and measured protein expression were observed (e.g., PD-L1: ρ=0.741, Ki-67: ρ=0.730). Immune markers were also moderately predicted, validating spatial learning of TME context. • **Conclusions:** This model enables scalable, biopsy-sparing prediction of proteomic profiles, offering real-time insight into tumor-immune dynamics and supporting immunotherapy decisions.

Notable Presentations at AACR 2025
AI / ML (7/20)

Date	Title	Author	Summary
28 April 2025	Artificial intelligence enables prediction of MET amplification & associated morphologic features from H&E-stained NSCLC specimens	Ylaine Gerardin	• **Introduction**: MET amplification (MET-amp) in NSCLC drives oncogenesis and influences prognosis. This study introduces an AI-based method to predict MET-amp from H&E-stained slides, bypassing the need for FISH. • **Methodology**: A multiple instance learning model using PLUTO embeddings was trained on 1,384 WSIs. MET-amp was predicted in 170 NSCLC slides (test set), and HP cell density was quantified using a logistic regression classifier trained on 6,597 annotated cells. • **Results:** MET-amp prediction AUROC was 0.74. HP cell classifier achieved 98% sensitivity and 84% specificity. MET-amp tumors showed significantly higher HP cell proportions (p=0.0004). • **Conclusions:** AI-based MET-amp prediction from H&E images is feasible and correlates with HP tumor morphology, supporting non-invasive screening for targeted therapy selection.
28 April 2025	Artificial intelligence-based quantification of PD-L1 staining intensity in non-small cell lung cancer: Beyond binary assessment	Tae-Yeong Kwak	• **Introduction**: PD-L1 quantification via manual Tumor Proportion Score (TPS) in NSCLC is subjective and binary. An AI-powered pipeline was developed to assess PD-L1 staining intensity continuously on a 0–100 scale. • **Methodology**: The pipeline integrates cancer localization and cellular compartment segmentation to analyze PD-L1 membrane staining in 366 IHC-stained NSCLC slides. Metrics were compared to expert-assessed TPS using Pearson's r. • **Results:** AI metrics strongly correlated with clinical TPS: Mean PD-L1 Intensity (r=0.9042), H-score (r=0.8995), and AI-TPS (r=0.8896). Intensity heterogeneity also correlated (SD r=0.7261). Adenocarcinomas showed higher intensity than squamous carcinomas (p<0.0001). • **Conclusions:** The AI pipeline enables objective, quantitative PD-L1 analysis, offering superior granularity and adaptability to novel biomarkers.

Notable Presentations at AACR 2025
AI / ML (8/20)

Date	Title	Author	Summary
28 April 2025	LINMAP: A framework for comprehensive cell division lineage reconstruction via molecular barcoding and machine learning	Lin Wang	• **Introduction**: Lineage tracing using CRISPR-Cas9 and single-cell RNA-Seq enables high-resolution tracking but is challenged by dynamic mutation patterns from homing guide RNAs (hgRNAs). • **Methodology**: LINMAP, a machine learning framework, models mutation transition probabilities across divisions, quantifying cell-cell distances to reconstruct lineage histories and division counts. • **Results:** In MMTV-PyMT and lung cancer mouse models, LINMAP accurately reconstructed lineage trees, predicted allele dynamics, distinguished monoclonal vs. polyclonal tumors, and mapped tumor evolution and cell state shifts. • **Conclusions:** LINMAP offers precise, scalable reconstruction of cell lineages, revealing tumor origins, metastatic routes, and drug resistance evolution—advancing cancer and developmental biology research.
28 April 2025	Utilizing machine learning to predict clinical staging with head and neck cancer gene expression datasets	Nathan DeMichaelis	• **Introduction**: Stagnant cure rates in head and neck cancer necessitate precision staging. This study applies ML to genomic datasets (Affymetrix, TCGA) to enhance T/N stage prediction. • **Methodology**: HPV-stratified TCGA and Affymetrix gene expression data were used to train/test models (BSVCs, RF, GB, LR) on early vs. advanced stage (T1/2 vs. T3+) and N0 vs. N1+. Feature selection and hyperparameter tuning were applied over 50 trials. • **Results:** RF and BSVCs significantly outperformed LR in all tasks. Best models achieved AUC-ROC up to 0.95 (Affymetrix N, BSVCs) and 0.954 (TCGA HPV+ T, RF). • **Conclusions:** ML models with tuning and gene selection robustly predict staging, offering a path to refine treatment decisions in head and neck cancer.

Notable Presentations at AACR 2025
AI / ML (9/20)

Date	Title	Author	Summary
28 April 2025	Artificial intelligence-powered spatial analysis of tumor-infiltrating lymphocytes predicts prognosis in gallbladder cancer after resection	Hyemin Kim	• **Introduction**: The prognostic role of tumor-infiltrating lymphocytes (TILs) in resected gallbladder cancer remains poorly defined. This study applies AI to classify immune phenotypes and assess survival outcomes. • **Methodology**: Lunit SCOPE IO analyzed H&E slides from 225 patients, categorizing TIL patterns as immune-inflamed (IIP), immune-excluded (IEP), or immune-desert (IDP). DFS and OS were analyzed, including stage-based subgroups. • **Results:** IIP (25.8%) and IEP (67.1%) predicted significantly better DFS/OS than IDP (7.1%). Multivariate analysis showed IIP conferred lowest risk of recurrence and death (DFS HR=0.28, p=0.001; OS HR=0.26, p=0.001). • **Conclusions:** AI-defined immune phenotypes are strong prognostic markers in gallbladder cancer, particularly in advanced-stage disease, supporting immune profiling for risk stratification.
28 April 2025	Implementing an AI triage platform for identification and management of patients suspected of cancer risk to improve elective recovery post pandemic	Miles Payling	• **Introduction**: The COVID-19 pandemic led to a 27% rise in UK USC cancer referrals without increased detection, overwhelming secondary care. GPs often default to USC pathways, bypassing triage. • **Methodology**: C the Signs AI tool analyzed 235,662 assessments (2020–2024) across 1,084 practices, stratifying patients into urgent, non-urgent, diagnostics, or excluded from cancer pathways. • **Results:** The platform safely diverted 21.7% from USC, reducing USC load by 61,099 patients. Conversion rate was 7.3%, surpassing NHS average (6.0%) by 20.9%. Only 0.0% required urgent admission. • **Conclusions:** C the Signs optimizes cancer triage, reduces unnecessary USC referrals, and maintains safety, offering scalable NHS efficiency gains.

Notable Presentations at AACR 2025
AI / ML (10/20)

Date	Title	Author	Summary
28 April 2025	Mechanistically explainable AI model for predicting synergistic cancer therapy combinations	Han Si	• **Introduction**: Drug resistance in cancer necessitates rational multi-drug combinations, yet in vitro/in vivo models lack translational fidelity. This study introduces an LLM-based framework integrating trial data and a knowledge graph to predict synergistic combinations with biological rationale. • **Methodology**: A RAG-enhanced Mistral v0.2 model was trained on DrugComboDb and 1,092 clinical trials. PrimeKG provided mechanistic insights. Validation included 42 unseen drug combinations across 8 modalities. • **Results:** The model achieved high performance (F1 = 0.80; recall = 0.92). ADC-based combinations performed best (F1 = 100%); IO-IO scored lowest (F1 = 62%). Predictions included mechanistic explainability. • **Conclusions:** This LLM-knowledge graph pipeline offers accurate, interpretable predictions for oncology drug combinations, enhancing clinical translation and accelerating synergistic therapy discovery.
28 April 2025	DeepSynBa: A deep learning method to improve drug combination predictions using full dose-response matrices and contextual features of cell lines and cancer indications	Marta Milo	• **Introduction**: Traditional synergy models oversimplify drug interactions by predicting a single score, limiting clinical utility. DeepSynBa addresses this by modeling full dose-response matrices for drug pairs. • **Methodology**: DeepSynBa, a deep learning framework, predicts drug pair responses using cell line-specific features and drug embeddings. A parameter-estimating layer captures potency and efficacy, enabling post-hoc synergy score computation • **Results:** On the NCI-ALMANAC dataset (~300,000 combinations), DeepSynBa outperformed comboFM and comboLTR, reducing RMSE by ~65%. It showed robust performance across 9 tissue types and novel drug/cell line settings. • **Conclusions:** DeepSynBa enhances synergy prediction by modeling detailed dose-response behavior, improving experimental design and dosage optimization for untested drug combinations.

Notable Presentations at AACR 2025
AI / ML (11/20)

Date	Title	Author	Summary
28 April 2025	TeloPred: A machine learning classification webserver for prediction of small molecules as telomerase inhibitors for anti-cancer drug development	Divpreet Kaur	• **Introduction**: Telomerase is active in ~90% of cancers, yet small-molecule inhibitor development has stagnated. TeloPred, a novel ML classifier, predicts telomerase inhibitors to streamline drug discovery. • **Methodology**: Using 281 ChEMBL compounds and 12 molecular fingerprints, six ML models were trained; Support Vector Classifier (SVC) achieved optimal performance. Feature selection and SHAP analysis enhanced interpretability; a natural compound library was screened. • **Results:** SVC achieved 87.2% test accuracy, with an enrichment factor of 21. Key inhibitory features included aromaticity and amide linkages. Screening reduced the search space by 83%, yielding 10 lead candidates. • **Conclusions:** TeloPred enables accurate, interpretable virtual screening for telomerase inhibitors, advancing anti-cancer drug development and supporting global precision oncology efforts.
28 April 2025	The development of neoantigen-derived peptide vaccine driven by AI epitope design and computer assisted epitope enhancement	Chi Han Samson Li	• **Introduction**: Neoantigen vaccines are promising but often limited by poor MHC-I presentation. This study couples an AI-based epitope predictor with in silico mutagenesis to enhance peptide presentation and immunogenicity. • **Methodology**: TP53-derived neoantigens were optimized for HLA-A02:01 binding using saturation mutagenesis. Peptides with improved AI-predicted scores were synthesized, validated by SPR, and tested in HLA-A02:01-humanized mice via ELISpot and ICS. • **Results:** Seven modified peptides showed strong HLA binding; six induced $CD8^+$ T-cell responses. One native peptide reactivated T cells, confirming cross-reactivity from modified vaccine peptides. • **Conclusions:** AI-guided epitope optimization enhances MHC-I presentation and T-cell activation, offering a precise, scalable approach for next-generation neoantigen cancer vaccines.

Notable Presentations at AACR 2025
AI / ML (12/20)

Date	Title	Author	Summary
29 April 2025	A multimodal deep learning approach to predict survival in never smoking lung cancer patients	Monjoy Saha	• **Introduction**: Lung cancer in never-smokers (LCINS) remains a major cause of mortality. This study evaluates a multimodal deep learning approach combining clinical, histopathological, and genomic data to predict survival in LCINS. • **Methodology**: From 495 LCINS patients, CNN-derived WSI features, clinical, and genomic data were integrated into a unified deep learning model optimized using Cox loss. Survival risk prediction was validated with and without genomic input. • **Results:** The model achieved high prognostic accuracy (C-index = 0.86). Risk-stratified Kaplan-Meier curves showed significant survival differences ($p \leq 0.05$). Genomic data alone added limited predictive value. • **Conclusions:** Multimodal modeling effectively predicts LCINS survival, outperforming gene-specific models and supporting personalized treatment strategies even in early-stage disease.
29 April 2025	Machine learning prediction of perineural invasion in hepatobiliary cancers	Jehad A. Yasin	• **Introduction**: Perineural invasion (PNI) worsens outcomes in hepatobiliary cancers. This study developed ML models to predict PNI, aiding risk stratification and treatment planning. • **Methodology**: From 433 cases in the MSKCC HCC 2024 dataset, 10 ML models were trained on clinical, demographic, and genomic features using an 80/20 split. Top models were interpreted via SHAP analysis. • **Results:** Logistic Regression (AUC=0.892), Gradient Boosting (0.889), and Random Forest (0.888) outperformed other models. Cancer subtype and tumor site were key predictors. Decision Tree showed highest precision (0.902); MLPs underperformed • **Conclusions:** ML accurately predicts PNI in hepatobiliary cancers, supporting personalized care by identifying aggressive tumor features preoperatively.

Notable Presentations at AACR 2025
AI / ML (13/20)

Date	Title	Author	Summary
29 April 2025	Deep learning model for cancer diagnosis in frozen section sentinel lymph nodes with limited annotations	Tae-Yeong Kwak	• **Introduction**: Frozen section (FS) histology supports intraoperative cancer diagnosis, but AI applications are hindered by stain and scanner variability. This study introduces a generalizable model to detect cancer in FS H&E-stained images. • **Methodology**: Using >31,000 WSIs from TCGA, Camelyon16, and hospital archives, a MIL-based model with fixed backbone and classifier-only training was developed. Minimal pathologist annotations and data augmentation were used. • **Results:** The MIL + classifier-only approach achieved high generalizability (AUC/ROC: 0.9241–0.9536) and superior specificity vs. full fine-tuning. It outperformed across FS and FFPE datasets from varied scanners. • **Conclusions:** Reducing stain/scanner variation enhances FS cancer detection, supporting robust, annotation-light AI deployment in pathology workflows.
29 April 2025	Machine learning prediction and single-cell landscape of distant organ metastasis in non-small cell lung cancer	Zaid Nassar Abu Rjai'	• **Introduction**: Accurate prediction of NSCLC metastasis by site can inform tailored management. This study integrates ML and scRNA-seq to analyze predictors and tumor microenvironment (TME) shifts across metastatic sites. • **Methodology**: Using MSKCC and GEO datasets, seven random forest classifiers (RFCs) predicted site-specific metastasis based on clinical/genomic features. scRNA-seq (n > 94,000 cells) profiled cellular composition in primary vs. brain metastases. • **Results:** RFCs performed best for mediastinal (AUC=0.61) and adrenal metastases (AUC=0.62), with FGA, MSI, TMB, and mutation count as top predictors. Brain metastases showed stromal/epithelial dominance, with COL1A1/2 upregulation indicating ECM remodeling. • **Conclusions:** ML enables site-specific NSCLC metastasis prediction. scRNA data reveals TME shifts, suggesting mechanistic targets in metastatic progression.

Notable Presentations at AACR 2025
AI / ML (14/20)

Date	Title	Author	Summary
29 April 2025	A machine learning model for predicting hyperprogressive disease risk in cancer immunotherapy: Integrating clinical and molecular data	Haitao Wang	• **Introduction**: Hyperprogressive disease (HPD) is a severe adverse outcome of immunotherapy. This study developed a machine learning (ML) model to predict HPD risk across solid tumors using integrated clinical and molecular data. • **Methodology**: Among 1,005 ICI-treated patients, 363 with complete pre-treatment data were used. Eight key HPD predictors were identified and modeled using random forest, compared against logistic regression. • **Results:** The ML model achieved AUC 0.87 (CV), 0.71 (test set), with 90% sensitivity and 78% specificity in CV. Logistic regression was less effective (AUC 0.66). • **Conclusions:** This first-of-its-kind, high-sensitivity HPD prediction model enables proactive immunotherapy risk management across multiple cancer types.
29 April 2025	Discovery of novel PARP1-selective inhibitors for treatment of brain tumors using artificial intelligence	Sarah Truong	• **Introduction**: Brain tumors are difficult to treat due to blood-brain barrier (BBB) limitations. First-gen PARP inhibitors lack CNS penetration and PARP1 selectivity. This study applies Deep Docking and generative AI to develop a PARP1-selective, brain-penetrant inhibitor. • **Methodology**: Billions of compounds were screened via Deep Docking against PARP1. Generative AI optimized leads for CNS penetrance, PARP1 selectivity, and pharmacologic properties. • **Results:** Hit compounds showed promising PARP1 selectivity, BBB permeability, and favourable pharmacokinetics. In vitro and in vivo validations confirmed lead viability. • **Conclusions:** Deep Docking + AI enables efficient discovery of CNS-penetrant PARP1 inhibitors, offering a novel therapeutic strategy for brain tumors.

Notable Presentations at AACR 2025
AI / ML (15/20)

Date	Title	Author	Summary
29 April 2025	Clinical significance of co localization index in rectal cancer: a deep learning approach to cell interaction analysis	Kimihiro Yamashita	• **Introduction**: Tumor tissues are complex ecosystems. This study uses deep-learning imaging cytometry (DL-IC) and a novel co-localization index (CLI) to quantify spatial interactions in the rectal cancer immune microenvironment. • **Methodology**: Forty surgical specimens were analyzed via Cu-Cyto DL-IC with a bit pattern kernel filtering algorithm to prevent cell count duplication. CLI quantified spatial interactions, especially between $CD8^+$ T cells and cancer cells. • **Results:** High CLI between cancer cells and $CD8^+$ T cells correlated with improved 5-year DFS ($p=0.041$); multivariate analysis confirmed its prognostic value. Three-way CLI with macrophages also proved independently significant. • **Conclusions:** CLI offers a reproducible, AI-powered method to quantify immune-cancer interactions, enhancing prognostic evaluation in rectal cancer.
29 April 2025	Comparing prognostic association of manual vs. artificial intelligence derived quantifications from baseline computed tomography scans in MYSTIC, a global phase 3 trial for treatment of metastatic non-small cell lung cancer	Harish RaviPrakash	• **Introduction**: RECIST SLD is standard for baseline tumor burden, but AI-derived metrics like IPRO and lung volumetric tumor burden (VTB) may enhance prognostication. • **Methodology**: In 672 NSCLC patients from the MYSTIC trial, AI-derived IPRO and VTB were compared to SLD using c-index, TD-AUC, and Cox models for OS prediction. • **Results:** IPRO showed the strongest OS association (c-index: 0.61, HR: 0.57), outperforming SLD (c-index: 0.56, HR: 0.76). VTB had similar performance to SLD (c-index: 0.57, HR: 0.68). • **Conclusions:** AI-derived IPRO provides superior OS stratification over traditional SLD, supporting its clinical utility in treatment assessment.

Notable Presentations at AACR 2025
AI / ML (16/20)

Date	Title	Author	Summary
29 April 2025	CT radiomics-based machine learning models for diagnosing para-aortic lymph node metastases in colorectal cancer	Yingqian Zhou	• **Introduction**: PALN metastasis in colorectal cancer is rare and hard to detect preoperatively. This study developed CT radiomics-based machine learning models to improve diagnostic accuracy. • **Methodology**: In 116 CRC patients, 1,037 radiomics features were extracted from CT scans of PALNs. Six key features were selected via LASSO regression. ML models (RF, SVM, XGBoost, LR) were evaluated using cross-validation. • **Results:** The random forest model showed best performance (AUC = 0.809; F1 = 0.905), outperforming size-based imaging criteria (NRI = 0.789, P < 0.001; IDI = 0.116, P = 0.014). • **Conclusions:** Radiomics-based ML provides a non-invasive, accurate method to predict PALN metastasis in CRC, improving upon traditional imaging assessments.
29 April 2025	Inactivation of CDK12 remodels the transcription machinery and promotes epigenetic plasticity	Jing Liang	• **Introduction**: CDK12 inactivation, though counterintuitive given its role in transcription, may confer a survival advantage in prostate cancer. This study explores its epigenetic and transcriptional consequences. • **Methodology**: Analysis of TCGA datasets revealed CDK12 truncations correlate with DNA methylation loss in prostate, breast, and ovarian cancers. In vitro validation confirmed this link. RNA Pol II interactome profiling via mass spectrometry identified compensatory protein recruitment upon CDK12 inhibition. • **Results:** CDK12 loss reduces DNA methylation and alters RNA Pol II interactions. Recruited proteins may represent synthetic lethal targets, currently under functional validation in cancer models. • **Conclusions:** CDK12 inactivation drives epigenetic plasticity and rewires transcription machinery, revealing potential synthetic lethal vulnerabilities for therapeutic exploitation.

Notable Presentations at AACR 2025
AI / ML (17/20)

Date	Title	Author	Summary
30 April 2025	Modelling COPD to lung cancer progression using machine learning frameworks	Tej Pandya	• **Introduction**: COPD is an independent lung cancer risk factor, but gene-environment interactions—particularly involving air pollution and inflammation—remain poorly understood. • **Methodology**: Using UK Biobank data (n=488,377), ML models (XGBoost, TabNet, Elastic Net) integrated germline SNPs, PM2.5 exposure, and clinical data to predict lung cancer risk in COPD patients (n=24,094). • **Results:** XGBoost achieved best performance (AUC=0.73), rising to 0.87 when limited to 10-year COPD survivors. Key predictors included inflammation-related SNPs (e.g., RAGE) and pollution exposure. • **Conclusions:** ML reveals that inflammation mediates gene-environment interactions driving lung cancer in COPD, supporting stratified prevention and broad ML application in cancer epidemiology.
30 April 2025	Predicting acute care utilization following cancer treatment using machine learning: A patient-centered approach to precision oncology	Arman Koul	• **Introduction**: Unplanned acute care utilization (ACU) post-cancer therapy is a CMS quality metric (OP-35) and reflects care gaps. This study developed ML models to predict 30-day ACU using structured and unstructured data. • **Methodology**: Data from 18,143 cancer patients (2010–2024) were modeled using XGBoost and Random Forest. Clinical notes were encoded with large language models to supplement structured EMR data. • **Results:** The best model (XGBoost) achieved AUROC 0.84; top predictive categories included anemia (AUROC 0.87) and infection (AUROC 0.86). Later therapy lines improved predictive accuracy. • **Conclusions:** ML enables high-accuracy prediction of post-treatment ACU, offering actionable insights for proactive, quality-driven cancer care across complex treatment trajectories.

Notable Presentations at AACR 2025
AI / ML (18/20)

Date	Title	Author	Summary
30 April 2025	Multicenter study on an artificial intelligence model for predicting NSCLC recurrence	Junho Lee	• **Introduction**: Accurate recurrence prediction in early-stage NSCLC is vital for guiding personalized care. This study updates a transformer-based RADAR model integrating multimodal data to enhance generalizability across institutions. • **Methodology**: Using 16,828 NSCLC cases from two hospitals (2008–2024), the model predicted 1-year recurrence. Performance was assessed via AUC, sensitivity, and specificity across institutions and stages. • **Results:** The updated RADAR model achieved an AUC of 0.858 (sensitivity: 74.5%, specificity: 82.1%), with stage-specific AUCs of 0.865 (I), 0.756 (II), and 0.731 (III). Performance varied by institution, highlighting generalizability challenges. • **Conclusions:** Multi-institutional integration improved NSCLC recurrence prediction. Ongoing refinement and external validation are essential for real-world application in precision oncology.
30 April 2025	Mapping T cell reactivity against the human genome using machine learning uncovers target specific TCRs against novel tumour antigens	Nathaniel J. Davies	• **Introduction**: T cell engagers (TCEs) hold promise in solid tumors but are limited by target specificity. The T-Cα platform redefines TCR discovery by enabling high-throughput identification of TCRs against HLA-presented targets. • **Methodology**: Billions of T cells from 100s of donors were screened against >50 novel genomic targets. A dataset of 10,000s of TCR-epitope pairs, including negatives, was generated to train ML models predicting TCR specificity and potency. • **Results:** The model achieved high predictive accuracy, generalizing to novel epitopes and identifying TCRs suitable for TCE development. Functional assays confirmed specificity and cross-reactivity. • **Conclusions:** T-Cα enables rapid, scalable TCR discovery and ML-driven prediction of TCR-target specificity, advancing TCE pipelines with IND-enabling studies expected in 2025.

Notable Presentations at AACR 2025
AI / ML (19/20)

Date	Title	Author	Summary
30 April 2025	Stratification of cell therapies in solid tumor organoids using deep learning-derived imaging metrics	Luca Lonini	• **Introduction**: Efficient preclinical evaluation of immunotherapies requires scalable, quantitative tools. This study integrates deep learning with PDO co-culture models to assess cell therapy efficacy across multiple cancer types. • **Methodology**: 27 cell therapies were tested on 15 PDO lines from 8 cancers. Brightfield images over 72 hours were analyzed using deep networks to predict viability and extract six explainable spatial phenotypes. • **Results:** Brightfield-based viability predictions correlated strongly with vital dye staining (r=0.76). Spatial phenotypes also predicted viability (r=0.70) and clustered therapies by type and compound exposure. • **Conclusions:** This high-throughput, explainable imaging platform enables robust assessment of immunotherapy impact on PDOs, supporting therapy stratification and optimization in cancer research.
30 April 2025	Global mapping of artificial intelligence applications in gastric cancer from 1993-2024	Trong Anh Vu Dam	• **Introduction**: AI technologies are transforming gastric cancer (GC) care. This study analyzes global trends, research themes, and development patterns in AI applications for GC (1993–2024). • **Methodology**: Using 1,717 WoS-indexed articles, VOSviewer, Latent Dirichlet Allocation, and dendrogram analysis were applied to map term co-occurrence, topic clusters, and research trajectories. • **Results:** China, Japan, and the U.S. led in output; LMICs were underrepresented. "Robotic vs. Laparoscopic Gastrectomy" showed declining interest, while tumor segmentation, chemotherapy prediction, and cfDNA biomarkers emerged as key trends. AI's role grew during COVID-19. • **Conclusions:** AI research in GC is expanding but unequally distributed. Future work should prioritize LMICs and develop tools for surgical planning and monitoring to improve outcomes and reduce system burdens.

Notable Presentations at AACR 2025
AI / ML (20/20)

Date	Title	Author	Summary
30 April 2025	Efficacy of chemoradiotherapy in older patients with advanced stage head and neck cancer: A propensity and machine learning analysis	Rasheed Omobolaji Alabi	• **Introduction**: With increasing HPV-driven and age-related HNSCC cases, optimal treatment for older patients remains unclear. This study used machine learning (ML) to assess the impact of chemoradiotherapy (CRT) vs. radiotherapy (RT) in patients ≥65 with stage III–IV HNSCC. • **Methodology**: Using SEER data (n=3,570), ML models (voting ensemble, XGBoost) stratified patients by overall survival (OS). Permutation feature importance (PFI) evaluated CRT's effect, and results were validated via propensity score matching (PSM). • **Results:** CRT was the top predictor of OS (model accuracy: 85.2%). PSM confirmed CRT's survival benefit over RT alone. Unexpectedly, stage IV patients showed better survival than stage III. • **Conclusions:** CRT improves OS in older advanced-stage HNSCC patients. Decisions should be based on clinical, not chronological, factors. Validation in trials and broader datasets is recommended.
30 April 2025	MAGNETICA: Machine-augmented generation of novel enhanced tomographic imaging for tumor insight and cancer assessment	Morteza Rezanejad	• **Introduction**: Early-phase cancer trials suffer from limited CT image data. MAGNETICA addresses this by generating anatomically realistic, clinically conditioned synthetic 3D CT images to support trial design and biomarker discovery. • **Methodology**: Using NSCLC-Radiomics data (n=422), a VAE and Latent Diffusion Model integrated clinical features (e.g., stage, histology, survival) and ControlNet-guided anatomical maps to generate high-fidelity CT volumes. • **Results:** Synthetic scans showed minimal deviation from real images (MAE = 0.12; KS = 0.07; KL = 3.81×10^{-11}), with 98.9% rated anatomically accurate. Radiomic features matched real distributions. • **Conclusions:** MAGNETICA produces realistic, clinically relevant synthetic CT images, enhancing early-phase oncology trial data diversity, supporting modeling of tumor heterogeneity, safety, and dosing.

Strategic Insights and Strategy Development is our focus