SABCS 2025 Clinical and AI / ML Preview

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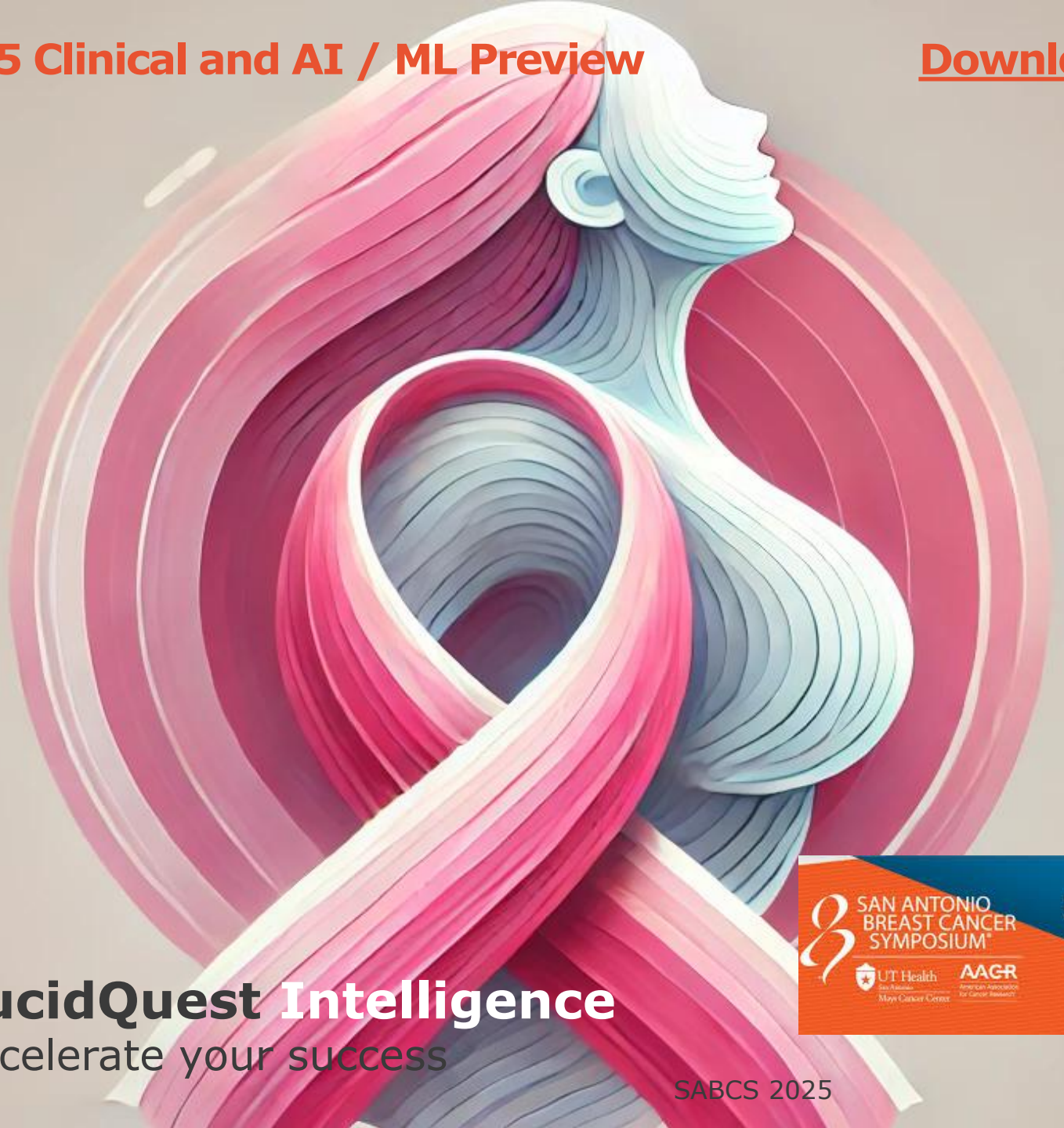

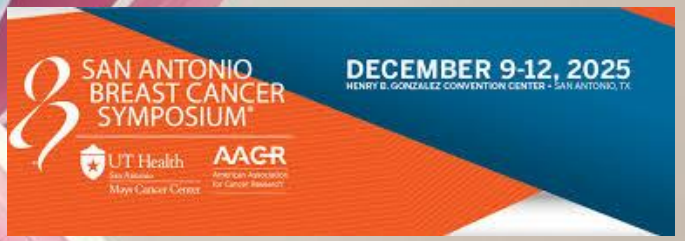

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SABCS 2025 – General Overview

- **Subtype-spanning evidence integration:** SABCS 2025 will synthesize Phase 3 and translational data across HR+/HER2−, HER2+, HER2-low, and TNBC, reshaping standards from in situ disease to metastatic settings
- **Biology-to-bedside continuum**: The meeting will connect experimental biology with therapeutic decisions, focusing on escalation and de-escalation strategies
- **Imaging, liquid biopsy, and MRD:** SABCS 2025 will highlight ctDNA, liquid biopsy, and advanced imaging (e.g., FDG-PET, TMIST) as decision tools for minimal residual disease and screening optimization
- **Trial diversity and disparities focus:** Presentations will emphasize outcomes in under-represented populations, including Black women and global cohorts, to inform equity-focused treatment algorithms
- **Practice-shaping guidelines alignment:** Sessions will align trial data with NCCN, ASCO, and ESMO guidelines, addressing immediate practice adoption
- **Multistakeholder translation into care:** The symposium will translate complex data into actionable insights for clinicians, trialists, and advocates, focusing on survivorship and quality of life

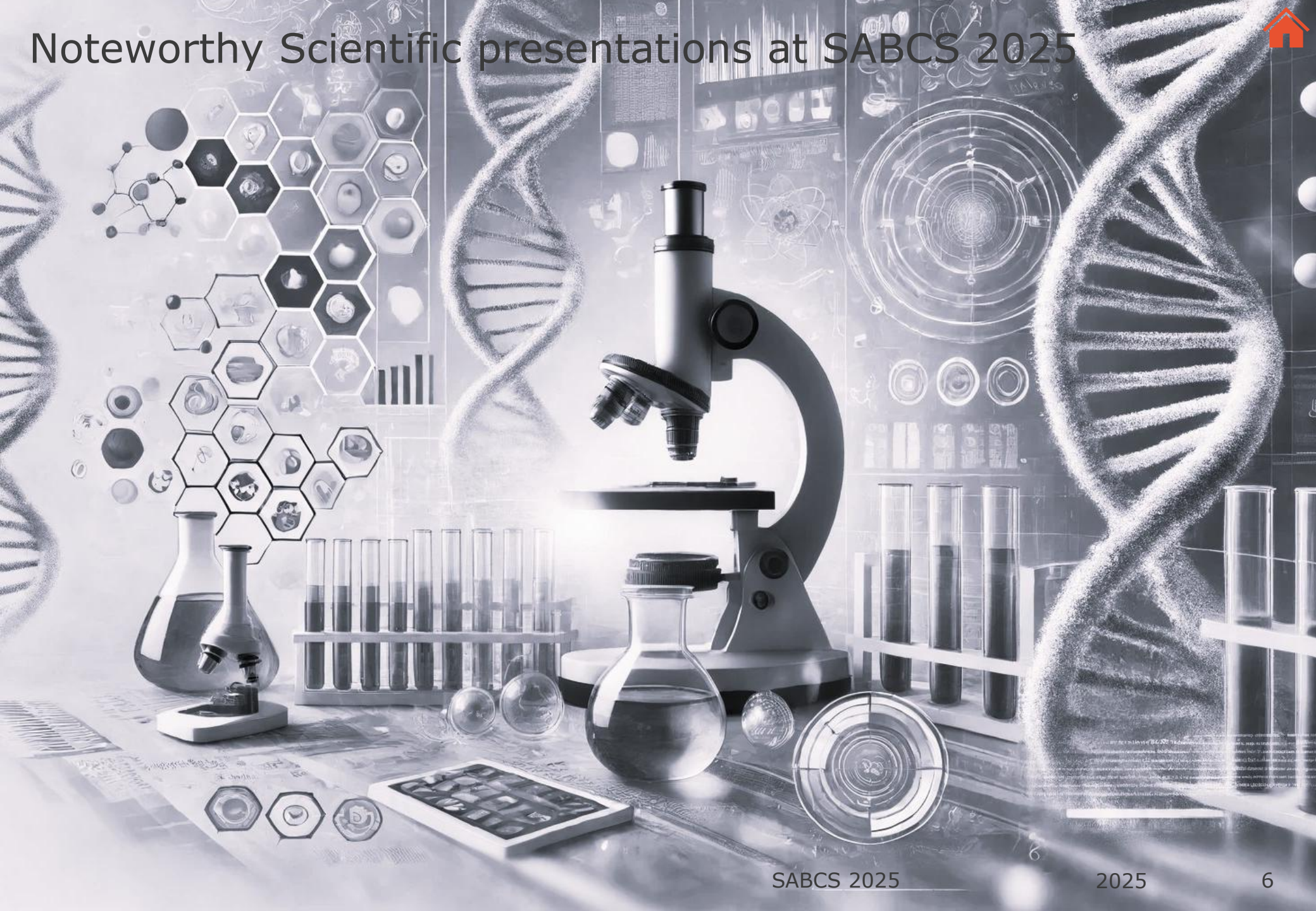
SABCS 2025– Conference Themes (1/2)

- **ADC intensification across disease stages:** Data will explore next-gen ADCs in HER2-low, HR+/HER2−, and TNBC, focusing on sequencing, combinations, and resistance mechanisms
- **Early TNBC biomarkers and tailoring:** Poster spotlights will prioritize early TNBC biomarker signatures, residual disease strategies, and adaptive post-neoadjuvant regimens to refine pCR-anchored risk stratification
- **HR+/HER2− escalation and de-escalation:** Trials will examine CDK4/6 inhibitor integration, chemotherapy omission, and adaptive endocrine strategies in genomically low-risk yet anatomically high-risk HR+/HER2− disease
- **Lobular breast cancer spotlight:** Dedicated ILC education and poster sessions will address distinct biology, imaging pitfalls, and tailored systemic approaches for invasive lobular carcinoma
- **Imaging-guided treatment adaptation:** Presentations will emphasize FDG-PET and advanced mammography (TMIST) for personalized therapy and screening strategies

SABCS 2025– Conference Themes (2/2)

- **Liquid biopsy and ctDNA-defined MRD:** Prospective registries will assess ctDNA assays like MAESTRO for predicting recurrence and guiding therapy in high-risk early breast cancer
- **Immunotherapy in early and metastatic settings:** Updates will refine chemo-immunotherapy strategies and explore combinations with PARP inhibitors or ADCs for early and advanced disease
- **Real-world outcomes and toxicity management:** Real-world data will characterize effectiveness and toxicity of ADCs, CDK4/6 inhibitors, and G-CSF regimens in metastatic settings
- **Survivorship, late effects, and supportive care:** Sessions will address cardiotoxicity, neurocognitive effects, fertility, and symptom management, integrating digital tools for survivorship
- **AI, digital pathology, and decision support:** Abstracts will showcase AI-driven slide analysis and risk models that enhance prognostication and treatment selection alongside genomic assays

Noteworthy Scientific presentations at SABCS 2025



Key Topics From Notable Presentations (1/10)

- **Triple-Negative Breast Cancer:** Advancements in chemotherapy combinations and the use of biomarkers such as Ki67, TILs, and immune signatures will be pivotal in improving survival outcomes and personalizing treatment strategies for TNBC patients at SABCS 2025

  - Residual TNBC and Post-Neoadjuvant Treatment Risk: Residual TNBC after neoadjuvant chemotherapy (NACT) carries a high risk of relapse, and integrating Ki67 and TILs could refine post-NACT risk stratification, guiding personalized therapy and better outcomes

  - Chemotherapy in TNBC: Carboplatin Efficacy: Carboplatin improves pCR and EFS in early and advanced TNBC. Although it offers no OS benefit, it remains a standard of care, with immune signatures serving as prognostic indicators for better EFS

  - Advanced Treatment Combinations for TNBC: New combinations like ADCs (e.g., TROP2-ADC) with immunotherapies (adebrelimab) are showing promising efficacy in pretreated advanced TNBC, offering potential in cases previously resistant to standard chemotherapy.

Key Topics From Notable Presentations (2/10)

- **DCIS / Early-Stage General:** The integration of personalized and less invasive approaches in managing early-stage breast cancer, particularly DCIS and axillary management, will likely become more prevalent, with ongoing research pushing for more individualized treatment strategies at SABCS 2025
  - Axillary Management Post-Neoadjuvant Endocrine Therapy (NET): After NET, axillary management remains unclear, but studies like ALTERNATE suggest that axillary surgery can be omitted in many cases with low-volume nodal disease, especially when BCS is achievable
  - Intensified Surveillance in High-Risk Early Breast Cancer: While intensive surveillance (including CT/PET-CT) may detect recurrences earlier, trials like INSPIRE show no clear benefit in terms of reducing recurrence-free survival (RFS) or distant metastasis-free survival (DMFS), warranting further investigation
  - Alternative Options for DCIS Management: Trials like LORETTA and RECAST focus on alternative strategies like tamoxifen for low-risk DCIS, with promising results for surgery-free survival. However, tamoxifen alone did not meet prespecified criteria, showing selective applicability for certain patient groups

Key Topics From Notable Presentations (3/10)

- **HER2-Low / HER2-Ultralow Breast Cancer:** At SABCS 2025, emerging data on HER3-targeted ADCs and T-DXd in HER2-low breast cancer will shape future treatment paradigms, while cross-resistance challenges from sequential ADCs will necessitate better biomarker-driven strategies
  - Sequential Topoisomerase-I ADC Use in HER2-Low MBC: Sequential use of topoisomerase-I antibody-drug conjugates (ADC) in HER2-low metastatic breast cancer (MBC) shows limited benefit due to cross-resistance. A need for predictive biomarkers to optimize ADC selection will be highlighted
  - Emerging HER3-Directed ADCs in HR+ HER2-Low Disease: HER3-targeted ADCs like YL202/BNT326 demonstrate promising efficacy in HR+ HER2-low metastatic breast cancer, providing new treatment options for previously underserved populations. Toxicity remains manageable with ongoing trials
  - T-DXd Efficacy in HER2-Low Metastatic Breast Cancer: Data from the DESTINY-Breast04 and DESTINY-Breast07 trials show strong efficacy of T-DXd in HER2-low MBC, highlighting its role in first-line and advanced stages. However, safety concerns, including ILD, remain important considerations

Key Topics From Notable Presentations (4/10)

- **HER2-Positive Breast Cancer:** There will be growing emphasis on optimizing HER2-targeted therapies through tailored sequencing and combination strategies for better disease control in both early and metastatic HER2+ breast cancer
  - Endocrine–HER2 Strategy Optimisation: ALTTO data are expected to position aromatase inhibitor–based endocrine therapy, including OFS in premenopausal women, as the preferred partner to anti-HER2 therapy in HR+/HER2+ early breast cancer
  - Stromal TILs as Predictive Biomarkers: Baseline stromal TILs will significantly predict pCR in HER2+ breast cancer, providing insights into immune-based risk stratification and influencing future HER2+ de-escalation strategies
  - HER2+ Advanced Breast Cancer: DP303c will outperform T-DM1 in HER2+ advanced breast cancer, showing significant improvements in PFS and ORR, positioning it as a promising new therapy with manageable safety

Key Topics From Notable Presentations (5/10)

- **HR+/HER2-Negative Breast Cancer:** Targeted therapies, including combination therapies with CDK4/6 inhibitors, BCL2 inhibitors, and next-generation SERDs, demonstrate promising clinical efficacy in ER+/HER2– metastatic breast cancer, with manageable safety profiles, highlighting the potential for personalized treatment strategies
  - CDK4/6 and BCL2 Inhibition: The PALVEN trial evaluated triplet therapy (letrozole, palbociclib, and venetoclax) in ER+/HER2–, BCL2+ metastatic breast cancer, showing strong efficacy with a 93% clinical benefit rate (CBR) and a progression-free survival (PFS) of 29.2 months. Toxicities were manageable, supporting further BCL2-CDK4/6 combinations
  - Next-Generation SERD (PF-07248144): In patients with ER+/HER2– metastatic breast cancer progressing after CDK4/6i and endocrine therapy (ET), PF-07248144 demonstrated superior objective response rates (ORR) and PFS compared to previous therapies, supporting its continued evaluation
  - Chidamide and Endocrine Therapy: In heavily pretreated HR+/HER2– advanced breast cancer, the combination of chidamide (an HDAC inhibitor) and fulvestrant showed encouraging disease control and manageable safety. Although ORR was 10%, the disease control rate (DCR) was 83.3%

Key Topics From Notable Presentations (6/10)

- **Metastatic Breast:** Innovative targeted therapies, including anti-metastatic nucleic acid treatments and novel immune-based approaches, offer promising efficacy and safety profiles in metastatic breast cancer, enhancing the precision of current treatment regimens
  - TTX-MC138 for Metastasis: TTX-MC138, a novel antisense oligonucleotide, demonstrated promising preclinical results in eradicating metastases. In Phase 0 and ongoing Phase 1/2 trials, it showed effective uptake by metastatic lesions and strong pharmacodynamic activity, with minimal toxicity, supporting its potential as a first-in-class anti-metastatic therapy
  - SYHX2011 - Novel Albumin-Bound Paclitaxel: SYHX2011, a new formulation of paclitaxel, achieved superior objective response rates (ORR) and significantly reduced hypersensitivity reactions compared to standard albumin-bound paclitaxel in patients with metastatic breast cancer, presenting a better-tolerated taxane option
  - Bria-IMT Immunotherapy: The Bria-IMT trial evaluated an allogeneic vaccine in combination with checkpoint inhibitors in heavily pretreated metastatic breast cancer patients. Early data showed that Bria-IMT is feasible, well-tolerated, and associated with promising biomarker-linked activity, supporting further clinical development

Key Topics From Notable Presentations (7/10)

- **Immunotherapy Across Subtypes :** Early detection of immune-related toxicities, proactive safety monitoring in ADC–IO regimens, and advanced ctDNA testing offer promising strategies for improving outcomes and personalizing treatment in metastatic breast cancer, enhancing the precision of immunotherapy
  - Immune-Related Toxicities as Predictors of Response: Early immune-related AEs such as muscle pain, joint pain, and mucositis were linked to higher odds of achieving a pCR in high-risk stage II/III breast cancer, suggesting that early symptoms could serve as biomarkers for predicting treatment outcomes and guiding therapy continuation
  - Proactive ILD Detection in ADC–IO Regimens: T-DXd combined with rilvegostomig, although associated with interstitial lung disease (ILD) risk, can be managed with six-weekly HRCT scans and real-time pulmonology reviews, preventing severe complications and allowing for continued treatment without major interruptions
  - ctDNA as a Prognostic Biomarker: ctDNA assays, particularly tissue-free methylation assays, were found to be highly predictive of relapse in high-risk TNBC patients, offering a scalable, biopsy-free option for monitoring minimal residual disease (MRD) and enabling personalized treatment strategies.

Key Topics From Notable Presentations (8/10)

- **Surgery & Radiotherapy:** Axillary surgery de-escalation, coupled with precise radiotherapy and tailored treatment plans, offers potential benefits for minimizing morbidity and optimizing outcomes in early and node-positive breast cancer, necessitating further investigation and personalized strategies
  - Tailored Axillary Surgery (TAS): TAS is a feasible, safe, and effective approach to reducing axillary morbidity in clinically node-positive breast cancer, with a similar non-TAS nodal positivity rate compared to SLN-positive cN0 trials. This supports further Phase III trials evaluating ALND omission within axillary de-escalation strategies
  - Axillary Surgery Omission in Node-Negative Disease: Omission of axillary surgery in early-stage, node-negative breast cancer does not compromise survival outcomes, offering a viable alternative for selected patients. Careful monitoring for slightly increased regional recurrence is still necessary
  - Radiotherapy's Role in Axillary De-Escalation: Incidental axillary irradiation in patients undergoing breast-conserving surgery (BCS) without sentinel lymph node biopsy (SLNB) shows substantial therapeutic benefit, highlighting the importance of considering radiotherapy alongside axillary surgery de-escalation

Key Topics From Notable Presentations (9/10)

- **Supportive Care, QoL, Toxicity, Lifestyle, Psychosocial:** Supportive care strategies, such as olanzapine for nausea, acupuncture for CIPN, and cryotherapy for nail toxicity, are crucial in managing treatment-related side effects and improving the quality of life in breast cancer patients. More research is needed to optimize these interventions and confirm their long-term benefits
  - Olanzapine's Impact on QOL: Olanzapine (OLZ) significantly improved QOL in breast cancer patients, particularly in those undergoing highly emetogenic chemotherapy, with nausea reduction being a primary mediator of this benefit. This supports OLZ integration into antiemetic regimens for these patients
  - Acupuncture for CIPN: Both real and sham acupuncture reduced chemotherapy-induced peripheral neuropathy (CIPN) symptoms in breast cancer patients on taxane therapy, though no significant differences between the two groups were observed. These findings suggest a nonspecific or placebo effect, warranting further investigation into supportive interventions for CIPN
  - Cryotherapy for Nail Toxicity: Cryotherapy significantly reduced docetaxel-induced nail toxicity in early breast cancer patients, making it an effective and scalable supportive-care strategy despite some discomfort during treatment sessions

Key Topics From Notable Presentations (10/10)

- **Screening, Prevention, Genetics, Disparities, Trial Enrollment:** Despite progress, underrepresentation of minority and young women in clinical trials persists. Addressing these disparities through tailored outreach, navigation tools, and inclusion in study designs is essential to ensure equitable participation and treatment benefits across all groups

  - Polygenic Risk Scores (PRS) in Genetic Carriers: PRS refines risk estimates for moderate-penetrance genes (ATM, CHEK2), but adds limited value for high-risk BRCA1/2 carriers. It supports gene-specific risk counseling

  - Age and Prognosis in BRCA1/2 Carriers: Very early age at diagnosis (≤30 years) does not worsen prognosis in BRCA1/2 carriers, suggesting that appropriate therapy minimizes age-related differences in survival

  - Tamoxifen and Endometrial Cancer Risk: Tamoxifen increases the risk of endometrial cancer in women under 54, emphasizing the need for vigilant monitoring in this population

Focus of Key Industry-Sponsored Sessions at SABCS 2025 (1/5)

- **Pfizer:**
  - Focus Areas: First-line therapy and maintenance in HER2+ metastatic breast cancer
  - Presentations will focus on personalizing first-line and maintenance therapy for HER2+ metastatic breast cancer to extend survival and elevate quality of life. Discussions will also cover how PROTAC ER degradation may shift the standard of endocrine therapies in metastatic breast cancer
- **AstraZeneca & Genentech:**
  - Focus Areas: HR+/HER2- metastatic breast cancer & Endocrine therapy
  - Sessions will explore optimizing treatment for frontline and heavily pretreated HR+/HER2- metastatic breast cancer, with a special focus on the integration of endocrine agents, CDK4/6 inhibitors, and targeted therapies to improve patient outcomes

Focus of Key Industry-Sponsored Sessions at SABCS 2025 (2/5)

- **Gilead Sciences & Helsinn Therapeutics:**
  - Focus Areas: Antibody-Drug Conjugates (ADCs) in Metastatic Breast Cancer
  - Investigators will discuss the role of ADCs in the management of triple-negative and HR-positive metastatic breast cancer, exploring the latest clinical findings and integration into current treatment regimens
- **MSD:**
  - Focus Areas: HR+/HER2- metastatic breast cancer & TROP2-targeting
  - Sessions will address the use of TROP2-targeting ADCs, immune checkpoint inhibitors (ICIs), and PARP inhibition in triple-negative breast cancer, along with the nuances of modern treatment paradigms for early-stage HR+/HER2- breast cancer

Focus of Key Industry-Sponsored Sessions at SABCS 2025 (3/5)

- **Celcuity, Inc:**
  - Focus Areas: Endocrine-resistant HR+/HER2- breast cancer
  - Discussions will highlight new approaches for managing endocrine-resistant HR+/HER2- advanced breast cancer, with a focus on integrating novel therapies to improve efficacy and patient outcomes
- **PeerView Institute for Medical Education:**
  - Focus Areas: CDK4/6 Inhibition & Endocrine therapies
  - Presentations will cover key steps to success with CDK4/6 inhibition in both early-stage and metastatic HR+/HER2- breast cancer, focusing on stratification, selection, sequencing, and specialty management. Additional discussions will explore new approaches to treating endocrine-resistant HR+/HER2- advanced breast cancer

Focus of Key Industry-Sponsored Sessions at SABCS 2025 (4/5)

- **Daiichi Sankyo, Inc. & AstraZeneca:**
  - Focus Areas: Antibody-Drug Conjugates (ADCs) in Breast Cancer
  - Presentations will focus on the earlier use of ADCs in breast cancer, exploring clinical breakthroughs and strategies to improve patient outcomes through innovative ADC applications
- **Arvinas:**
  - Focus Areas: PROTAC ER Degradation in Metastatic Breast Cancer
  - Sessions will explore the expanding arsenal of endocrine therapies for HR+/HER2- metastatic breast cancer, emphasizing how PROTAC ER degradation could shift treatment standards and provide new therapeutic options for patients

Focus of Key Industry-Sponsored Sessions at SABCS 2025 (5/5)

- **Stemline Therapeutics (A Menarini Group):**
  - Focus Areas: Endocrine therapy & Targeted therapies in HR+/HER2- breast cancer
  - Investigators will discuss the optimal management strategies for HER2-positive breast cancer, with a focus on innovative approaches to endocrine therapy and the role of targeted therapies in improving clinical outcome

Notable Presentations And Late-breaking Sessions At SABCS 2025

Notable Presentations At SABCS 2025
Triple-Negative Breast Cancer (TNBC) (1/7)

Date	Title	Author	Summary
09 Dec 2025	Prognostic Markers in Residual Tumors after neoadjuvant chemotherapy (NACT) for Early Triple-negative Breast Cancer (TNBC) – a Pooled Analysis from nine Neoadjuvant GBG/AGO-B Trials	Johannes Holtschmidt	• **Introduction:** Residual TNBC after NACT carries high relapse risk, and pCR alone incompletely reflects prognosis. Ki67 and TILs may better characterize biologic response and residual risk. • **Methodology:** Across nine GBG/AGO-B trials, 640 TNBC patients with residual invasive disease had paired baseline and post-NACT Ki67/TILs assessed. Primary endpoint was DDFS; OS secondary. • **Results:** Residual Ki67 >15% predicted worse DDFS (HR 1.71) and OS (HR 2.02). Combined Ki67 >15% + TILs ≤10% identified the poorest-risk group (5y OS 48%). Low Ki67 + high TILs conferred best outcomes, even within ypT1N0 disease. • **Conclusions:** Integrating Ki67 and TILs in residual TNBC refines post-NACT risk stratification and may guide personalized post-neoadjuvant therapy.
09 Dec 2025	Pooled analysis of the BrighTNess, CALGB 40603 (Alliance), and GeparSixto clinical trials identifies the impact of neoadjuvant carboplatin on pCR and survival in early-stage triple-negative breast cancer	Brooke M Felsheim	• **Introduction:** TNBC remains aggressive despite pCR being strongly prognostic. Carboplatin became SOC after KEYNOTE-522, yet its precise benefit and predictive biomarkers remain unclear. • **Methodology:** Pooled data from BrighTNess, CALGB 40603, and GeparSixto (n=1084) evaluated carboplatin's effect on pCR, EFS, OS, and biomarker relevance (gBRCA, eight immune/hypoxia signatures) using mixed-effects logistic and Cox models. • **Results:** Carboplatin improved pCR (OR 1.89) and EFS (HR 0.71) but not OS. gBRCA carriers derived EFS benefit (HR 0.50) without pCR/OS gains. Six immune signatures predicted higher pCR; four correlated with better EFS/OS, but none predicted carboplatin benefit. • **Conclusions:** Carboplatin improves pCR and EFS in stage II–III TNBC, supporting its SOC role. Immune signatures are prognostic but not predictive, highlighting unmet need for carboplatin-specific biomarkers.

Notable Presentations At SABCS 2025
Triple-Negative Breast Cancer (TNBC) (2/7)

Date	Title	Author	Summary
09 Dec 2025	Adjuvant epirubicin plus cyclophosphamide followed by taxanes with or without carboplatin for early stage triple-negative breast cancer (RJBC 1501): a randomized controlled phase III trial	Xiaosong Chen	• **Introduction:** Early-stage TNBC carries high recurrence risk; the value of adding adjuvant carboplatin to EC-T remains uncertain. • **Methodology:** RJBC 1501 randomized 786 post-surgery TNBC patients 1:1 to EC-T vs EC-TCb. Primary endpoint was DFS; secondary endpoints included DDFS, OS, and safety. • **Results:** Carboplatin significantly improved DFS (HR 0.66), DDFS (HR 0.61), and OS (HR 0.39). Three-year DFS increased from 89.8% to 93.1%. Hematologic grade 3–4 toxicity was higher with EC-TCb (49.9% vs 38.7%), mainly neutropenia and thrombocytopenia. • **Conclusions:** Adjuvant carboplatin meaningfully improves survival in early-stage TNBC with manageable added toxicity.
09 Dec 2025	Effect of adjuvant carboplatin intensified chemotherapy versus standard chemotherapy on survival in women with high-risk early-stage triple-negative breast cancer (CITRINE): a phase 3 randomized trial	Yin Liu	• **Introduction:** High-risk early-stage TNBC has substantial recurrence risk, and the value of adding carboplatin to standard anthracycline/taxane adjuvant chemotherapy remains debated. • **Methodology:** In this open-label phase III trial (NCT04296175), 808 women with operable high-risk TNBC were randomized 1:1 to EC→weekly paclitaxel ± carboplatin. Primary endpoint: DFS; secondary endpoints: RFS, D-DFS, OS, safety. • **Results:** Carboplatin significantly improved 3-year DFS (92.3% vs 85.8%; HR 0.64), RFS (HR 0.59), D-DFS (HR 0.61), and OS (98.0% vs 94.0%; HR 0.41). Benefit was consistent across subgroups. Grade 3–4 toxicity increased (66.7% vs 55%) but without treatment-related deaths. • **Conclusions:** Adjuvant carboplatin meaningfully enhances survival in high-risk TNBC with acceptable incremental toxicity

Notable Presentations At SABCS 2025
Triple-Negative Breast Cancer (TNBC) (3/7)

Date	Title	Author	Summary
09 Dec 2025	Impact of Immune Checkpoint Inhibition (CPI) on Fertility in Young Women with Early Triple-Negative Breast Cancer (TNBC) receiving neoadjuvant Chemotherapy (NACT): A Prospective Substudy of the NSABP B-59/GBG-96-GeparDouze Trial	Mattea Reinisch	• **Introduction:** NACT causes substantial ovarian toxicity in young TNBC patients, but the added effect of checkpoint inhibitors (CPI) on ovarian failure is unclear. • **Methodology:** In this prospective substudy (≤45 yrs), patients received anthracycline/cyclophosphamide/taxane/carboplatin NACT ± atezolizumab. CIOF was defined by postmenopausal FSH/E2 levels. FSH, E2, and AMH were measured at baseline, end of therapy, and 6–24 months post-NACT. • **Results:** Among 133 evaluable patients, CIOF occurred in 34.2% at EOT and persisted in 10% at 24 months, with higher rates in the CPI arm (7.5% vs 2.5%). AMH dropped universally at EOT; recovery remained limited (≈26%). FSH stayed postmenopausal only with CPI. • **Conclusions:** CPI-NACT increases ovarian failure risk and reduces hormonal recovery, underscoring the need for proactive fertility counselling.
10 Dec 2025	Safety analysis of ASCENT-03, a phase 3 study of sacituzumab govitecan (SG) vs chemotherapy (chemo) for previously untreated advanced triple-negative breast cancer (TNBC) in patients (pts) who are not candidates for PD-(L)1 inhibitors (PD-[L]1i)	Sara Hurvitz	• **Introduction:** ASCENT-03 showed SG improves PFS over chemotherapy in untreated advanced TNBC, but detailed safety profiling is essential for clinical adoption. • **Methodology:** Pts were randomized 1:1 to SG or chemotherapy (taxane or gemcitabine+carboplatin). Exposure-adjusted incidence rates, severity, timing, and supportive-care use for key TEAEs were evaluated. • **Results:** Among 551 pts, grade ≥3 TEAEs were similar (SG 66% vs chemo 62%). SG caused more diarrhea (54%/9%) but comparable neutropenia to chemo (68%/45%). EAIRs of neutropenia were similar despite longer SG exposure. Dose reductions/discontinuations were fewer with SG; G-CSF and antidiarrheals were more frequently required. • **Conclusions:** SG shows a manageable, predictable safety profile, comparable severe toxicity, and fewer treatment modifications than chemotherapy, supporting its frontline use with proactive AE management.

Notable Presentations At SABCS 2025
Triple-Negative Breast Cancer (TNBC) (4/7)

Date	Title	Author	Summary
10 Dec 2025	Preliminary data from a global multicohort Phase2 randomized trial of pumitamig (PD-L1 × VEGF-A bsAb) + chemotherapy for 1L/2L+ locally advanced/metastatic TNBC	Peter Schmid	• **Introduction:** Pumitamig, a PD-L1/VEGF-A bispecific antibody, aims to enhance immune activation and VEGF-A blockade, with prior promising activity in Chinese TNBC cohorts. • **Methodology:** This global phase II trial evaluated pumitamig (15–20 mg/kg) plus nab-paclitaxel or other chemotherapies in 1L/2L+ LA/mTNBC. Endpoints included ORR, tumor shrinkage, ctDNA clearance, and safety. • **Results:** Among 69 pts, Cohort 1 achieved uORR 69.2% and cORR 56.4%, with ≥40% mean tumor reduction and ctDNA clearance up to 71% at 20 mg/kg. Cohort 2 showed uORR 64.7%. Responses were consistent across CPS levels. Grade ≥3 AEs occurred in 31–45%, with no new safety signals. • **Conclusions:** Pumitamig plus chemotherapy demonstrates robust, PD-L1–independent activity and manageable toxicity, supporting advancement into phase III evaluation.
11 Dec 2025	Exploratory phase II trial of camrelizumab (an anti-PD-1 antibody) combined with apatinib (a VEGFR-2 inhibitor) and chemotherapy as a neoadjuvant therapy for triple-negative breast cancer (NeoPanDa03): efficacy, safety and biomarker analysis	Ting Luo	• **Introduction:** TNBC relies heavily on chemotherapy but outcomes remain suboptimal. This study evaluates an intensified neoadjuvant regimen combining camrelizumab, apatinib, and alternating chemotherapy. • **Methodology:** Single-arm Phase II trial (n=35) used camrelizumab, apatinib, nab-paclitaxel, and EC across 12 cycles. Immune, genomic, and microenvironmental analyses integrated Olink proteomics and RNA-seq. Novel predictive (PRPscore) and efficacy (EAscore) systems were developed. • **Results:** tpCR reached 67.6% and ORR 94.1%. Grade 3–4 hepatotoxicity was most common; no major safety signals. pCR tumors showed higher TP53 mutation rates; non-pCR tumors had more HRD-high status, reduced CD4+ T-cells, and activated fibroblasts. PRPscore predicted pCR (AUC 0.823); EAscore evaluated response (AUC 0.93). • **Conclusions:** This camrelizumab–apatinib–chemotherapy regimen demonstrated strong efficacy and acceptable safety. Dual-score systems offer promising tools for personalized neoadjuvant TNBC management.

Notable Presentations At SABCS 2025
Triple-Negative Breast Cancer (TNBC) (5/7)

Date	Title	Author	Summary
11 Dec 2025	Septin9 isoforms predict taxane efficacy in triple negative breast cancer	Jycole Bush	• **Introduction:** Taxanes are central to breast cancer therapy, yet no biomarkers predict response. Mechanistically distinct SEPT9 isoforms—oncogenic sept9_i1 and microtubule-nonbinding sept9_i2—may influence taxane sensitivity. • **Methodology:** A retrospective metastatic cohort and a prospective neoadjuvant study assessed sept9 isoform expression (qRT-PCR, IHC) and correlated levels with survival and pCR. Isogenic cell lines interrogated mechanistic effects on microtubule dynamics. • **Results:** TNBC tumors showed low sept9_i1 and high sept9_i2. Elevated sept9_i2 correlated with improved overall survival in TNBC and trended toward higher pCR. In vitro, sept9_i1 reduction modestly increased taxane efficacy; sept9_i2's clinical benefit was not replicated mechanistically. Taxanes shifted septin–cytoskeleton interactions. • **Conclusions:** Sept9_i2 emerges as a promising taxane-response biomarker, particularly in TNBC. Further functional validation is required to confirm causality and guide isoform-informed treatment strategies.
11 Dec 2025	Efficacy of a novel BCL-xL degrader, DT2216, in the treatment of triple-negative breast cancer	Yuxiang Lin	• **Introduction:** TNBC has limited treatment options and poor outcomes. BCL-xL is overexpressed in TNBC and promotes chemoresistance, but conventional BCL-xL inhibitors cause thrombocytopenia. DT2216, a PROTAC, selectively degrades BCL-xL in tumors while sparing platelets. • **Methodology:** Bioinformatic profiling, TNBC vs ER+ cell line assays, BCL-xL knockdown studies, DT2216 monotherapy testing, and combination assays with paclitaxel/carboplatin were performed; in vivo validation is ongoing. • **Results:** BCL-xL was elevated in TNBC and linked to poor prognosis. TNBC cells were highly dependent on BCL-xL. DT2216 selectively inhibited TNBC growth and synergistically enhanced paclitaxel and carboplatin cytotoxicity. • **Conclusions:** DT2216 shows strong subtype-specific activity and synergy with chemotherapy, supporting its potential as a novel therapeutic strategy for TNBC pending in vivo confirmation.

Notable Presentations At SABCS 2025
Triple-Negative Breast Cancer (TNBC) (6/7)

Date	Title	Author	Summary
11 Dec 2025	Real World Analysis of Efficacy, Toxicity, and Treatment Patterns of Pembrolizumab-Containing Regimens for Older Adults with Early-Stage Triple Negative Breast Cancer	Claire Smith	• **Introduction:** Older adults with early-stage TNBC are underrepresented in pembrolizumab trials, limiting evidence on efficacy and tolerability. • **Methodology:** A real-world review of women ≥65 (n=85) assessed RDI, toxicities, hospitalizations, discontinuation, IRAEs, and pCR following neoadjuvant pembrolizumab-based regimens. • **Results:** Median RDI was 90%; only 55% reached ≥85%. Hospitalizations (41%), early discontinuation (41%), IRAEs (39%), and three treatment-related deaths occurred. Patients >70 had more IRAEs and lower RDI. pCR was 43% and not linked to age or RDI • **Conclusions:** High toxicity and modest pCR highlight the need for safer regimens in older TNBC patients.
11 Dec 2025	Real-world efficacy of non-anthracycline neoadjuvant chemo-immunotherapy in early-stage triple negative breast cancer: a retrospective two site cohort study	Amanda K Mennie	• **Introduction:** Optimal neoadjuvant therapy for lower-risk (T1–T2 N0) TNBC is unclear, particularly regarding anthracycline omission. • **Methodology:** Retrospective analysis of 83 early TNBC cases (2021–2024) comparing pCR between KEYNOTE-522 and non-anthracycline carboplatin/paclitaxel+pembrolizumab. TIL status assessed as a predictive factor. • **Results:** pCR rates were similar (57.6% K522 vs 70.8% non-anthracycline; p=0.45). TIL-positive tumors had significantly higher pCR (75.8% vs 52%; p=0.032). No baseline imbalances explained differences. • **Conclusions:** Non-anthracycline chemoimmunotherapy may be effective for selected early TNBC. TILs remain a promising predictive biomarker warranting further validation

Notable Presentations At SABCS 2025
Triple-Negative Breast Cancer (TNBC) (7/7)

Date	Title	Author	Summary
11 Dec 2025	Risk and Pattern of Relapse in Triple-Negative Breast Cancer with Pathological Complete Response after Neoadjuvant Treatment: Updated Results from the European GAMBIT Real-world Study	Maria Vittoria Dieci	• **Introduction:** Although pCR after NAT improves TNBC outcomes, relapse remains heterogeneous. Identifying high-risk biology post-pCR is critical. • **Methodology:** GAMBIT included 2,458 stage I–III TNBC patients; 1,193 achieved pCR. TILs (n=691) and first distant relapse site were analyzed using competing-risk models; DRFS was the primary endpoint. • **Results:** Clinical nodal positivity independently predicted worse DRFS (HR 2.38) and OS (HR 3.19). cN+/low-TILs patients showed markedly inferior 5-year DRFS (83%) and OS (86%). Despite lower overall CNS relapse vs RD, CNS-only relapse rates were similar; cN+/low-TILs exhibited CNS relapse patterns resembling RD. • **Conclusions:** pCR does not ensure uniformly favorable prognosis. cN+/low-TILs define a high-risk subgroup requiring post-pCR risk-adapted strategies and CNS-directed therapeutic escalation.
12 Dec 2025	Trop2-directed antibody-drug conjugate shr-a1921 combined with pd-l1 inhibitor adebrelimab for patients with advanced triple negative breast cancer: results from a phase 2, multi-cohort, open-label, non-controlled trial	Tao Wang	• **Introduction:** New ADC–immunotherapy combinations may enhance activity in advanced HER2-negative/TNBC, but clinical data are scarce. • **Methodology:** In this phase II open-label trial, pretreated advanced TNBC patients received SHR-A1921 (TROP2-ADC) plus adebrelimab Q3W. Primary endpoint: ORR; secondary endpoints included DCR, CBR, DoR, PFS, OS, and safety. • **Results**: Among 15 pts (53% PD-L1–negative; 87% visceral disease), confirmed ORR was 46.7%, DCR 86.7%, median DoR 4.6 mo, and median PFS 5.1 mo. Responses occurred irrespective of PD-L1 status. TRAEs were universal but mostly grade 1–2; grade ≥3 events occurred in 13%. • **Conclusions:** SHR-A1921 plus adebrelimab shows promising efficacy with manageable toxicity in pretreated TNBC, supporting further development.

Notable Presentations At SABCS 2025
DCIS / Early-Stage General (1/7)

Date	Title	Author	Summary
09 Dec 2025	Surgical outcomesin the ALTERNATE trial (Alliance A011106) -a randomized phase 3 neoadjuvant endocrine therapy (NET) trial in postmenopausal women with clinical stage II/III estrogen receptor positive (ER+) and HER2 negative (HER2-) breast cancer (BC)	Ann Marilyn Leitch	• **Introduction:** Limited guidance exists for axillary management after neoadjuvant endocrine therapy (NET), where pCR is rare. ALTERNATE evaluated real-world surgical patterns in ER+/HER2– stage II/III disease. • **Methodology:** 933 postmenopausal patients received 6 months of anastrozole, fulvestrant, or both. Standard-of-care breast surgery and mandatory SLNB±ALND were performed to assess PEPI/RCB. Surgeons pre-declared BCS eligibility; imaging and pathology informed post-NET decisions. • **Results:** BCS was achieved in 69.9%, including 43.8% initially ineligible. Despite low nodal pCR, many node-positive patients had only 1–2 positive LNs. SLNB-alone use aligned with Z0011—common in BCS but less in mastectomy. • **Conclusions:** NET substantially increases BCS feasibility. Low-volume nodal disease post-NET suggests ALND omission may be appropriate, though long-term recurrence data are needed.
10 Dec 2025	Randomized phase III study comparing intensive follow-up with standard follow-up in post-operative high risk breast cancer <INSPIRE trial: JCOG1204>: the early analysis of Relapse-free survival and Onset of recurrence	Takashi Hojo	• **Introduction:** Despite guideline-recommended annual mammography, advances in systemic therapy, imaging, and MRD assays raise interest in intensified surveillance. INSPIRE tested whether early detection improves outcomes in high-risk postoperative breast cancer. • **Methodology:** In this phase III trial, 1034 patients were randomized to standard follow-up (annual MMG, tumor markers) versus intensive follow-up (MMG, semiannual CT/PET-CT, frequent tumor markers). Primary endpoint was OS; secondary endpoints included RFS and DMFS. • **Results:** After 83-month median follow-up, 7-year RFS (73.0% vs 73.6%) and DMFS (74.1% vs 75.5%) were identical between arms. Intensive surveillance detected recurrence earlier but did not reduce recurrence rates. • **Conclusions:** Intensive imaging accelerates detection but offers no RFS/DMFS benefit. Longer follow-up is needed to determine OS impact.

Notable Presentations At SABCS 2025
DCIS / Early-Stage General (2/7)

Date	Title	Author	Summary
10 Dec 2025	2.5-year follow-up results of a five-fraction external beam radiotherapy accelerated partial breast irradiation for early-stage breast cancer after breast-conserving surgery	Nikolai Strusberg Fernandez	• **Introduction:** APBI offers a shorter, targeted alternative to whole-breast irradiation. This study evaluates feasibility and safety of the 5-fraction Florence regimen in carefully selected early-stage patients. • **Methodology:** Aretrospective review of 54 women treated with 30 Gy/5-fraction external-beam APBI, meeting strict criteria (pTis/pT1–2, ≤30 mm, node-negative). Outcomes included toxicity (CTCAE v5.0), recurrence, and treatment tolerance over ~35 months of follow-up. • **Results:** No locoregional or distant recurrences occurred. Toxicity was minimal—only grade 1 acute (24.1%) and late (7.4%) events, with rare asymptomatic fat necrosis/fibrosis. • **Conclusions:** The 5-fraction APBI regimen is highly feasible, well tolerated, and provides excellent short-term control, reinforcing its role as a standard option for selected early-stage patients.
10 Dec 2025	Preliminary Results from the NEOMET Trial: Nutritional and Exercise Interventions During Neoadjuvant Chemotherapy in Early Breast Cancer	Ida Taglialatela	• **Introduction:** Metabolic status influences neoadjuvant chemotherapy (NAT) response in early breast cancer. Prior SeNEOAD metabolomics identified fatty-acid deficits in non-pCR patients, supporting supplementation strategies • **Methodology:** NEOMET randomizes patients to NAT alone or combined with omega-3/hexadecenoic-acid supplementation, supervised exercise, or both. Body composition (BIA) and QoL (EORTC QLQ-C30/BR45) were assessed pre- and post-NAT. • **Results:** Among 27 enrolled, 15 with paired data showed worsening global QoL but improved physical functioning. Lean body mass trended upward (44.9→46.4 kg), muscle mass increased, and toxicities were comparable across arms. • **Conclusions:** Early findings show feasibility and safety of metabolic–exercise interventions during NAT, with signals toward preserved muscle mass and functional benefit pending full metabolomic analyses.

Notable Presentations At SABCS 2025
DCIS / Early-Stage General (3/7)

Date	Title	Author	Summary
10 Dec 2025	Omitting Sentinel Lymph Node Dissection After Neoadjuvant Treatment in Early Breast Cancer: Interim Results from the VENUS Randomized Clinical Trial	Giuliano M Duarte	• **Introduction:** SLND omission after neoadjuvant therapy (NAT) remains understudied. VENUS evaluates the safety of omitting axillary surgery in clinically/ultrasound N0 early breast cancer, including patients treated with NAT. • **Methodology:** Interim analysis of 788 women randomized to SLND or no axillary surgery. NAT and upfront-surgery cohorts were compared for tumor biology, SLND positivity, and early axillary recurrence over 22 months. • **Results:** Only 8% received NAT, characterized by younger age and aggressive subtypes (HER2+, TNBC). SLND positivity was lower post-NAT (4.2% vs 19.9%). No axillary recurrences occurred. • **Conclusions:** Early findings support continued NAT patient enrollment. SLND omission appears feasible, though small NAT numbers warrant longer follow-up.
11 Dec 2025	Early dynamics of tumor microenvironment in triple negative or ER-low breast cancer: updated analyses from window of opportunity (WOO) MEDIOLA trial of olaparib and durvalumab	Jiwon Koh	• **Introduction:** Early immune–metabolic shifts during PARP inhibition may predict neoadjuvant response in TNBC/ER-low disease. • **Methodology:** Fifty-four patients received 4 weeks of olaparib + durvalumab before NAC with serial PET, biopsies, PD-L1, RNAseq, mIHC, and AI-based H&E segmentation. • **Results:** pCR was 70.4%. Early metabolic and tumor-cell reductions at 2 weeks strongly associated with fHRD and pCR. PARP inhibition triggered rapid TC decline, marked CD8+ T-cell expansion, and subtype shifts (Basal→LumA; BLIS→BLIA). Relapsing tumors showed EMT and cell-cycle pathway upregulation. • **Conclusions:** Two-week microenvironmental changes best predicted pCR, underscoring PARP-driven immune activation and the value of longitudinal biopsies.

Notable Presentations At SABCS 2025
DCIS / Early-Stage General (4/7)

Date	Title	Author	Summary
11 Dec 2025	Omission of Axillary Dissection in ypN1mi Breast Cancer Patients after Neoadjuvant Chemotherapy: Preliminary Results from the NEONOD2 Trial	Damiano Gentile	• **Introduction:** Whether ALND is necessary for initially cN+ patients who convert to cN0 after NAC but have SLN micrometastasis remains unclear. NEONOD2 tests safety of ALND omission. • **Methodology:** Prospective trial enrolling cN+ patients downstaged to cN0 post-NAC. SLNB categorized patients as ypN1mi (experimental) or ypN0 (standard). Primary endpoint: RFS. • **Results:** Among 449 patients, 70 had ypN1mi. At 21.8-month follow-up, recurrences were low (4.3% vs 1.4%), with no isolated axillary failures and no deaths in the micrometastatic group. • **Conclusions:** Early findings support safe ALND omission pending longer follow-up.
11 Dec 2025	The single-arm confirmatory trial of tamoxifen alone without surgery for low-risk DCIS of the breast with ER-positive HER2-negative (LORETTA trial: JCOG1505)	Hiroji Iwata	• **Introduction:** DCIS incidence is rising, prompting interest in nonsurgical options. LORETTA tests tamoxifen (TAM) alone for ER-positive, low-risk DCIS. • **Methodology:** Single-arm trial enrolling women ≥40 with NG1–2, HER2-negative, ≤25 mm DCIS. Patients received TAM 20 mg/day without surgery. Primary endpoint: 5-year CIPIC, with efficacy confirmed if the upper 95% CI ≤7%. • **Results:** Among 341 patients, 5-year CIPIC was 9.8%, exceeding the prespecified threshold. Invasion correlated with imaging size, not grade or biomarkers. Surgery-free survival was 82%; grade ≥3 AEs occurred in 3.8%. • **Conclusions:** TAM alone did not meet criteria but showed low event rates, suggesting selective applicability.

Notable Presentations At SABCS 2025
DCIS / Early-Stage General (5/7)

Date	Title	Author	Summary
11 Dec 2025	Radiation doses and fractionation schedules in non-low-risk ductal carcinoma in situ in the breast (BIG 3-07/TROG 07.01): final 10-year analysis of a randomised, factorial, multicentre, open-label, phase 3 study	Boon H Chua	• **Introduction:** WBI lowers recurrence in DCIS, but the added benefit of a tumor-bed boost for non–low-risk DCIS required long-term validation. • **Methodology:** In this international phase III trial (n=1608), patients received conventional or hypofractionated WBI with or without a 16-Gy boost. Primary endpoint: time to local recurrence • **Results:** At 10.2-year median follow-up, boost significantly improved local-recurrence–free survival (93% vs 87%; HR 0.49). Disease-recurrence rates favored boost; OS was similar. Toxicities (induration, pain) were higher with boost. Fractionation had no impact. • **Conclusions:** Boost reduces recurrence but increases late toxicity; hypofractionation remains safe.
11 Dec 2025	Wisdom and mypebs: personalized breast cancer screening trials operating in distinct international contexts	Katherine Leggat-Barr	• **Introduction:** WISDOM and MyPeBS are large US–EU/Israel risk-based screening trials evaluating whether personalized breast cancer screening maintains safety while reducing unnecessary imaging. • **Methodology:** Both randomized women aged ~40–74 to risk-based vs standard screening, using BCSC+PRS models and risk-tiered screening frequencies. Recruitment differed: opportunistic (US) vs systematic (EU). • **Results:** Risk distributions were nearly identical across trials. Low-risk screening frequency differed most (biennial ≥50 in WISDOM vs 4-year interval in MyPeBS). Baseline contrasts included higher BMI, biopsies, family history, HRT use, and education in WISDOM. • **Conclusions:** Aligned risk structures and complementary practice differences enhance generalizability and potential practice impact.

Notable Presentations At SABCS 2025
DCIS / Early-Stage General (6/7)

Date	Title	Author	Summary
11 Dec 2025	Neoadjuvant Aromatase Inhibitor Therapy Decreases Radiographic Tumor Size: Initial Results from the NAOMI Trial	Lillian Lawrence	• **Introduction:** ER-positive breast cancers frequently respond to neoadjuvant aromatase inhibitors (AIs), but radiographic assessment of early response is understudied. • **Methodology:** Forty postmenopausal women with stage I–III ER+/HER2− disease had pre- and post-AI imaging (mean AI duration 6.7 weeks). Tumor size changes on mammography/ultrasound were compared with pathology. • **Results:** Mean tumor size decreased from 19.4 mm to 14.8 mm (p<.001), with shrinkage in 68%. Larger baseline tumors showed greater reduction. Correlation between post-AI imaging and pathology was moderate (r=0.69). • **Conclusions:** Short-course neoadjuvant AI yields measurable radiographic shrinkage. Imaging may guide surgical planning, though lobular tumors require separate evaluation.
11 Dec 2025	Initial results from RECAST DCIS: Multicenter platform trial testing active surveillance and novel endocrine therapy agents for DCIS management	Kelly C Hewitt	• **Introduction:** DCIS is biologically heterogeneous, and many cases are overtreated. RECAST evaluates whether upfront endocrine therapy can identify patients suitable for long-term active surveillance (AS). • **Methodology:** Hormone receptor–positive DCIS patients undergo baseline MRI and are randomized to four endocrine regimens. MRI at 3 and 6 months assesses response; those with favorable imaging may continue AS for 3 years. Primary endpoint: proportion remaining on AS at 7 months. • **Results:** Among >50 enrolled, AEs were only grade 1–2. Of 25 evaluable at ≥6 months, 88% remained on AS; imaging progression occurred in 8%. One invasive cancer was detected at surgery. • **Conclusions:** Early data support safety, feasibility, and strong AS retention, highlighting endocrine response as a tool for individualized DCIS management.

Notable Presentations At SABCS 2025
DCIS / Early-Stage General (7/7)

Date	Title	Author	Summary
11 Dec 2025	Five-year analysis of distant disease-free survival (DDFS) across key subgroups from the phase 3 NATALEE trial of ribociclib (RIB) plus a nonsteroidal aromatase inhibitor (NSAI) in patients with HR+/HER2– early breast cancer (EBC)	Sara Hurvitz	• **Introduction:** Distant recurrence remains a major threat in high-risk HR+/HER2– EBC. NATALEE previously showed invasive and distant recurrence benefits with ribociclib (RIB) + NSAI. • **Methodology:** Patients with stage IIA–III disease were randomized to RIB + NSAI vs NSAI alone. The prespecified 5-year landmark analysis assessed DDFS across anatomic and clinical subgroups. • **Results:** With 55.5-month follow-up, RIB + NSAI significantly improved DDFS (HR 0.709) and distant-recurrence–free survival (HR 0.699). Benefits were consistent across stages IIA–IIIC and nodal groups (N0 HR 0.539; N+ HR 0.723), with fewer distant recurrences at all metastatic sites. • **Conclusions:** DDFS benefits persist two years post-RIB, supporting adjuvant RIB + NSAI as a recurrence-reducing strategy across broad high-risk HR+/HER2– subgroups.
12 Dec 2025	Pathologic complete response rates (pCR) after the novel HER2 ADC ARX788: Results from the I-SPY2.2 trial	Paula R Pohlmann	• **Introduction:** I-SPY2.2 evaluates response-adaptive neoadjuvant strategies using molecular Response Predictive Subtypes (RPS). ARX788, a next-generation HER2 ADC, was tested in HER2+/Luminal (S6) and HER2+/non-Luminal (S5) disease. • **Methodology:** Patients received ARX788 Q3W×4 in Block A with MRI-guided early-surgery decisions. Bayesian models compared pCR to subtype-specific Dynamic Controls drawn from historical I-SPY cohorts. • **Results:** Among 100 patients, pCR reached 63% overall; 82% achieved RCB0/1 without AC. Forty underwent surgery after Block A, 82% with RCB0/1. S6 subtype pCR (39%) exceeded its DC (17%). Toxicities included ocular events (95%, 9% grade 3) and rare pneumonitis. • **Conclusions:** ARX788 shows strong subtype-driven efficacy enabling chemotherapy de-escalation, reinforcing response-adaptive, molecularly guided neoadjuvant treatment.

Notable Presentations At SABCS 2025
HER2-Low / HER2-Ultralow Breast Cancer (1/5)

Date	Title	Author	Summary
10 Dec 2025	Evidence Accumulates Against Sequencing Topo1-ADCs in HER2-Low Metastatic Breast Cancers: results from International, retrospective, real-world ADC-Low-Europe cohort.	Francois Poumeaud	• **Introduction:** Sequential topoisomerase-I ADC use is recommended in HER2-low MBC, but emerging data suggest limited benefit from a second ADC due to potential cross-resistance. • **Methodology:** A European retrospective study of 331 HER2-low MBC patients treated with sacituzumab govitecan (SG) and trastuzumab deruxtecan (T-DXd), evaluating progression-free survival on ADC2 (PFS2) • **Results:** Median PFS2 was only 2.6 months. Primary resistance rose from 25% on ADC1 to 66% on ADC2. Consecutive ADC1→ADC2 sequencing improved PFS2 modestly (3.0 months). T-DXd as ADC2 outperformed SG. • **Conclusions:** Sequential TOPO1-ADCs yield poor outcomes, reinforcing the need for predictive biomarkers and optimized ADC1 selection.
10 Dec 2025	First disclosure of efficacy and safety data for YL202/BNT326 (HER3 antibody-drug conjugate [ADC]) in advanced or metastatic HR+/HER2 null and HER2-low breast cancer: Phase 2 trial results	Jian Zhang	• **Introduction:** YL202/BNT326 is a HER3-targeting topoisomerase-I ADC developed for HR+ metastatic breast cancer with HER2-null to HER2-low expression—populations with limited ADC options. • **Methodology:** In this phase 2 trial (n=75), patients previously treated with CDK4/6 inhibitors and endocrine therapy received YL202/BNT326 (2.0–3.0 mg/kg Q3W). Primary endpoints: ORR and recommended dose; secondary endpoints: DCR, PFS, OS, safety. • **Results:** All patients were evaluable: early data show promising activity across HER2-null and HER2-low groups. TRAEs occurred in 93%, mostly low-grade cytopenias and nausea; grade ≥3 events were infrequent (19%), with no discontinuations or deaths. • **Conclusions:** YL202/BNT326 demonstrates encouraging efficacy with manageable toxicity in HR+ HER2-null/low disease, supporting continued development and combination studies.

Notable Presentations At SABCS 2025
HER2-Low / HER2-Ultralow Breast Cancer (2/5)

Date	Title	Author	Summary
11 Dec 2025	Updated results and an exploratory analysis of ESR1m circulating tumor DNA (ctDNA) dynamics from SERENA-6, a phase 3 trial of camizestrant (CAMI) + CDK4/6 inhibitor (CDK4/6i) for emergent ESR1 mutations (ESR1m) during first-line (1L) endocrine-based therapy and ahead of disease progression in patients (pts) with HR+/HER2- advanced breast cancer (ABC)	François-Clément Bidard	• **Introduction:** SERENA-6 evaluates whether switching from AI to camizestrant (CAMI) at ctDNA-detected ESR1 mutations—before clinical progression—improves outcomes in HR+/HER2– advanced breast cancer on first-line CDK4/6 inhibition. • **Methodology:** Patients on ≥6 months of AI+CDK4/6i were randomized at ESR1m detection to CAMI+CDK4/6i vs continued AI+CDK4/6i. Primary endpoint: PFS; exploratory: ESR1m ctDNA dynamics. • **Results:** With 18.7-month follow-up, CAMI significantly prolonged PFS across all subgroups. ESR1m allele frequency fell ~100% by week 8 with CAMI but rose markedly on continued AI. Discontinuations were rare; no new safety signals. • **Conclusions:** Early switch to CAMI+CDK4/6i durably improves PFS and suppresses ESR1m expansion, supporting a mutation-triggered treatment-adaptation strategy.
11 Dec 2025	Clinico-pathological and genomic features of HER2-low early Breast Cancer (eBC). Results of retrospective analysis of seven adjuvant trials by the Hellenic Cooperative Oncology Group (HeCOG)	Sotirios Lakis	• **Introduction:** HER2-low breast cancers span luminal and TNBC phenotypes, but their molecular distinctiveness remains unclear, especially for guiding ADC use. • **Methodology:** Across seven adjuvant trials (n=2,751), HER2-low, HER2-zero, and HR subtypes were centrally assigned using IHC/FISH. TMA-based clinicopathologic analysis and NGS (n=1,120) evaluated subtype distribution, ERBB2 copy number, and heterogeneity. • **Results:** HER2-low tumors were predominantly HR+. Within HR+ disease, Luminal B was enriched in HER2-low, while HER2-zero showed more Luminal A and more PIK3CA mutations. ERBB2 copy number increased progressively from HER2-zero → HER2-low_d → HER2-low_c. HER2-low status did not affect survival. • **Conclusions:** HER2-low reflects distinct ER-pathway biology but does not independently influence prognosis; ERBB2 copy-number gradients mirror HER2 IHC variability.

Notable Presentations At SABCS 2025
HER2-Low / HER2-Ultralow Breast Cancer (3/5)

Date	Title	Author	Summary
11 Dec 2025	First clinical data of DB-1310 (HER3-targeted antibody-drug-conjugate), in patients with pretreated hormone receptor-positive/HER2-negative breast cancer: efficacy and safety data from a phase 1/2a trial	Hua Mu	• **Introduction:** HER3-directed ADCs are emerging therapies in breast cancer. DB-1310 couples a high-internalizing HER3 antibody with a topo-I payload, showing early activity across solid tumors. • **Methodology:** In this phase 1 trial, patients with advanced HR+/HER2– BC received DB-1310 Q3W (3.0–5.5 mg/kg). Primary objective was safety; secondary endpoints included ORR, DCR, DoR, PFS, and OS. • **Results:** Among 15 evaluable HR+/HER2– patients, ORR was 53% (62% at 5–5.5 mg/kg), DCR 87%, and median PFS 14.8 months. Toxicities were mainly hematologic; ≥G3 TRAEs occurred in 43% overall, with low discontinuation (4.3%) and no TRAE-related deaths.. • **Conclusions:** DB-1310 demonstrates strong activity and manageable safety in pretreated HR+/HER2– disease, supporting continued clinical development.
12 Dec 2025	Interim analysis results for the effectiveness and safety of trastuzumab deruxtecan in patients with HER2-low breast cancer and brain metastases: The HALLOW study	Naoki Niikura	• **Introduction:** DESTINY-Breast04 excluded patients with active brain metastases (BMs). HALLOW evaluates real-world T-DXd outcomes in HER2-low mBC with current or prior BMs • **Methodology:** Among ~600 planned patients, 42 had investigator-diagnosed BMs; 33 were Brain-ICR confirmed (including active BMs). Intracranial PFS/ORR were assessed by Brain-ICR; systemic PFS/OS and safety by investigators. • **Results:** Median IC-PFS was 8.0 months; IC-ORR 9.1%. Median PFS was 6.7 months; OS not reached. Grade ≥3 TEAEs occurred in 43%; ILD in 5% including one grade-5 case. • **Conclusions:** Early data suggest T-DXd offers intracranial activity and manageable safety in HER2-low mBC with active BMs.

Notable Presentations At SABCS 2025
HER2-Low / HER2-Ultralow Breast Cancer (4/5)

Date	Title	Author	Summary
12 Dec 2025	Trastuzumab deruxtecan (T-DXd) monotherapy and T-DXd + pertuzumab in patients (pts) with previously untreated HER2+ unresectable/metastatic breast cancer (mBC): final results from DESTINY-Breast07	Fabrice André	• **Introduction:** DESTINY-Breast07 evaluated T-DXd ± pertuzumab as first-line therapy for HER2+ metastatic breast cancer, preceding the positive Phase 3 DESTINY-Breast09 results. • **Methodology:** HER2+ untreated mBC patients received T-DXd 5.4 mg/kg Q3W alone or with pertuzumab. Endpoints included safety, ORR, duration of response, PFS, PFS2, and OS. • **Results:** With ~38-month follow-up, ORR was high (79% T-DXd; 84% T-DXd+P). Responses were durable, with ~68% ongoing at 36 months. Median PFS and OS were not reached. Grade ≥3 AEs occurred in 57–62%; ILD/pneumonitis in ~14%. • **Conclusions:** T-DXd ± pertuzumab shows strong and durable first-line activity with expected toxicity, aligning with DESTINY-Breast09 findings.
12 Dec 2025	Impact of HER2 kinase domain mutations on trastuzumab deruxtecan efficacy in HER2 low metastatic breast cancer	Yoshiya Horimoto	• **Introduction:** HER2-low MBC eligibility for T-DXd is based on protein expression, yet the impact of HER2 kinase-domain mutations on treatment response is poorly understood. • **Methodology:** Twenty-five Japanese women with HER2-low MBC treated with T-DXd underwent ddPCR testing for four functional HER2 mutations (L755S, D769Y, V777L, V842I). Time to treatment discontinuation (TTD) was compared by mutation status and mutation burden. • **Results:** Mutation frequencies were high: V842I (92%), L755S (64%), D769Y (32%). L755S was associated with shorter TTD (32 vs 41 weeks). Multiple mutations led to significantly shorter TTD (30 vs 52 weeks). • **Conclusions:** HER2 kinase-domain mutations—particularly L755S and multi-mutation profiles—may reduce T-DXd sensitivity, warranting further biomarker-driven validation.

Notable Presentations At SABCS 2025
HER2-Low / HER2-Ultralow Breast Cancer (5/5)

Date	Title	Author	Summary
12 Dec 2025	Efficacy of systemic therapy in HER2-low breast cancer with CNS metastases: a "real-world" experience	Bipin Ghimire	• **Introduction:** CNS metastases are rising in breast cancer, but systemic options for HER2-low disease remain poorly defined. This study evaluates real-world intracranial responses to upfront systemic therapy. • **Methodology:** Sixteen HER2-low patients with CNS metastases and no concurrent local therapy were retrospectively analyzed. Responses were assessed using RANO-BM/RANO-LM. • **Results:** ORR was 31%, DCR 56%, median PFS 2 months. Benefit was greatest in HER2 IHC 2+ tumors (ORR 67%, DCR 100%) and with T-DXd (DCR 75%). Chemotherapy showed limited activity aside from rare complete responses. • **Conclusions:** Systemic efficacy in HER2-low CNS disease is modest, but T-DXd and HER2 2+ biology show promise, underscoring the need for dedicated prospective studies.
12 Dec 2025	Herthena-breast04: a phase 3, randomized, open-label study evaluating the efficacy and safety of patritumab deruxtecan (HER3-DXd) versus treatment of physician's choice in hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2−) unresectable locally advanced or metastatic breast cancer	Barbara Pistilli	• **Introduction:** HR+/HER2− metastatic breast cancer progressing after CDK4/6 inhibitors has limited options, with chemotherapy and ADCs offering modest benefit. HER3 overexpression drives resistance, supporting HER3-DXd development. • **Methodology:** HERTHENA-Breast04 is a global phase 3 trial randomizing ~1000 HR+/HER2− patients post-CDK4/6i+ET to HER3-DXd vs treatment of physician's choice across six regimens. Key endpoints: PFS and OS by BICR, with ORR, DOR, safety, and PROs as secondary measures. • **Results:** Enrollment begins Q3 2025; imaging at fixed 6- and 12-week intervals; treatment continues until progression/toxicity. • **Conclusions:** This pivotal trial will define whether HER3-DXd can outperform standard chemotherapy/ADC options in post-CDK4/6i HR+/HER2− disease.

Notable Presentations At SABCS 2025
HER2-Positive Breast Cancer (1/7)

Date	Title	Author	Summary
10 Dec 2025	Her2climb-05: a randomized, double-blind, phase 3 study of tucatinib versus placebo in combination with trastuzumab and pertuzumab as maintenance therapy for her2+ metastatic breast cancer	Erika Hamilton	• **Introduction:** Optimal endocrine therapy for HR+/HER2+ EBC is unresolved. ALTTO enables long-term comparison of SERMs vs aromatase inhibitors (AIs) in patients receiving modern chemotherapy plus anti-HER2 therapy. • **Methodology:** This 10-year analysis included 2,651 centrally confirmed HR+/HER2+ patients receiving CT+trastuzumab-based regimens. Patients switching ET were excluded. Outcomes—DFS, TTDR, OS—were compared using multivariable Cox models. Premenopausal subgroups evaluated SERM, SERM+OFS, and AI±OFS. • **Results:** AI significantly improved 10-year DFS (80.1% vs 76.5%; aHR 0.65) and TTDR (aHR 0.65) across all clinical and tumor subsets. In premenopausal women, AI±OFS yielded the best DFS (90%). OS was similar between groups. • **Conclusions:** AIs provide superior long-term disease control vs SERMs in HR+/HER2+ EBC, supporting AI-based strategies across menopausal groups.
10 Dec 2025	Tumor infiltrating lymphocytes (TILs) and pathologic complete response (pCR) in stage II/III HER2+ breast cancer treated with taxane, trastuzumab, and pertuzumab (THP): secondary results from the ECOG-ACRIN-1181/CompassHER2 pCR trial	Sunil S Badve	• **Introduction:** The predictive value of stromal TILs (sTILs) in HER2+ breast cancer remains uncertain. EA1181 provides a uniform THP-treated cohort to reassess their association with pCR. • **Methodology:** Among 2141 patients, 1328 had evaluable biopsies. sTILs were quantified on full-face H&E sections as continuous and categorical variables (≥10%, ≥30%, ≥60%). Multivariable Cox models assessed associations with pCR. • **Results:** Overall pCR was 44.5% (64% HER2+/ER−; 33% HER2+/ER+). Higher sTILs strongly correlated with higher pCR across subtypes ($p<0.001$). Categorical ≥10% and ≥30% cutoffs predicted pCR, especially in HER2+/ER+ tumors. • **Conclusions:** Baseline sTILs significantly predict pCR to THP, supporting immune-based risk stratification and informing future HER2+ de-escalation/optimization trials.

Notable Presentations At SABCS 2025
HER2-Positive Breast Cancer (2/7)

Date	Title	Author	Summary
10 Dec 2025	Efficacy and safety of DP303c versus T-DM1 in HER2-positive advanced breast cancer: Interim analysis of a randomized, open-label, phase 3 trial	N/A	• **Introduction:** HER2+ advanced breast cancer progressing after trastuzumab/taxane lacks effective options in China. DP303c, a novel HER2-targeted MMAE-ADC, was compared with T-DM1. • **Methodology:** In this randomized phase III trial (N=448), adults with previously treated HER2+ ABC received DP303c 3.0 mg/kg Q3W or T-DM1 3.6 mg/kg Q3W. Primary endpoint was BIRC-assessed PFS; secondary endpoints included ORR, CBR, OS, and safety. • **Results:** DP303c significantly improved PFS (8.8 vs 5.8 mo; HR 0.56; p<0.0001) and ORR (62.8% vs 42.8%). Benefit was consistent by investigator review. Safety was manageable, mainly ocular and neuropathic events, with low discontinuation. • **Conclusions:** DP303c outperformed T-DM1 with clinically meaningful PFS and ORR gains and acceptable tolerability, supporting it as a promising new HER2+ ABC therapy.
10 Dec 2025	Safety and efficacy of trastuzumab deruxtecan and concomitant radiation therapy in breast cancer patients: an international retrospective cohort study	Luca Visani	• **Introduction:** T-DXd is standard after trastuzumab/taxane failure in HER2+/HER2-low metastatic breast cancer. Limited evidence exists on the safety of concurrent radiotherapy (RT), a frequent component of metastatic care. • **Methodology:** In this multicentre European retrospective cohort (N=147), 67 patients received RT within 1 month before or during uninterrupted T-DXd. Ablative RT followed ESTRO OligoCare EQD2≥50 Gy criteria. Primary endpoint: >G2 toxicity associations. • **Results:** Concurrent RT did not increase overall >G2 toxicity (p=0.30), acute (p=0.31), or late toxicity (p=0.59). ILD/pneumonitis rates were similar (10.5% RT vs 8.8% no-RT). Only one radionecrosis case occurred. Discontinuation rates were comparable. • **Conclusions:** Concurrent RT with T-DXd appears safe, without excess severe toxicity, supporting its use in routine metastatic management.

Notable Presentations At SABCS 2025
HER2-Positive Breast Cancer (3/7)

Date	Title	Author	Summary
11 Dec 2025	Trastuzumab Combined with Pyrotinib and Capecitabine as Postoperative Adjuvant Therapy in Non-Pathological Complete Response HER2-Positive Early Breast Cancer Following Neoadjuvant Therapy: A Multicenter Phase II Study	Jie Zhang	• **Introduction:** HER2+ early breast cancer patients without pCR after neoadjuvant therapy face high recurrence risk. Building on KATHERINE, this study evaluates adjuvant trastuzumab + pyrotinib + capecitabine as an alternative escalation strategy. • **Methodology:** In this single-arm, multicenter study (N=102), eligible non-pCR patients received one year of trastuzumab and pyrotinib plus six cycles of capecitabine. Primary endpoint: 3-year iDFS; secondary endpoints: DDFS, OS, safety. • **Results:** At 25-month median follow-up, 2-year iDFS was 91.3% and DDFS 96.8%. Grade ≥3 AEs occurred in 21.6%—mainly diarrhea (13.7%). Treatment interruptions (64.7%) and dose reductions (36.3%) were frequent but manageable. • **Conclusions:** Adjuvant trastuzumab + pyrotinib + capecitabine shows promising disease-control with acceptable toxicity in non-pCR HER2+ early breast cancer, supporting further validation.
11 Dec 2025	Efficacy and safety of disitamab vedotin combined with pyrotinib as neoadjuvant therapy for HER2-positive breast cancer: a phase II trial	Tianyu Zeng	• **Introduction:** Dual HER2 blockade plus chemotherapy is effective but toxic. This phase II trial tested the first chemo-free neoadjuvant strategy using RC48 (HER2-ADC) + pyrotinib (pan-HER TKI) in HER2+ breast cancer. • **Methodology:** Dual HER2 blockade plus chemotherapy is effective but toxic. This phase II trial tested the first chemo-free neoadjuvant strategy using RC48 (HER2-ADC) + pyrotinib (pan-HER TKI) in HER2+ breast cancer. • **Results:** Among 17 evaluable patients (all HR−/HER2+), pCR was 53.3% and ORR 88.2%. No EFS events or deaths occurred. Grade ≥3 TRAEs were mainly transient hepatic dysfunction; no discontinuations. • **Conclusions:** RC48 + pyrotinib produced high response rates with manageable toxicity, supporting further evaluation as a chemo-free neoadjuvant option for HER2+ disease.

Notable Presentations At SABCS 2025
HER2-Positive Breast Cancer (4/7)

Date	Title	Author	Summary
11 Dec 2025	Efficacy and safety of 12-week adjuvant docetaxel plus trastuzumab in patients with node-negative HER2-positive breast cancer (tumors ≤1cm): results from the SOBER prospective single-arm trial	Shuning Ding	• **Introduction:** Management of HER2-positive, node-negative tumors ≤1 cm remains undefined. This phase II trial evaluated short-course adjuvant docetaxel + trastuzumab • **Methodology:** Seventy-eight patients with HER2-positive T1mic/T1a/T1b node-negative breast cancer received 12 weeks of docetaxel with concurrent trastuzumab. Primary endpoint: 3-year DFS; secondary endpoints: OS, BCSS, safety. • **Results:** With 45.2-month median follow-up, 3-year DFS was 96.9% and 5-year DFS 89.8%; OS was 100% and 96% at 3 and 5 years. No BCSS events occurred. LVEF decline >10% was absent; neutropenia (23.7%) was the most common AE. • **Conclusions:** Short-course docetaxel + trastuzumab yields excellent survival and manageable toxicity in HER2-positive tumors ≤1 cm.
11 Dec 2025	Cross-country Treatment Practices after pCR Following Neoadjuvant Trastuzumab (H) and Pertuzumab (P) in HER2+ Early Breast Cancer: Preliminary Results from the PEARL-HER2 Study	Soraia Lobo-Martins	• **Introduction:** Post-pCR management of HER2+ early breast cancer varies globally, and the benefit of continuing adjuvant pertuzumab (HP) versus trastuzumab (H) alone after neoadjuvant HP remains unclear. • **Methodology:** PEARL-HER2 is a retrospective international cohort (2014–2023) evaluating diagnostic patterns and adjuvant therapy use in 649 pCR patients across multiple countries • **Results:** Marked variation emerged: routine MRI in Spain/Portugal/Belgium vs 15% in Turkey; PET favored in Turkey/Belgium; anthracycline-free regimens common in Argentina (100%) and Belgium (34%). Adjuvant HP use exceeded 90% in Belgium but <9% in Iberian countries. With 44-month follow-up, relapse rate was low (5.4%), but 51% were CNS events • **Conclusions:** Substantial international disparities reflect differences in access, reimbursement, and staging practices. High CNS relapse proportion underscores need for optimized post-pCR strategies; PEARL-HER2 follow-up will define the value of adjuvant pertuzumab.

Notable Presentations At SABCS 2025
HER2-Positive Breast Cancer (5/7)

Date	Title	Author	Summary
12 Dec 2025	Efficacy of second- or third-line Tucatinib, Trastuzumab, and Capecitabine (TTC) following trastuzumab deruxtecan (T-DXd) in HER2-positive metastatic breast cancer: A multicenter French cohort study.	Jean Sebastien Frenel	• **Introduction:** T-DXd is the standard second-line therapy for HER2+ MBC, but optimal sequencing afterward is undefined. The tucatinib–trastuzumab–capecitabine (TTC) regimen is a leading post–T-DXd option with limited real-world evidence. • **Methodology:** A multicenter French cohort (17 centers) included HER2+ MBC patients receiving TTC in 2L/3L immediately after T-DXd. Endpoints: PFS (primary), TTNT, OS, ORR. • **Results:** Among 103 patients, median PFS was 4.7 months, OS 12.3 months, ORR 30.2%. Longer T-DXd responders (>18 months) and patients with brain metastases showed improved PFS. • **Conclusions:** TTC demonstrates meaningful activity post–T-DXd, supporting its role as an effective later-line option.
12 Dec 2025	Evorpacept (ALX-148) combined with trastuzumab deruxtecan in patients with HER2 positive/HER2low metastatic breast cancer (mBC): results from the PRE-ISPY phase Ib trial	PAULA R POHLMANN	• **Introduction:** Despite T-DXd advances, HER2+/HER2-low metastatic breast cancer remains incurable. Evorpacept, a CD47 blocker enhancing phagocytosis, may potentiate T-DXd activity. • **Methodology:** PRE-ISPY Phase I/Ib enrolled 30 previously treated, T-DXd–naïve HER2+/HER2-low patients across dose-finding (30 vs 45 mg/kg) and expansion cohorts with standard T-DXd. Primary endpoints: safety, RP2D, ORR. • **Results:** No DLTs; RP2D established at evo 45 mg/kg + T-DXd. TEAEs mainly grade 1–2; grade ≥3 in 47%, no grade 5. cORR 33%, DCR 73%; mPFS 8.6 months, not reached in HER2+. • **Conclusions:** Evo+T-DXd shows manageable safety and promising activity, supporting further evaluation

Notable Presentations At SABCS 2025
HER2-Positive Breast Cancer (6/7)

Date	Title	Author	Summary
12 Dec 2025	Early use of CDK4/6 inhibitor combined with endocrine therapy plus anti-HER2 antibody may get more survival benefit in HR+/HER2+ advanced breast cancer: result from a phase II single-arm mini cohort study (CABC016)	Yaxin Liu	• **Introduction:** Rationale stems from ER–HER2 cross-talk driving resistance; adding CDK4/6 inhibition to anti-HER2 + ET may replicate PATINA-like benefit without chemotherapy • **Methodology:** CABC016 is a single-arm phase II trial of palbociclib + trastuzumab/inetetamab ± pertuzumab + ET in HR+/HER2+ MBC. Primary endpoint: PFS; secondary endpoints: ORR, DCR, OS, safety. • **Results:** Among 47 pts, mPFS was 16.5 months; mOS 34.9 months (immature). ET-naïve pts showed striking benefit (mPFS 22.0 vs 8.3 months). Earlier-line use yielded longest PFS (up to 24.1 months). ORR 34% (46% ET-naïve); DCR 88%. Efficacy preserved in stable brain disease. Toxicities were manageable, dominated by neutropenia. • **Conclusions:** Palbociclib + ET + anti-HER2 therapy provides meaningful chemotherapy-free activity, especially as first-line and in ET-naïve disease
12 Dec 2025	Impact of Prior T-DM1 Exposure on the Efficacy of Trastuzumab Deruxtecan in HER2-Positive Metastatic Breast Cancer	Seyda Gunduz	• **Introduction:** Sequencing of HER2-targeted ADCs is poorly understood. Whether prior T-DM1 exposure compromises subsequent T-DXd efficacy is clinically relevant for optimizing metastatic HER2+ treatment pathways. • **Methodology:** A multicenter retrospective cohort across 21 Turkish centers assessed the effect of prior T-DM1 on PFS under T-DXd. Cox models estimated progression risk; 199 patients were analyzed. • **Results:** T-DM1-pretreated patients progressed more frequently (47% vs 13.8%). Prior T-DM1 significantly increased progression risk (HR 3.03; p=0.002). Median PFS was 12.1 months with prior T-DM1, while not reached in T-DM1-naïve patients (p=0.001). • **Conclusions:** Prior T-DM1 exposure substantially reduces T-DXd benefit, emphasizing the importance of optimal ADC sequencing in HER2+ MBC.

Notable Presentations At SABCS 2025
HER2-Positive Breast Cancer (7/7)

Date	Title	Author	Summary
12 Dec 2025	Intracranial Activity and Systemic Efficacy of Trastuzumab Deruxtecan in Breast Cancer Patients with Brain Metastases	Zouina Sarfraz	• **Introduction:** Brain metastases in metastatic HER2-positive breast cancer remain difficult to treat. This meta-analysis assesses the intracranial and systemic efficacy of T-DXd, a HER2-targeted ADC with emerging CNS penetration. • **Methodology:** Fourteen eligible studies (RCTs, prospective trials, cohorts) were pooled using random-effects models. Outcomes included IC-CBR, IC-ORR, systemic PFS, and 12-month OS. Heterogeneity was quantified via I^2. • **Results:** T-DXd achieved high intracranial benefit (IC-CBR 81%) and strong IC-ORR (62%). Mean systemic PFS was 12.6 months and 12-month OS was 81%. • **Conclusions:** T-DXd provides substantial CNS activity and survival benefit, outperforming historical HER2-targeted therapies.
12 Dec 2025	NRG-BR008: A phase III randomized trial of radiotherapy optimization for low-risk HER2-positive breast cancer (HERO)	Melissa P Mitchell	• **Introduction:** Excellent 10-year locoregional control in early-stage HER2+ breast cancer raises the question of whether radiotherapy (RT) can be safely omitted after breast-conserving surgery (BCS) when modern systemic HER2-targeted therapy is given. • **Methodology:** NRG-BR008 is a phase III randomized non-inferiority trial enrolling T1N0 or post-neoadjuvant ypT0N0 HER2+ patients. Participants receive standard RT + HER2 therapy versus HER2 therapy alone. Primary endpoint: recurrence-free interval (RFI). Target accrual: 1,300 patients. • **Results:** Accrual reached 103/1,300 by July 2025. Final RFI events (n=38) are expected after 4.5 additional years of follow-up. • **Conclusions:** This trial will determine whether RT can be safely omitted in carefully selected low-risk HER2+ patients receiving optimal systemic therapy.

Notable Presentations At SABCS 2025
HR+/HER2-Negative Breast Cancer (1/7)

Date	Title	Author	Summary
10 Dec 2025	Progression free survival and exploratory endpoints from PALVEN: a phase 1b study of palbociclib, letrozole and venetoclax in ER and BCL2-positive metastatic breast cancer	Geoffrey J Lindeman	• **Introduction:** CDK4/6 inhibitors induce senescence, limiting apoptosis; BCL2 blockade may restore apoptotic sensitivity. PALVEN evaluates triplet endocrine–CDK4/6–BCL2 inhibition in ER+/HER2–, BCL2+ metastatic breast cancer. • **Methodology:** Postmenopausal women (≤2 prior metastatic lines) received letrozole, palbociclib, and venetoclax. Assessments occurred every 8–12 weeks. Endpoints included PFS, OS, CBR, biomarker modulation, and toxicity. • **Results:** Among 15 evaluable patients, CBR was 93%, PFS 29.2 months, and PR loss with ≥50% Ki67 reduction was universal. Toxicities were mainly grade ≥3 neutropenia without infections. • **Conclusions:** Triplet therapy showed strong, durable activity with manageable myelosuppression, supporting further BCL2–CDK4/6–ET combination development.
10 Dec 2025	Dose optimization of PF-07248144, a first-in-class KAT6 inhibitor, in patients with ER+/HER2− metastatic breast cancer: results from phase 1 study to support the recommended phase 3 dose	Yeon Hee Park	• **Introduction:** ER+/HER2− mBC progressing after CDK4/6i+ET lacks effective targeted options. PF-07248144, a next-generation SERD/SERCA modulator, was evaluated to define optimal dosing and activity. • **Methodology:** Patients received PF-07248144 at 5 mg or 1 mg QD with/without fulvestrant. Safety, PK/PD, and RECIST-based efficacy were assessed across 107 treated patients. • **Results:** The 5 mg+FUL regimen showed superior ORR (37.2%), longer DoR (15.8 mo), and PFS (10.7 mo). Toxicities were manageable, dominated by reversible neutropenia, with no pneumonitis reported. • **Conclusions:** PF-07248144 5 mg+FUL demonstrated optimal benefit–risk and meaningful antitumor activity, supporting ongoing phase 3 evaluation.

Notable Presentations At SABCS 2025
HR+/HER2-Negative Breast Cancer (2/7)

Date	Title	Author	Summary
10 Dec 2025	Chidamide combined with fulvestrant in the treatment of HR-positive,HER2-negative advanced breast cancer after failure of previous endocrine therapy: A single-arm, single-center, phase 2 study	La Zou	• **Introduction:** HR+/HER2– advanced breast cancer progressing after endocrine therapy requires new combinations. Chidamide, an HDAC inhibitor, previously improved PFS with endocrine therapy, prompting evaluation with fulvestrant. • **Methodology:** Women aged 18–75 with HR+/HER2– advanced disease after ≥1 prior ET received chidamide 30 mg twice weekly plus fulvestrant 500 mg. Primary endpoint was PFS; secondary endpoints included ORR, DoR, DCR, OS, and safety. • **Results:** Among 30 patients (80% visceral disease), ORR was 10% and DCR 83.3%. Seventeen percent remained on therapy at cutoff. • **Conclusions:** Chidamide–fulvestrant showed encouraging disease control and acceptable safety in heavily pretreated HR+/HER2– disease.
10 Dec 2025	Palbociclib, pembrolizumab, and endocrine therapy in HR+/HER2- metastatic breast cancer: Updated results from a phase I/II trial	Alexis LeVee	• **Introduction:** ICIs have uncertain benefit in HR+/HER2– MBC. This study evaluates pembrolizumab added to palbociclib + endocrine therapy in first-line disease. • **Methodology:** Phase I/II, single-center trial across 3 cohorts; pembrolizumab was given concurrently or sequentially with palbociclib + ET. Primary endpoint: ORR; secondary: PFS, OS, safety. • **Results:** Among 43 first-line patients, ORR was 62.8%, PFS 27.1 months, OS 56.8 months. Toxicities were mainly hematologic (G3: 90.7%), with pneumonitis in 14.3%. • **Conclusions:** Adding pembrolizumab produced higher ORR vs PALOMA-2 and acceptable safety, supporting biomarker-driven evaluation.

Notable Presentations At SABCS 2025
HR+/HER2-Negative Breast Cancer (3/7)

Date	Title	Author	Summary
10 Dec 2025	The ADELA study: a double-blind, placebo-controlled, randomized phase 3 trial of elacestrant + everolimus versus elacestrant + placebo in ER+/HER2- advanced breast cancer (ABC) patients with ESR1-mutated tumors progressing on endocrine therapy (ET) + CDK4/6i	Antonio Llombart-Cussac	• **Introduction:** Endocrine + CDK4/6 inhibition remains 1L SOC in ER+/HER2− ABC, but resistance—especially ESR1 mutations—drives progression. Dual ER and PI3K/AKT/mTOR targeting provides strong biologic rationale. • **Methodology:** ADELA is a global, randomized, double-blind phase 3 trial comparing elacestrant + everolimus vs elacestrant + placebo in ESR1-mutated ER+/HER2− ABC progressing after ≥6 months of ET+CDK4/6i. Primary endpoint: BICR-assessed PFS. • **Results:** Early-phase data show elacestrant + everolimus achieving median PFS 8.3 months with manageable toxicity, supporting RP2D selection (345 mg + 7.5 mg). • **Conclusions:** ADELA will clarify whether adding everolimus meaningfully improves PFS in ESR1-mutated CDK4/6i-resistant disease.
10 Dec 2025	Phase II trial of pembrolizumab in combination with paclitaxel in the hormone receptor-positive metastatic breast cancer enriched with tumor mutational burden determined by whole exome sequencing: Korean Cancer Study Group trial (KCSG BR20-16)	Joohyuk Sohn	• **Introduction:** Chemotherapy is required for HR+/HER2− MBC resistant to ET/CDK4/6i; pembrolizumab alone is ineffective. This trial tests whether TMB-enriched selection can enhance ICI benefit. • **Methodology:** Multicenter phase II; fresh biopsies underwent WES-based TMB assessment. Patients with high TMB received pembrolizumab + weekly paclitaxel. Primary endpoint: ORR. • **Results:** Among 23 enrolled, ORR was 65.2%; mPFS 7.5 months; DoR 4.3 months. Higher TMB correlated with greater shrinkage. irAEs predicted longer PFS (9.1 vs 5.8 months). • **Conclusions:** TMB-guided pembrolizumab + paclitaxel shows meaningful activity and acceptable safety, supporting biomarker-driven immunochemotherapy.

Notable Presentations At SABCS 2025
HR+/HER2-Negative Breast Cancer (4/7)

Date	Title	Author	Summary
10 Dec 2025	Impact of sarcopenia on efficacy and toxicity profile of CDK4/6 inhibitors in HR+/HER2- metastatic breast cancer patients: a real-world analysis	Denise Drittone	• **Introduction:** Sarcopenia is common in cancer and may influence toxicity and outcomes, but its relevance in HR+/HER2− mBC treated with first-line CDK4/6i+ET is unclear. • **Methodology:** Retrospective study of 75 patients; sarcopenia quantified via AI-based L3 CT muscle segmentation (SMI <38.5 cm²/m²). Survival and toxicity associations assessed using Cox models and logistic regression. • **Results:** Sarcopenia prevalence was 56%. It did not affect PFS (27 vs 23 mo) or OS (51 vs 47 mo). Sarcopenia strongly correlated with grade 3/4 toxicity (61% vs 37%). Lower BMI predicted sarcopenia (p=0.01). • **Conclusions:** Sarcopenia is not prognostic but increases toxicity risk, supporting routine body-composition evaluation and proactive supportive care in CDK4/6i-treated patients.
10 Dec 2025	First-in-human, phase 1a/b study of GDC-4198 (RGT-419B), a next generation CDK4/2 inhibitor, in patients with hormone receptor positive HER2- locally advanced/metastatic breast cancer (LA/mBC) who progressed on prior CDK4/6 inhibitors	Seth A Wander	• **Introduction:** GDC-4198 is a next-generation CDK4/2 inhibitor designed to overcome resistance after CDK4/6i in HR+/HER2− advanced breast cancer. • **Methodology:** Phase 1, first-in-human, 3+3 dose-escalation trial evaluated GDC-4198 monotherapy (25–150 mg QD; 150 mg BID) and combination with an aromatase inhibitor. Primary endpoint was safety; secondary endpoint exploratory antitumor activity. • **Results:** Among 32 treated patients, toxicity was manageable with only 16% grade ≥3 TRAEs and no discontinuations or treatment-related SAEs. MTD not reached. Four confirmed partial responses occurred at higher monotherapy doses. • **Conclusions:** GDC-4198 shows good tolerability and early antitumor activity post-CDK4/6i, supporting continued dose escalation and expansion.

Notable Presentations At SABCS 2025
HR+/HER2-Negative Breast Cancer (5/7)

Date	Title	Author	Summary
10 Dec 2025	Esr1 mutations and use of the oral serd elacestrant in metastatic breast cancer patients in austria: results from the agmt_mbc-registry	Simon P Gampenrieder	• **Introduction:** ESR1 mutations, a key mechanism of AI resistance in HR+/HER2− MBC, have gained clinical importance following EU approval of elacestrant and the integration of routine ESR1 testing. • **Methodology:** Analysis of evaluable patients in the AGMT national MBC registry (n=2,956). ESR1 testing performed via liquid biopsy or tissue per local practice; mutation patterns and treatment decisions documented. • **Results:** Only 4.5% underwent ESR1 testing; 27.5% were mutation-positive, identifying six variants, with 21% harboring multiple mutations. Half of ESR1-mutant patients started elacestrant. Frequent co-mutations included PIK3CA, TP53, and BRCA2, influencing treatment choices. • **Conclusions:** Findings show underuse of ESR1 testing yet high clinical relevance. Mutation patterns and co-alterations support personalized endocrine and targeted therapy strategies, including elacestrant and PI3K inhibition.
10 Dec 2025	Prognostic impact of type and location of germline BRCA2 pathogenic or likely pathogenic variants in patients with HR+/HER2- advanced breast cancer: results from the multicenter real-world PAMBRACA study	Emma Zattarin	• **Introduction:** BRCA2 variant type and exon location influence cancer risk, but their prognostic relevance in HR+/HER2− advanced breast cancer (aBC) treated with CDK4/6i is unclear. • **Methodology:** PAMBRACA retrospectively analyzed BRCA2 LP/PV carriers receiving CDK4/6i+ET, with half later treated with PARPi. Variant class, coding consequence, truncation status, and exon location were correlated with OS and PFS using left-truncated and multivariable Cox models. • **Results:** Among 72 pts, 65% had INDELs and 86% truncating variants; 56% were located in exon 11. No LP/PV type or location was associated with OS or PFS. Worse OS correlated only with >3 metastatic sites and postmenopausal status. • **Conclusions:** BRCA2 variant characteristics did not impact CDK4/6i or PARPi effectiveness, supporting treatment decisions independent of mutation subtype.

Notable Presentations At SABCS 2025
HR+/HER2-Negative Breast Cancer (6/7)

Date	Title	Author	Summary
10 Dec 2025	Ribo-age: age-stratified descriptive analysis of adverse drug reactions in patients with advanced breast cancer treated with ribociclib plus nonsteroidal aromatase inhibitors: preliminary results	Tamara Díaz-Redondo	• **Introduction:** Ribociclib plus NSAI improves survival in HR+/HER2− ABC, but real-world Spanish safety data are limited. • **Methodology:** A retrospective cohort assessed adults starting 1L RIB+NSAI (2021–2023) with 12-month follow-up. Safety, discontinuations, exposure time, and age-stratified PFS were evaluated from medical records. • **Results:** Among 147 pts, median follow-up was 23.8 months and treatment duration 18.4 months. Twenty-four-month PFS was similar in ≤65 vs >65 yrs (63.3% vs 65.5%). AEs occurred in 141 pts; 10.9% discontinued due to toxicity. No new safety signals emerged. • **Conclusions:** RIB+NSAI shows favorable, age-independent tolerability and consistent effectiveness in real-world Spanish practice.
10 Dec 2025	Palbociclib in real clinical practic: Results of a single-center observational study	Aleksandr Sultanbaev	• **Introduction:** Real-world evidence on palbociclib in HR+/HER2− mBC remains limited; evaluating outcomes outside trials is clinically relevant. • **Methodology:** Retrospective review of 323 pts treated at a single oncology center assessed clinicopathologic features, antitumor response, PFS, OS, and toxicity using clinical, radiologic, and pathologic records. • **Results:** Median age was 62. Partial response occurred in 16.7%, stable disease in 65.6%, progression in 17.8% (DCR 82.4%). Median PFS was 13 months. Grade 3 AEs occurred in 23 pts (notably hepatotoxicity 47.8%, neutropenia 21.7%). No discontinuations. First-line use yielded best outcomes. OS was slightly lower than PALOMA trials (median 31 months). • **Conclusions:** Findings align with RCTs, confirming palbociclib's real-world effectiveness and manageable toxicity in HR+/HER2− mBC.

Notable Presentations At SABCS 2025
HR+/HER2-Negative Breast Cancer (7/7)

Date	Title	Author	Summary
11 Dec 2025	Primary Results from the HR+/HER2- Cohort of TBCRC-053 (P-RAD): A Randomized Trial of No, Low, or High Dose Preoperative RADiation with Pembrolizumab and Chemotherapy in Node-Positive, HER2-Negative Breast Cancer	Gaorav Gupta	• **Introduction:** Rising DCIS detection has renewed interest in nonsurgical management, but long-term safety remains uncertain. LORETTA evaluates tamoxifen (TAM) alone for carefully selected low-risk DCIS. • **Methodology:** Single-arm, multicenter trial in Japan enrolling ER+, HER2−, NG1–2, ≤25 mm DCIS without comedo necrosis or invasive features. Patients ≥40 received TAM 20 mg/day only. Primary endpoint: 5-year CIPIC ≤7% • **Results:** Among 341 pts, 5-year CIPIC was 9.8% (CI 5.2–16.1%), exceeding threshold. Eighteen invasive events occurred. Larger imaging-defined size predicted invasion. OS (98.8%), contralateral DFS (97.5%), and surgery-free survival (82%) were high. Grade ≥3 AEs: 3.8%. • **Conclusions:** TAM alone failed the predefined efficacy threshold but showed low invasive event rates and limited need for surgery, suggesting potential use in rigorously selected low-risk DCIS.
11 Dec 2025	Sustained Ovarian Function Suppression with Triptorelin in Premenopausal HR+ HER2− Breast Cancer: Results from the Second Interim Analysis of the ROSE Study	Alessandra Fabi	• **Introduction:** Ovarian function suppression (OFS) is essential for premenopausal HR+/HER2− early breast cancer. Real-world evidence on triptorelin's endocrine effectiveness across treatment settings is limited. • **Methodology:** ROSE is a multicenter observational study assessing hormonal suppression in premenopausal stage I–IIIA patients receiving triptorelin plus endocrine therapy, with or without chemotherapy or abemaciclib. OFS was defined as estradiol <30 pg/mL over 18 months. • **Results:** Among 103 patients, OFS rates were 84.2%, 91.5%, and 93.0% at 6, 12, and 18 months. Median estradiol remained ~12–14 pg/mL; FSH rose appropriately. Suppression was consistent across AI vs tamoxifen, chemotherapy vs none, and 1- vs 3-month formulations. • **Conclusions:** Triptorelin produced durable, uniform OFS across treatment combinations, supporting its robust endocrine effect and the value of long-term hormonal monitoring.

Notable Presentations At SABCS 2025
Metastatic Breast (1/8)

Date	Title	Author	Summary
10 Dec 2025	Phase 1 Clinical Testing of a First-in-Class Antisense Oligonucleotide Therapeutic against Advanced Solid Tumors of Multiple Tissue Origins	Zdravka Medarova	• **Introduction:** miR-10b is a key metastasis driver. TTX-MC138, an antisense oligonucleotide with innate tumor tropism, eradicates metastases in preclinical models and may offer a novel therapeutic class for advanced cancers. • **Methodology:** A Phase 0 microdose study evaluated delivery of Cu64-labeled TTX-MC138 to metastatic lesions and PK/PD effects. An ongoing Phase 1/2 BOIN-designed trial administers monthly dosing across four levels (0.8–4.8 mg/kg) to previously treated advanced solid tumors. • **Results:** Phase 0 confirmed metastatic uptake, drug stability, 18.7-hour half-life, and robust PD activity. In Phase 1/2 (n=16), no DLTs/SAEs emerged; PK scaled with dose and remained consistent. miR-10b inhibition reached ~66% at 24 hours. • **Conclusions:** TTX-MC138 demonstrates favorable delivery, safety, and target engagement, supporting further clinical development as a first-in-class anti-metastatic nucleic acid therapy.
10 Dec 2025	Efficacy and safety of Albumin-Bound Paclitaxel (SYHX2011) in Patients with Advanced Breast Cancer: A Multicenter, Randomized, Double-blind Phase III study	Cuizhi Geng	• **Introduction:** Albumin-bound paclitaxel improves drug delivery but commonly causes rash. SYHX2011, a novel formulation replacing most albumin with mannitol/sucrose, may enhance efficacy and reduce hypersensitivity. • **Methodology:** In this double-blind phase III trial (N=459), patients with unresectable/metastatic breast cancer were randomized 1:1 to SYHX2011 vs standard PAB (260 mg/m² q3w). Primary endpoint was IRC-assessed ORR, with noninferiority then superiority testing; rash incidence was a key secondary endpoint. • **Results:** SYHX2011 achieved higher ORR (35.8% vs 25.8%; RR 1.38, p=0.0124), meeting noninferiority and superiority. Rash rates were markedly lower (Cycle 1–2: 13.6% vs 34.3%; whole treatment: 16.2% vs 42.6%, both p<0.0001). Grade ≥3 TRAEs were similar, mainly hematologic. • **Conclusions:** SYHX2011 delivers superior efficacy with substantially reduced rash, representing a potentially better-tolerated taxane option for advanced breast cancer.

Notable Presentations At SABCS 2025
Metastatic Breast (2/8)

Date	Title	Author	Summary
10 Dec 2025	Impact of Prior Therapy, Genotype Matching, and Biomarkers in the Bria-ABC Phase 3 Trial	Giuseppe Del Priore	• **Introduction:** Bria-IMT™, an allogeneic whole-cell vaccine expressing TAAs and GM-CSF, aims to activate innate and adaptive immunity in heavily pretreated metastatic breast cancer (MBC). Bria-ABC evaluates Bria-IMT ± checkpoint inhibition (CPI) vs physician's choice. • **Methodology:** This phase III RCT randomized patients 1:1:1 to Bria-IMT+CPI, Bria-IMT, or TPC; subsequent enrollment continues 1:1 (Bria-IMT+CPI vs TPC). Feasibility, PFS trends, and biomarker associations were assessed using KM and stratified analyses. • **Results:** Among 107 treated patients (median 6 prior lines), mPFS was 2.9 months. Prior CDK4/6i predicted longer PFS (3.8 vs 2.1 mo). Favorable NLR yielded significantly improved PFS (~4.5 vs 2.5 mo). Patients without CTCs or with reduced CAML size had better outcomes. Toxicity was mostly grade 1–2; no Bria-IMT–related discontinuations. • **Conclusions:** Bria-IMT is feasible, well tolerated, and shows early biomarker-linked activity even in ultra-refractory MBC, supporting continued trial evaluation and future biomarker-driven design refinements.
10 Dec 2025	Real-world efficacy of everolimus in ER+/HER2- metastatic breast cancer following CDK4/6 inhibitors: a multicenter registry-based study	Hikari Kiyohara	• **Introduction:** Everolimus is a standard post-CDK4/6i option, yet evidence in CDK4/6-pretreated ER+/HER2– metastatic breast cancer remains limited. This study assessed its real-world effectiveness and predictors of treatment durability. • **Methodology:** A retrospective ABCD registry analysis included 169 ER+/HER2– patients previously treated with CDK4/6i. Clinical, pathological, and treatment variables were evaluated. TTF and OS were estimated by Kaplan–Meier; prognostic factors were tested using Cox models. • **Results:** Median TTF was 4.1 months and OS 28.7 months; ORR was 9%. Multivariate predictors of shorter TTF included non-ductal histology, prior chemotherapy, and ≥4 metastatic sites. TTF declined progressively with increasing risk factors. • **Conclusions:** Everolimus shows modest benefit post-CDK4/6i, with clear clinicopathologic predictors of poorer durability, guiding personalized sequencing decisions in advanced ER+/HER2– disease.

Notable Presentations At SABCS 2025 Metastatic Breast (3/8)

Date	Title	Author	Summary
10 Dec 2025	Enrolment of Patients with Metastatic Lobular Breast Cancer in Clinical Trials in the Multicenter ESME Cohort	Eleonora De Maio	• **Introduction:** ILC differs biologically from NST yet remains underrepresented in trials, potentially limiting tailored evidence for metastatic ILC. • **Methodology:** Using the nationwide ESME MBC registry (2008–2023), trial enrolment was compared across ILC, NST, and mixed subtypes. A "trial-eligible" ILC subgroup underwent multivariable analysis. • **Results:** Among 32,722 pts, trial enrolment was lower in ILC vs NST (12.6% vs 16.2%). First-line participation was similarly reduced (7.4% vs 9.5%). ILC pts entered more phase III but fewer phase I trials. Only grade II predicted enrolment. • **Conclusions:** ILC shows systematic under-enrolment, underscoring access disparities and the need for ILC-specific trial strategies.
11 Dec 2025	A real-world prospective observational multi-national study in adult patients with breast cancer treated with extended adjuvant neratinib: interim results from the NERLYFE study	Rupert Bartsch	• **Introduction:** Neratinib improves iDFS in HR+/HER2+ EBC but causes clinically significant diarrhoea. Real-world data are needed to optimize prophylaxis and maintain adherence. • **Methodology:** NERLYFE is a European PASS evaluating diarrhoea-related discontinuation over the first 3 months in patients receiving neratinib for up to 12 months. Dosing, prophylaxis use, and diarrhoea patterns were assessed. • **Results:** Among 113 patients, 14% discontinued due to diarrhoea—lower with prophylaxis (10% vs 21%) and with <240 mg starting dose (12% vs 15%). Any-grade diarrhoea occurred in 88% (20% grade 3), typically within 7 days. Prophylaxis halved median duration of grade ≥3 diarrhoea (6.5 vs 13 days). • **Conclusions:** Prophylaxis meaningfully reduces diarrhoea severity and discontinuations, supporting optimized supportive care to maintain neratinib benefit in HR+/HER2+ EBC.

Notable Presentations At SABCS 2025
Metastatic Breast (4/8)

Date	Title	Author	Summary
11 Dec 2025	A phase 1/2, first-in-human study of AVZO-021, a selective cyclin-dependent kinase 2 inhibitor (CDK2i), as a monotherapy and in combination for patients with advanced solid tumors, including hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) breast cancer and cyclin E1 (CCNE1)-amplified solid tumors: preliminary safety and efficacy results	Alberto J Montero	• **Introduction:** CCNE1 overexpression and CDK2 activation drive resistance to CDK4/6 inhibitors in HR+/HER2− mBC. AVZO-021, a selective CDK2 inhibitor, is being tested to overcome this escape pathway. • **Methodology:** In this phase 1 dose-escalation study, AVZO-021 (20–220 mg QD) is evaluated as monotherapy and combined with ET, CDK4/6i, sacituzumab govitecan, or carboplatin. Key endpoints include safety, PK, and early activity. • **Results:** Among 47 treated patients (68% breast cancer), no DLTs or discontinuations occurred up to 220 mg. Common TEAEs were fatigue, nausea, anemia, and vomiting. PK showed robust target coverage and 14-hour half-life. Combination cohorts showed no new safety concerns. • **Conclusions:** AVZO-021 demonstrates favorable tolerability, pharmacology, and rationale for combination strategies, supporting continued development in CDK4/6-resistant HR+/HER2− mBC.
12 Dec 2025	Rhenium (186Re) obisbemeda (rhenium nanoliposome,186RNL) for the treatment of leptomeningeal metastases (LM): Phase 1 dose escalation study results	Andrew Brenner	• **Introduction:** Leptomeningeal metastases carry dismal outcomes. 186Re-Obisbemeda (Reyobiq™) delivers intraventricular beta radiation with gamma imaging capability and a long half-life optimized for CSF distribution. • **Methodology:** ReSPECT-LM was a phase I 3+3 dose-escalation study (6.6–109.96 mCi) administering a single intraventricular dose via Ommaya reservoir to assess MTD/MFD, safety, and preliminary activity. • **Results:** Among 29 treated patients, 45% had breast cancer. DLTs occurred only at high doses (cohorts 5–6). RP2D was 44.10 mCi with no serious AEs. Breast-cancer–specific clinical benefit (CR/PR/SD) reached 67%, with 87.5% CSF-TCE responses. Across early cohorts, median OS was 9 months—substantially exceeding historical ~4 months. • **Conclusions:** Reyobiq is safe, delivers high therapeutic CSF radiation, and shows encouraging radiographic, clinical, and CSF-molecular activity, supporting ongoing multidose optimization studies.

Notable Presentations At SABCS 2025
Metastatic Breast (5/8)

Date	Title	Author	Summary
12 Dec 2025	Pyrotinib or placebo in combination with trastuzumab and docetaxel for untreated HER2-positive metastatic breast cancer: long-term survival results from the phase 3 PHILA study	Binghe Xu	• **Introduction:** PHILA evaluated pyrotinib + trastuzumab + docetaxel (PyroHT) vs HT as first-line therapy in HER2+ metastatic breast cancer, previously demonstrating significant PFS and OS benefit. • **Methodology:** In this double-blind phase 3 trial, 590 untreated HER2+ MBC patients were randomized 1:1 to PyroHT or HT. Primary endpoint was investigator-assessed PFS; updated OS results were analyzed after ~45.5 months' follow-up. • **Results:** PyroHT sustained significant OS benefit (HR 0.74) with 5-year OS of 65.7% vs 58.5% and durable PFS advantage (HR 0.44) with 29% vs 4% remaining progression-free at 5 years. Benefit was consistent across subgroups, including prior trastuzumab exposure. PyroHT delayed onset of brain metastases (16.6 vs 9.1 months). Diarrhea rates declined markedly after docetaxel discontinuation. • **Conclusions:** Long-term data confirm durable OS and PFS improvements with PyroHT, reinforcing dual HER2 blockade with pyrotinib + trastuzumab as a strong first-line standard for HER2+ MBC.
12 Dec 2025	Jbcrg-m06/emerald post-hoc analysis by physician's choice of docetaxel or paclitaxel: efficacy and safety of eribulin mesylate vs taxanes combined with trastuzumab and pertuzumab as first-line for her2-positive locally advanced or metastatic breast cancer	Norikazu Masuda	• **Introduction:** JBCRG-M06/EMERALD showed eribulin was non-inferior to taxanes when paired with trastuzumab + pertuzumab in first-line HER2+ LABC/mBC. This post-hoc analysis compared outcomes by taxane type. • **Methodology:** Patients were randomized to eribulin or taxane (docetaxel or paclitaxel). Survival was assessed using Kaplan–Meier and log-rank tests; safety and response patterns were explored by waterfall and swimmer plots. • **Results:** Among 222 taxane-treated patients, 84% received docetaxel and 16% paclitaxel. PFS and OS were similar between docetaxel and paclitaxel groups. AE profiles were comparable across arms, but peripheral sensory neuropathy was highest with paclitaxel, and neutropenia was lowest with docetaxel. • **Conclusions:** Docetaxel and paclitaxel produced equivalent efficacy with dual HER2 blockade. Paclitaxel caused more neuropathy, supporting individualized taxane selection in HER2+ LABC/mBC.

Notable Presentations At SABCS 2025
Metastatic Breast (6/8)

Date	Title	Author	Summary
12 Dec 2025	Clinical predictors for first-line treatment duration in HER2-positive metastatic breast cancer Results from the AGMT_MBC-Registry	Gabriel Rinnerthaler	• **Introduction:** CLEOPATRA established THP as the 1L standard for HER2+ MBC, but DESTINY-Breast09 suggests some patients may benefit more from T-DXd–based regimens. Identifying patients with long THP durability may guide 1L selection. • **Methodology:** Using the Austrian AGMT_MBC registry, HER2+ MBC patients treated with 1L THP were analyzed. TTNT was modeled via multivariable Cox regression with stepwise AIC-based variable selection. A risk score derived from the linear predictor stratified patients into low, intermediate, and high-risk groups. • **Results:** Among 218 patients, significant predictors of shorter TTNT included brain metastases (HR 2.22), pleural metastases (HR 3.41), disease-free interval <24 months (HR 1.98), and older age. Risk-score stratification showed markedly shorter TTNT in intermediate- (HR 1.79) and high-risk groups (HR 5.39) versus low-risk. One-year treatment continuation was 84% in low-risk vs 45% in high-risk patients. • **Conclusions:** A clinically grounded risk model identified HER2+ MBC patients likely to derive prolonged benefit from 1L THP. This approach may help reserve T-DXd–based regimens for higher-risk patients; external validation is needed.
12 Dec 2025	Utidelone plus bevacizumab for the treatment of HER2-positive breast cancer brain metastases (U-BOMB-HER): A multicenter, single-arm phase IIstudy	Min Yan	• **Introduction:** Brain metastases in HER2+ MBC remain difficult to treat after failure of trastuzumab, TKIs, and increasingly ADCs. Leveraging utidelone's BBB penetration and bevacizumab's anti-edema effects, U-BOMB-HER evaluated this combination in a refractory setting. • **Methodology:** This multicenter, single-arm phase II cohort enrolled HER2+ MBC patients with progressive brain metastases post-trastuzumab and TKI. Patients received utidelone (30 mg/m² days 1–5) plus bevacizumab (15 mg/kg day 1) every 21 days. Primary endpoint was CNS-ORR (RECIST 1.1). Secondary endpoints included CNS-DCR, PFS, CNS-PFS, OS, and safety. • **Results:** Among 50 evaluable patients (52% prior ADCs), CNS-ORR reached 54.0% and CNS-DCR 92.0%. Median PFS was 8.6 months and median OS 11.0 months. Activity was observed across radiotherapy-naïve and post-RT groups. Toxicities were frequent but manageable; grade 3 events included neuropathy (6%), neutropenia (16%), leukopenia (8%), and hypertension (12%) with no grade ≥4 events. • **Conclusions:** Utidelone plus bevacizumab shows meaningful CNS efficacy and acceptable tolerability in HER2+ TKI-refractory brain metastases, supporting further development of this regimen.

Notable Presentations At SABCS 2025
Metastatic Breast (7/8)

Date	Title	Author	Summary
12 Dec 2025	Safety analysis of phase 3 ASCENT-04 study of sacituzumab govitecan (SG) + pembrolizumab (pembro) vs chemotherapy (chemo) + pembro for previously untreated PD-L1+ metastatic triple-negative breast cancer (mTNBC)	Kevin Kalinsky	• **Introduction:** SG + pembrolizumab significantly improved PFS vs chemotherapy + pembro in PD-L1+ mTNBC (ASCENT-04). A detailed safety evaluation was conducted to contextualize the observed efficacy benefit. • **Methodology:** Pts were randomized 1:1 to SG + pembro or physician's-choice chemotherapy + pembro. Safety analyses included exposure-adjusted incidence rates (EAIRs), severity, onset, duration, and supportive-care use for key toxicities—neutropenia, diarrhea, and immune-mediated AEs (imAEs). G-CSF prophylaxis and AE-related dose modifications were assessed. • **Results:** Across 441 patients, EAIRs were broadly comparable between arms. Neutropenia was manageable with G-CSF, with lower grade ≥3 rates in SG + pembro (35% with prophylaxis) vs chemo + pembro (50%). Diarrhea was more frequent with SG + pembro (70% vs 29%) but mostly grade 1–2 and rarely caused dose reductions (5%) with no discontinuations. Colitis occurred in 6% and 1% respectively, typically manageable. Overall, SG + pembro had fewer discontinuations and no amplification of pembrolizumab-related imAEs. • **Conclusions:** SG + pembro shows a favorable, manageable safety profile with expected toxicity patterns and no imAE exacerbation, supporting its strong benefit–risk balance in PD-L1+ mTNBC.
12 Dec 2025	Trial in progress: Phase 1 Study Targeting DNA Methyltransferases in Metastatic Triple-Negative Breast Cancer (NCI Protocol #10546)	Roberto Leon-Ferre	• **Introduction:** Preclinical work shows DNMT3A predicts sensitivity to DNMT inhibition and that DNMT blockade enhances immune activation and potentiates paclitaxel and ICI activity. • **Methodology:** This phase 1, open-label, multicenter trial evaluates oral ASTX727 (decitabine/cedazuridine) + paclitaxel + pembrolizumab in metastatic TNBC. A 3+3 design tests 5 ASTX727 dose levels to establish the RP2D, followed by a 6-patient expansion. Key endpoints include safety, RP2D determination, antitumor activity, methylation changes, immune modulation, and correlations with DNMT3A expression. Eligible pts have TNBC, ECOG ≤2, 0–3 prior metastatic lines, and may have previously received ICIs. • **Results:** As of June 20, 2025, 10 pts have been treated in dose-finding. Enrollment and dose escalation remain ongoing. No efficacy or safety outcomes beyond dosing status are yet available. • **Conclusions:** This first-in-human combination targeting DNMT-driven epigenetic vulnerability in TNBC is feasible and progressing through dose escalation. Upcoming RP2D, safety, immune-modulation, and methylation-response data will clarify the regimen's therapeutic potential and role in DNMT3A-expressing TNBC.

Notable Presentations At SABCS 2025 Metastatic Breast (8/8)

Date	Title	Author	Summary
12 Dec 2025	A Real-World Multicenter Study in China: Efficacy and Safety of Sacituzumab Govitecan in Heavily Pretreated HER2-Negative Metastatic Breast Cancer Patients and Brain Metastases	Xu Liang	• **Introduction:** Sacituzumab govitecan (SG) improves survival in mTNBC and HR+/HER2– MBC, but real-world evidence in Chinese patients—especially those with brain metastases—is limited. • **Methodology:** This multicenter retrospective study analyzed 58 HER2– MBC patients treated with SG (2023–2024). Outcomes included rwPFS, rwOS, ORR, DCR, intracranial activity, and safety, with subgroup analyses by subtype and CNS involvement. • **Results:** Overall ORR was 34.5% and DCR 81%; median rwPFS 4.41 months and rwOS 16.3 months. TNBC and HR+/HER2– subgroups showed comparable benefits. In 12 patients with brain metastases, ORR was 25%, icORR 41.6%, icPFS 14.9 months, and rwOS 17.5 months. SG toxicity was manageable, with lower neutropenia rates supported by G-CSF prophylaxis. • **Conclusions:** SG demonstrated meaningful systemic and intracranial activity with favorable tolerability in Chinese HER2– MBC, supporting its expanding real-world role, including for CNS-involved disease.

Notable Presentations At SABCS 2025 Immunotherapy Across Subtypes (1/8)

Date	Title	Author	Summary
09 Dec 2025	Early Adverse Symptoms Predict Response to Treatment Among Patients in the I-SPY Trial	Amrita Basu	• **Introduction:** This study evaluated whether early patient-reported symptoms predict pCR in high-risk stage II/III breast cancer. • **Methodology:** Among 288 I-SPY2 patients, 33 PRO-CTCAE symptoms were captured in cycles 1–3. Odds ratios and Wilcoxon tests assessed associations between early moderate/severe AEs and pCR. MRI-derived ΔFTV quantified early volumetric response with multiple-testing correction. • **Results:** Early muscle pain, joint pain, headache, and mucositis strongly correlated with higher pCR odds (OR ≈ 2.6–3.6). Responders showed higher-grade muscle pain/palpitations and lower neuropathy. Limb swelling significantly aligned with ΔFTV reduction. • **Conclusions:** Early immune-linked symptoms function as sentinel biomarkers of response, supporting PRO-guided monitoring to optimize personalization and therapy continuation.
10 Dec 2025	Real-time monitoring for drug-induced interstitial lung disease with Trastuzumab Deruxtecan and Rilvegostomig combination therapy prevents persistent, symptomatic disease: Safety insights from the I-SPY2.2 platform trial	Ciara C OSullivan	• **Introduction:** ADC–IO combinations such as T-DXd + rilvegostomig carry substantial ILD risk, necessitating proactive detection frameworks to maintain safety during neoadjuvant therapy. • **Methodology:** In I-SPY2.2, 51 stage II/III patients received T-DXd + rilve with intensified monitoring: HRCT every 6 weeks, baseline/serial PFTs, 6MWT, and real-time centralized pulmonology adjudication. Predefined ILD criteria guided treatment holds/escalation. • **Results:** Eight ILD events (15.7%) occurred: grade 1 (n=5), grade 2 (n=2), grade 3 (n=1). All were HRCT-detected; PFTs/6MWT were non-informative. Symptoms resolved in 14–55 days; steroids managed higher-grade cases. No severe complications or ICU needs. • **Conclusions:** Six-weekly HRCT with centralized real-time review enables early ILD recognition, mitigates severity, and preserves treatment continuity—providing a scalable pulmonary-safety model for high-risk ADC–IO regimens.

Notable Presentations At SABCS 2025 Immunotherapy Across Subtypes (2/8)

Date	Title	Author	Summary
10 Dec 2025	Tumor-informed circulating tumor DNA analysis to assess molecular residual disease for prognosis and prediction of benefit from palbociclib in the PALLAS trial	Heather A Parsons	• **Introduction:** PALLAS evaluates whether palbociclib adds benefit to adjuvant endocrine therapy and integrates ctDNA-based MRD as a prognostic biomarker in stage II–III HR+/HER2– disease. • **Methodology:** Among 1280 randomly selected participants, tumor tissue and matched normal DNA underwent WES/WGS to generate personalized Signatera assays. Plasma was collected at C1D1, C6D1, and EOT. MRD (MTM/mL) was correlated with DRFI using Cox models under blinded conditions. • **Results:** Ongoing analyses will report MRD positivity and MTM/mL associations with 7-year DRFI across treatment arms. • **Conclusions:** PALLAS will deliver the first randomized phase III evidence on ctDNA-defined MRD in HR+/HER2– adjuvant therapy.
10 Dec 2025	Tissue-free circulating tumour DNA detection in patients with early triple negative breast cancer from the c-TRAK-TN trial	Niamh Cunningham	• **Introduction:** ctDNA predicts recurrence in early TNBC, but tumour-informed assays are resource-intensive. This study compared a tissue-free methylation assay with ddPCR in high-risk patients. • **Methodology:** c-TRAK-TN enrolled 159 patients with serial plasma collected up to 2 years. ddPCR tracked patient-specific variants; 1062 timepoints were tested with Guardant Reveal. Concordance and lead time were assessed. • **Results:** Reveal succeeded in 95.3% of samples, detecting ctDNA in 34% and strongly predicting relapse (HR 20.6). Overall concordance with ddPCR was 94.5%. Reveal detected ctDNA earlier in 44.8% vs 6.9% and showed longer lead time (7.9 vs 5.7 months). • **Conclusions:** Tissue-free ctDNA testing accurately anticipates relapse and often outperforms ddPCR, offering scalable, biopsy-free MRD surveillance.

Notable Presentations At SABCS 2025 Immunotherapy Across Subtypes (3/8)

Date	Title	Author	Summary
10 Dec 2025	A predictive gene signature for benefit from dose-dense adjuvant chemotherapy in patients with high-risk early breast cancer: results from the PANTHER phase III trial	Dimitrios Salgkamis	• **Introduction:** Dose-dense chemotherapy improves outcomes, but only SET2,3 previously predicted benefit; proliferation–immune biology may refine escalation selection. • **Methodology:** In PANTHER, 481 sequenced tumors were profiled for mitotic (MKS) and immune (IKS/IAS) modules. Combined MKS–immune strata were correlated with BCRFS, EFS, DDFS, and OS over 10.2 years using multivariable models. • **Results:** A molecular subgroup (32.6%) showed marked DD-ACT benefit (HR 0.29), while others did not (HR 1.22; p_interaction = 0.02). Sensitive tumors exhibited low mitotic/immune kinase expression or high mitosis with cold immunity. • **Conclusions:** A robust gene signature predicts DD-ACT benefit across endpoints, supporting external validation.
10 Dec 2025	Translational analysis of cerebrospinal fluid (CSF) and plasma circulating tumor DNA (ctDNA) from breast cancer patients (pts) with leptomeningeal disease (LMD) treated with trastuzumab deruxtecan (T-DXd) in the DEBBRAH trial	Amanda Fitzpatrick	• **Introduction:** LMD carries dismal outcomes and limited trial inclusion; CSF ctDNA may enable sensitive monitoring of T-DXd activity in HER2-positive/HER2-low disease. • **Methodology:** Seven cytology-confirmed LMD patients in DEBBRAH Cohort 5 received T-DXd. Serial CSF and plasma cfDNA underwent shallow WGS (ichorCNA) to quantify tumour fraction alongside intracranial (RANO-BM) and extracranial (RECIST) response. • **Results:** Baseline CSF ctDNA was detectable in all patients versus plasma in 3/7. All four with serial CSF sampling showed ctDNA reduction; two achieved complete clearance within 1–2 cycles. Progression was predominantly extracranial, reflected by rising plasma ctDNA. • **Conclusions:** CSF ctDNA is a highly sensitive biomarker for LMD response and warrants integration into LMD-focused trials.

Notable Presentations At SABCS 2025 Immunotherapy Across Subtypes (4/8)

Date	Title	Author	Summary
10 Dec 2025	Artificial Intelligence-Based Histopathology Model Predicts Recurrence Risk in Older Patients with Early HR+/HER2− Breast Cancer: Results from the Basel University Hospital Cohort	Elena Diana Chiru	• **Introduction:** Risk-stratification in HR+/HER2− early breast cancer is unreliable in older patients, especially with intermediate ODX scores. ATX, an AI model integrating H&E histology and clinical data, may improve prognostication. • **Methodology:** ATX scores were computed for 267 patients (40 ≥70 y). Prognostic accuracy for DFI was assessed using C-index and HRs. Reclassification of ODX-intermediate cases and validation across five external cohorts were evaluated. • **Results:** In ≥70 y patients, ATX showed strong performance (C-index 0.79; HR 2.12), outperforming ODX. ATX reclassified 77% of ODX-intermediate cases and remained robust across 611 external elderly patients. • **Conclusions:** ATX delivers superior, generalizable risk prediction and resolves intermediate-score ambiguity, supporting individualized therapy in older adults.
10 Dec 2025	Early on-treatment PD-L1 expression and stromal tumor infiltrating lymphocytes (sTILs) refine the prediction of EFS in the NeoTRIP trial	Matteo Dugo	• **Introduction:** On-treatment sTILs and PD-L1 predict EFS in TNBC, particularly with atezolizumab. This study sought baseline determinants of PD-L1 up-regulation and tested combined on-treatment biomarker performance. • **Methodology:** NeoTRIP randomized 280 patients to CT vs CT/A. Baseline and D1C2 samples underwent sTIL/PD-L1 assessment, RNA-seq, and IMC. EFS was analyzed by Kaplan–Meier. Differential biology underlying PD-L1 conversion was evaluated with FDR correction. • **Results:** No robust baseline predictors emerged. PD-L1 converters showed interferon-enriched signatures; enrichment patterns differed by arm. Only in CT/A did combined D1C2 sTILs+PD-L1 significantly improve EFS prediction (p=0.01), with PD-L1+/sTIL-High achieving the best 5-year EFS (0.86). • **Conclusions:** On-treatment sTILs+PD-L1 provides independent predictive–prognostic value under immunotherapy, irrespective of pCR, warranting validation in pembrolizumab-treated cohorts.

Notable Presentations At SABCS 2025 Immunotherapy Across Subtypes (5/8)

Date	Title	Author	Summary
11 Dec 2025	Three-year event-free survival from a phase 2 study of peri-operative immune checkpoint inhibition and cryoablation in women with hormone receptor-negative, HER2-negative early stage/resectable breast cancer (ipilimumab/nivolumab cohort)	Heather L McArthur	• **Introduction:** Residual TNBC after NAC carries poor prognosis (3-yr EFS <60%). Preclinical synergy between cryoablation and ICI prompted evaluation of peri-operative ipilimumab/nivolumab plus cryo to enhance antitumor immunity. • **Methodology:** Fifteen patients with resectable, high-risk TNBC and ≥1 cm residual disease post-NAC received ipi/nivo 1–5 days before cryo, followed by surgery and adjuvant nivo. Capecitabine was recommended. Primary endpoint was 3-yr EFS; safety and survival endpoints were secondary. • **Results:** At 49.5 months, 3-yr EFS was 66.7%, exceeding historical benchmarks. Five recurrences occurred; 3-yr DDFS was 73.3% and OS 80%. Grade ≥3 AEs occurred in 40%, mainly immune-related; cryo toxicity was minimal. • **Conclusions:** Peri-operative ICI plus cryo shows promising long-term benefit and manageable toxicity, supporting cryo-augmented immunotherapy as a potential strategy in high-risk early TNBC.
11 Dec 2025	Heating up cold tumors: single-cell mapping of immune and adenosine pathway reprogramming in luminal B breast cancer (Neo-CheckRay trial)	Marcela Carausu	• **Introduction:** Luminal B breast cancer is immunologically "cold," limiting pCR with NACT. Neo-CheckRay tested whether SBRT-based immune priming plus PD-L1 and adenosine blockade could enhance antitumor immunity. • **Methodology:** Single-cell RNA-seq of 78 tumor/LN samples from 28 patients across baseline, week 6, and surgery profiled immune states. Cell fractions and transcripts were compared across arms using Wilcoxon tests with rigorous QC. • **Results:** Baseline CXCL13+ myeloids and IL2RA+ T cells predicted pCR under ICB. SBRT+NACT induced LN DC expansion and reduced suppressive macrophages. Arm 3 uniquely restored cytotoxic balance, maintained CXCL13+ myeloids, activated cGAS–STING/IFN signaling, and remodeled adenosine pathways by shifting CD73/CD39 to vasculature with increased ADA/ADK, unlike suppressive remodeling in non-responders. • **Conclusions:** Effective conversion of immune-cold tumors requires coordinated priming, PD-L1 blockade, and vascular-centric adenosine remodeling—supporting mechanistic synergy of oleclumab with ICB.

Notable Presentations At SABCS 2025 Immunotherapy Across Subtypes (6/8)

Date	Title	Author	Summary
11 Dec 2025	Updated results and an exploratory analysis of ESR1m circulating tumor DNA (ctDNA) dynamics from SERENA-6, a phase 3 trial of camizestrant (CAMI) + CDK4/6 inhibitor (CDK4/6i) for emergent ESR1 mutations (ESR1m) during first-line (1L) endocrine-based therapy and ahead of disease progression in patients (pts) with HR+/HER2- advanced breast cancer (ABC)	François-Clément Bidard	• **Introduction:** ESR1 mutations drive resistance to AI+CDK4/6i. SERENA-6 tests whether switching to camizestrant (CAMI) at ESR1m emergence—before radiologic progression—improves outcomes. • **Methodology:** In this randomized phase III trial, 315 HR+/HER2– ABC patients with on-treatment ESR1m were assigned to CAMI+CDK4/6i vs continued AI+CDK4/6i. PFS was primary; ctDNA ESR1m allele-frequency shifts from baseline to C3D1 were exploratory. • **Results:** Final PFS confirmed significant benefit across subgroups. CAMI induced near-complete ESR1m suppression (median −100%) versus a marked increase on continued AI (+66.7%); 24.4% of AI-treated patients had >500% ESR1m expansion vs 0.8% on CAMI. Safety remained favorable. • **Conclusions:** Early switch to CAMI+CDK4/6i at molecular progression prolongs PFS, suppresses ESR1m evolution, and delays need for chemotherapy/ADCs, supporting proactive ESR1m-guided treatment adaptation.
11 Dec 2025	Safety Run-In Phase of the ATRiBRAVE trial: a Phase II Study Evaluating Ceralasertib Priming Followed by Durvalumab/Nab-Paclitaxel to Restore Immunotherapy Sensitivity in Advanced Triple Negative Breast Cancer (TNBC)	Valentina Guarneri	• **Introduction:** TRiBRAVE evaluates ceralasertib priming plus durvalumab–nab-paclitaxel in TNBC relapsing after prior ICI and chemotherapy. • **Methodology:** This single-arm phase II trial uses ceralasertib (7-day priming, then q28), durvalumab (q28), and nab-paclitaxel. A 3+3 safety run-in assessed dose-limiting toxicities to determine the recommended ceralasertib dose. • **Results:** Two DLTs at 240 mg BID mandated de-escalation; 160 mg BID showed no DLTs in 6 patients, completing SRP. AEs were hematologic, manageable, and without grade 5 events or discontinuations. Durvalumab toxicity was typical. • **Conclusions:** Ceralasertib 160 mg BID with durvalumab–nab-paclitaxel is feasible and tolerable, supporting continued phase II evaluation.

Notable Presentations At SABCS 2025 Immunotherapy Across Subtypes (7/8)

Date	Title	Author	Summary
12 Dec 2025	A single preoperative pembrolizumab dose plus a single subablative radiotherapy fraction (7 Gy) elicits anti-tumor immune response and increases stromal tumor infiltrating lymphocytes in triple negative breast cancer: a phase 1b/2 study	Julia Tchou	• **Introduction:** Chemo-ICB improves TNBC outcomes but may overtreat small cT1N0 tumors. Low-dose RT can prime immunity. This study tested whether single-dose pembrolizumab plus sub-ablative RT induces robust immune activation without chemotherapy. • **Methodology:** In this phase 1b/2 trial, 30 early-stage patients received pre-operative pembrolizumab ± 7 Gy RT. Co-primary endpoints were feasibility and immune activation (sTIL increase, Ki67+ T-cell expansion). Tumor shrinkage >30% (TΔ30) defined response. PBMC phenotyping, TCR sequencing, and spatial transcriptomics were exploratory. • **Results:** RT+pembro significantly improved TΔ30 (56% vs 0%) and raised sTILs from median 20→50% overall and 40→60% in TNBC; high-sTIL TNBC doubled (27%→54%). Responders showed expansion of activated/proliferating T cells, diversified TCRs, and cGAS–STING/antigen-presentation signatures. • **Conclusions:** A single-dose pembro+RT regimen safely induces strong immune priming, increasing high-sTIL TNBC proportion—supporting its use as a chemotherapy-free induction strategy enabling adjuvant-omission trials.
12 Dec 2025	Phase I Study of Stereotactic Radiation and Sacituzumab Govitecan with Zimberelimab in the Management of Metastatic Triple Negative Breast Cancer with Brain Metastases	Kamran A Ahmed	• **Introduction:** TNBC brain metastases have poor outcomes. Sacituzumab govitecan (SG) shows BBB penetration, and SRS can enhance immune access. Combining SG, PD-1 blockade, and SRS may yield synergistic intracranial activity. • **Methodology:** In this phase I/II single-arm trial, adults with measurable TNBC brain metastases received SRS followed by SG (10 mg/kg D1/8 q3w) plus zimberelimab (360 mg q3w). Phase I used a 3+3 design to assess neurologic DLTs. • **Results:** Three enrolled patients experienced no intracranial DLTs. Neutropenia (100%) and fatigue were the main AEs. All achieved intracranial partial responses; systemic responses ranged from PR to PD. Two remain on treatment. • **Conclusions:** SG+zimberelimab with SRS is safe and shows early intracranial activity, supporting continued evaluation in phase II.

Notable Presentations At SABCS 2025
Immunotherapy Across Subtypes (8/8)

Date	Title	Author	Summary
12 Dec 2025	A phase 1b/2 clinical investigation of invikafusp alfa (STAR0602), a first-in-class dual T-cell agonist, in combination with sacituzumab govitecan in patients with metastatic TNBC or HR+/HER2- MBC (START-002 trial)	Steven J Isakoff	• **Introduction:** Invikafusp alfa, a dual Vβ6/Vβ10 T-cell agonist with FDA Fast Track status, expands tumor-reactive $CD8^+$ T cells and shows activity post–PD(L)1 therapy. Sacituzumab govitecan (SG) enhances immunogenicity. START-002 tests whether combining both amplifies anti-tumor immunity in metastatic breast cancer. • **Methodology:** This phase 1b/2 open-label study evaluates SG (D1/8 q21d) plus STAR0602 (D8). A 5-patient safety run-in at 0.04 mg/kg precedes dose selection (0.02–0.08 mg/kg). Two Simon two-stage phase II cohorts enroll mTNBC and HR+/HER2– mBC. • **Results:** Enrollment in safety run-in is ongoing; dose escalation and expansion will assess tolerability and preliminary ORR by RECIST/iRECIST. • **Conclusions:** START-002 will define the safety and early efficacy of combining SG with selective T-cell activation, aiming to enhance immunogenicity in advanced breast cancer.

Notable Presentations At SABCS 2025 Surgery & Radiotherapy (1/8)

Date	Title	Author	Summary
10 Dec 2025	Feasibility of Tailored Axillary Surgery (TAS) in Patients with Clinically Node-Positive Breast Cancer in the Upfront Surgery Setting: Results of a Prospective, Single-Arm, Multicenter Phase II Trial	Kaori Terata	• **Introduction:** This phase II trial evaluated TAS feasibility, procedural consistency, and predictors of residual nodal disease. • **Methodology:** In this single-arm, multicenter Japanese study (jRCTs061220113), TAS included removal of the marked node, sentinel lymph nodes (SLNs), and palpable nodes, followed by mandatory ALND. Eligible patients had upfront surgery, biopsy-confirmed nodal metastasis, 1–3 suspicious level I nodes, and cT1–T3 tumors. The primary endpoint was non-TAS nodal positivity. Multivariable logistic regression assessed clinicopathologic predictors. • **Results:** 212 pts were enrolled (median age 53.5). Marked node retrieval was 100%, though 30% lacked SLN tracer uptake. Median TAS nodes retrieved: 4 (including 2 metastatic). ALND removed a median of 18 nodes. TAS identification rate was 100%. Non-TAS nodal positivity was 38.7% (82/212). Predictors included fewer TAS nodes removed (OR 0.85) and more positive TAS nodes (OR 1.50). Clinical T stage and imaging-defined suspicious nodes were not significant. Major complications were infrequent (bleeding 4.3%, infection 3.7%). • **Conclusions:** TAS is feasible, safe, and reliably identifies metastatic nodes in cN+ disease. Non-TAS positivity was comparable to false-negative rates in SLN-positive cN0 trials despite higher tumor burden.
10 Dec 2025	Omission of Axillary Surgery in Early Breast Cancer with Negative Lymph Nodes: A Systematic Review and Meta-Analysis of Randomized Clinical Trials	Giuliano M Duarte	• **Introduction:** Axillary surgery is increasingly questioned in early-stage, node-negative breast cancer as systemic therapy improves and morbidity concerns rise. • **Methodology:** A PRISMA-compliant meta-analysis (PROSPERO CRD420250653779) evaluated RCTs comparing omission of axillary surgery versus SLNB/AD. Seven trials (8,806 patients) were analyzed for OS, DFS, and axillary recurrence using RevMan 5.4 with RoB-2 bias assessment. • **Results:** Omission showed no OS (OR 1.02) or DFS detriment (OR 0.80). Axillary recurrence was higher without surgery (OR 0.18 favoring surgery) but remained uncommon. • **Conclusions:** Axillary surgery can be safely omitted in selected node-negative patients, with careful monitoring for slightly increased—but still low—regional recurrence.

Notable Presentations At SABCS 2025
Surgery & Radiotherapy (2/8)

Date	Title	Author	Summary
11 Dec 2025	Axillary surgery in breast cancer patients with one to three sentinel node macrometastases and breast-conserving therapy: Secondary results of the INSEMA trial	Toralf Reimer	• **Introduction:** Axillary staging guides prognosis and adjuvant therapy in early breast cancer. INSEMA evaluated de-escalation by omitting SLNB (Rando1) or avoiding cALND in SLNB-positive patients (Rando2). • **Methodology:** In this multicenter phase III trial, cN0 patients undergoing BCS with WBI were randomized 1:1 to SLNB alone versus cALND if SLNB showed 1–3 macrometastases. The per-protocol population (n=386) served as the primary analytic set. Primary outcome: invasive DFS non-inferiority. • **Results:** Non-inferiority of SLNB alone was not met (HR 1.69). Five-year iDFS was 86.6% vs 93.8% (SLNB vs cALND). OS and locoregional recurrence were comparable. SLNB alone significantly reduced lymphedema and functional morbidity. • **Conclusions:** SLNB alone showed similar survival but a numerical iDFS disadvantage. Morbidity benefits support continued evaluation; 10-year results are awaited.
11 Dec 2025	Insights of applied radiotherapy among patients undergoing breast-conserving surgery with or without axillary sentinel lymph node biopsy: secondary results from the INSEMA trial	Guido Hildebrandt	• **Introduction:** Axillary surgery de-escalation must be evaluated alongside radiotherapy, as incidental axillary irradiation may influence oncologic outcomes. INSEMA previously showed SLNB omission is safe in cN0 BCS patients at 5 years. • **Methodology:** This pre-planned secondary analysis assessed axillary dose distribution in 5,154 INSEMA participants across 108 radiotherapy centers. Axillary levels I–III were contoured per RTOG. Relative doses and patterns of RNI, fractionation, and boost use were compared between SLNB vs. no-SLNB arms. • **Results:** Most patients (95.7%) received WBI; 58% with standard tangents. Incidental axillary irradiation was substantial: >50% received ≥85% of breast dose to level I. SLNB patients received significantly higher doses in levels I–III and more frequent RNI (4.0% vs 0.9%). Fractionation and boost patterns were similar. Among patients without RT, iDFS did not differ. • **Conclusions:** Half of INSEMA patients received unintentional therapeutic-level axillary irradiation, particularly after SLNB. Higher incidental dose—and not surgery alone—may contribute to favorable outcomes, underscoring the need to interpret axillary de-escalation in the context of RT fields.

Notable Presentations At SABCS 2025
Surgery & Radiotherapy (3/8)

Date	Title	Author	Summary
11 Dec 2025	Primary Results from the HR+/HER2- Cohort of TBCRC-053 (P-RAD): A Randomized Trial of No, Low, or High Dose Preoperative RADiation with Pembrolizumab and Chemotherapy in Node-Positive, HER2-Negative Breast Cancer	Gaorav Gupta	• **Introduction:** Screen-detected DCIS is rising, prompting interest in nonsurgical management. Early prospective data suggested feasibility, but short follow-up limits confidence. LORETTA evaluated tamoxifen (TAM) alone for strictly defined low-risk DCIS. • **Methodology:** This single-arm confirmatory trial enrolled women ≥40 years with ER+, HER2–, NG1–2 DCIS ≤25 mm, no comedo necrosis, and no invasive disease on multimodal imaging. TAM 20 mg/day was given without surgery. The primary endpoint was 5-year ipsilateral invasive cancer incidence (CIPIC), with efficacy defined by an upper 95% CI ≤ 7%. • **Results:** Among 341 patients (median age 53), median follow-up was 36 months. DSMC halted the trial early: 5-year CIPIC was 9.8% (95%CI 5.2–16.1%), exceeding the predefined threshold. Tumor diameter predicted invasive events; other factors did not. Surgery-free survival was 82%; contralateral events were rare; OS was 98.8%. Grade ≥3 toxicity was 3.8%. • **Conclusions:** TAM alone did not meet the efficacy criterion, though absolute invasive event and surgery rates were low. Endocrine-only management may be considered for highly selected low-risk ER+/HER2– DCIS but remains investigational pending longer follow-up.
11 Dec 2025	Radiation doses and fractionation schedules in non-low-risk ductal carcinoma in situ in the breast (BIG 3-07/TROG 07.01): final 10-year analysis of a randomised, factorial, multicentre, open-label, phase 3 study	Boon H Chua	• **Introduction:** Non-low-risk DCIS carries substantial recurrence risk after breast-conserving surgery. While WBI reduces recurrence, the long-term benefit of adding a tumor-bed boost and the impact of dose-fractionation remain uncertain. • **Methodology:** This international phase III trial randomized 1,608 women with non-low-risk DCIS to boost vs no boost after conventional (50 Gy/25F) or hypofractionated (42.5 Gy/16F) WBI. Stratification included age, endocrine therapy, and center. Primary endpoint: time to local recurrence; secondary endpoints included disease recurrence, OS, and toxicity. • **Results:** After 10.2 years, boost significantly reduced local recurrence (10-yr 93% vs 87%; HR 0.49). Disease-recurrence–free survival improved (87% vs 79%). OS was similar (96% vs 94%). Toxicity increased with boost (induration and pain). No interaction with fractionation; hypofractionation performed equivalently. • **Conclusions:** A tumor-bed boost provides durable recurrence reduction in non-low-risk DCIS at the cost of higher late toxicity. Hypofractionated WBI is safe and effective across boost strategies.

Notable Presentations At SABCS 2025
Surgery & Radiotherapy (4/8)

Date	Title	Author	Summary
12 Dec 2025	Radiation Therapy Followed by Intrathecal (IT) Trastuzumab/Pertuzumab in the Management of HER2⁺ Breast Leptomeningeal Disease: Interim Results from a Phase II Multi-Institutional Study	Kamran Ahmed	• **Introduction:** HER2+ leptomeningeal disease (LMD) has poor prognosis and limited therapeutic options. Intrathecal (IT) HER2-directed therapy is emerging as a targeted strategy. • **Methodology:** This multi-institutional phase II trial (NCT04588545) evaluated OS after radiation followed by IT trastuzumab (80 mg) plus pertuzumab (80 mg). Eligible patients had MRI and/or CSF-confirmed LMD, KPS ≥60, and no limits on prior therapies. • **Results:** Twenty patients were enrolled. Median OS and LMD-PFS were not reached; 12-month OS was 86% and LMD-PFS 65%. Responses included 20% CR, 25% PR, and 55% SD. Treatment was well tolerated with mainly fatigue, headache, and nausea. • **Conclusions:** Interim findings show promising survival and manageable toxicity, supporting continuation to stage II.
12 Dec 2025	Vacuum Assisted Excision (VAE): A single-step approach to the diagnosis and percutaneous treatment of Early Breast Cancer (THE VAE BReast 01 TRIAL)	Henrique Lima Couto	• **Introduction:** Vacuum-assisted excision (VAE) is expanding from benign and B3 lesions toward minimally invasive management of small breast cancers, but margin status remains a critical limitation. • **Methodology:** This prospective study enrolls women with unifocal ≤1.5 cm BI-RADS 4–5 tumors. VAE combined with percutaneous cavity-margin sampling is assessed for complete oncologic excision. Diagnostic performance metrics and patient-reported outcomes (BreastQ) are collected. • **Results:** Data will evaluate sensitivity, specificity, residual disease rates, safety, cosmetic outcomes, and patient experience. • **Conclusions:** If margin-negative excision is feasible, VAE may represent a safe, low-morbidity, percutaneous treatment option for selected early breast cancers.

Notable Presentations At SABCS 2025
Surgery & Radiotherapy (5/8)

Date	Title	Author	Summary
12 Dec 2025	Targeted axillary dissection vs axillary node clearance in patients with positive axillary nodes in early breast cancer: a multicentre, pragmatic, phase 3 randomised controlled trial	Shelley Potter	• **Introduction:** Node-positive breast cancer often undergoes axillary node clearance (ANC), a morbid procedure with high long-term toxicity and unclear benefit in low-volume disease. • **Methodology:** TADPOLE is a UK multicentre phase III RCT randomizing cN0, biopsy-proven low-volume nodal-positive patients 2:1 to targeted axillary dissection (TAD) vs ANC. Co-primary endpoints: 12-month lymphoedema and 5-year locoregional recurrence. QA frameworks and ART prohibition in TAD ensure protocol fidelity. • **Results:** Consensus surgical standards established; recruitment begins September 2025 across 40 sites with an internal pilot. • **Conclusions:** If TAD reduces morbidity without compromising control, it could replace ANC and transform UK axillary management.
12 Dec 2025	A phase III trial evaluating De-escalation of Breast Radiation (DEBRA) following breast-conserving surgery of stage 1, HR+, HER2-, RS ≤18 breast cancer: NRG-BR007	Julia R White	• **Introduction:** Early-stage ER/PR+, HER2– tumors often have low genomic risk; assays such as Oncotype DX® may enable radiotherapy (RT) de-escalation after breast-conserving surgery (BCS). • **Methodology:** BR007 randomizes women aged 50–69 with stage I, node-negative, RS ≤ 18 disease to BCS+RT+endocrine therapy (ET) vs BCS+ET alone. Primary endpoint is in-breast recurrence; secondary endpoints include breast preservation, survival outcomes, and patient-reported metrics. Non-inferiority margin is a 4% 10-year IBR difference. • **Results:** Accrual targets 1,670 pts; 1,349 randomized by July 2025. • **Conclusions:** If RT omission is non-inferior, genomic-guided de-escalation could reduce overtreatment in low-risk stage I breast cancer.

Notable Presentations At SABCS 2025 Surgery & Radiotherapy (6/8)

Date	Title	Author	Summary
12 Dec 2025	Cryoablation versus Breast Surgery in the Local Treatment of Early-Stage Breast Cancer: Protocol for the CRYSTAL-SIX Trial (CRYoablation for Small Tumors As Local Treatment)	Vanessa Monteiro Sanvido	• **Introduction:** Growing interest in minimally invasive local therapy has positioned cryoablation as a potential alternative to surgery in small, node-negative breast cancers. • **Methodology:** CRYSTAL–SIX randomizes 750 women with T1N0 tumors to cryoablation (no axillary surgery) vs surgery, with ultrahypofractionated RT when indicated. Endpoints include 5-year local control, costs, survival, recurrence, liquid-biopsy monitoring, and patient-reported outcomes. • **Results:** Recruitment began March 2025; trial integrates de-escalated local therapy with CTC-based monitoring. • **Conclusions:** If non-inferior, cryoablation may provide a safe, less invasive, cost-effective alternative, redefining early breast cancer local management.
12 Dec 2025	Dose-dense Paclitaxel with Empegfilgrastim vs weekly Paclitaxel in luminal B HER2-negative early breast cancer (PULSE trial)	Petr Krivorotko	• **Introduction:** Luminal B/HER2– breast cancer responds poorly to standard NCT, with pCR rates ~20%, and no trials have compared weekly vs biweekly paclitaxel. • **Methodology:** This single-center phase II non-inferiority trial tests biweekly paclitaxel after ddAC with empegfilgrastim against matched historical weekly paclitaxel controls (1:3 matching). Primary endpoint: pCR; secondary: RCB 0–I, EFS, dose intensity, surgery rates, safety. • **Results:** Prospective enrollment receives ddAC→biweekly paclitaxel; analysis uses logistic regression and time-to-event models. • **Conclusions:** Findings will determine whether biweekly paclitaxel maintains efficacy, supporting design of a future phase III de-escalation trial.

Notable Presentations At SABCS 2025 Surgery & Radiotherapy (7/8)

Date	Title	Author	Summary
12 Dec 2025	Small: open surgery versus minimally invasive vacuum-assisted excision for small screen-detected breast cancer – a UK phase III randomised multi-centre trial	Stuart McIntosh	• **Introduction:** Screening increasingly detects small, indolent ER+/HER2– tumors, prompting evaluation of minimally invasive alternatives to avoid overtreatment. • **Methodology:** SMALL is a phase III RCT randomizing 800 women (2:1) to vacuum-assisted excision (VAE) vs surgery for screen-detected, grade 1, ≤15 mm tumors with negative axillary staging. Co-primary endpoints: second-procedure rates (non-inferiority) and 5-year local recurrence after VAE. • **Results:** Across 49 centers, 640 patients enrolled; QRI-guided recruitment optimization improved accrual and communication fidelity. • **Conclusions:** Completion in 2026 may establish VAE as a safe, less morbid alternative to surgery for highly selected low-risk screen-detected cancers.
12 Dec 2025	Rossini-platform: a 'basket factorial multi arm multi stage (mams)' platform trial in surgical site infection – the breast surgery pillar	Katherine Fairhurst	• **Introduction:** SSI is the most frequent postoperative complication in breast surgery, impairing recovery, delaying adjuvant therapy, and increasing recurrence risk. • **Methodology:** ROSSINI-Platform is a multicentre, NIHR-funded basket factorial MAMS trial evaluating multiple SSI-prevention strategies (prophylactic antibiotics, Granudacyn® irrigation, DACC dressings) versus standard care in 4,280 breast surgery patients, stratified by key risk factors. • **Results:** Eligibility excludes primary whole-breast reconstruction; SSI is assessed via hospital review and a digital wound hub with patient-submitted images. Secondary endpoints include QoL, cost-effectiveness, and wound complications. • **Conclusions:** This platform aims to generate rapid, practice-changing evidence to standardise SSI prevention nationally and internationally.

Notable Presentations At SABCS 2025
Surgery & Radiotherapy (8/8)

Date	Title	Author	Summary
12 Dec 2025	Radiant study: Phase 1b study of pre-op radiation with abemaciclib and letrozole in early-stage hormone-receptor positive breast cancer	Mridula George	• **Introduction:** CDK4/6 inhibitors show radiosensitizing synergy in HR+/HER2– disease, supporting investigation of concurrent preoperative RT plus endocrine therapy. • **Methodology:** RADIANT is a single-arm phase 1b trial (N=15) testing abemaciclib + letrozole with preoperative RT using a BOIN dose-escalation design. Eligible pts have cT1c–T2N0 HR+/HER2– tumors and Oncotype RS ≤25. • **Results:** Treatment includes 3 cycles NET/CDK4/6i, concurrent RT with abemaciclib 100–50 mg BID, then 2 post-RT cycles, followed by surgery. Safety is assessed via DLTs; efficacy via RCB. • **Conclusions:** The trial aims to define tolerability and early activity of CDK4/6i-RT combinations to enable future neoadjuvant de-escalation strategies.

Notable Presentations At SABCS 2025
Supportive Care, QoL, Toxicity, Lifestyle, Psychosocial (1/7)

Date	Title	Author	Summary
10 Dec 2025	Nausea as a Mediator of Olanzapine's effect on Quality-of-Life Improvement in Patients Receiving Highly or Moderately Emetogenic Chemotherapy Insights from a Phase III NCORP RCT	Luke J Peppone	• **Introduction:** This secondary analysis examined whether olanzapine's (OLZ) QOL benefits are mediated through nausea reduction, including subgroup effects by chemotherapy emetogenicity. • **Methodology:** From a Phase III NCORP trial, 310 breast cancer patients with moderate nausea after Cycle 1 were randomized to OLZ, prochlorperazine, or placebo. Nausea was diary-reported; QOL was measured with FACT-G. Structural equation modeling assessed mediation. • **Results:** OLZ improved QOL at T3 (MD 4.67), with 50.5% mediated by nausea reduction. Effects were strongest in highly emetogenic chemotherapy: FACT-G MD 6.50 (59% mediated) and physical well-being MD 3.20 (72% mediated). No significant benefit was seen with MEC. • **Conclusions:** More than half of OLZ's QOL benefit is driven by nausea control, supporting its integration into antiemetic regimens, particularly for highly emetogenic chemotherapy.
10 Dec 2025	Acupuncture for Preventing Progression of Taxane-Induced Peripheral Neuropathy (ATP) Beyond Cryotherapy: A Phase II Randomized, Double-Blinded, Sham-Controlled Trial	Iris Zhi	• **Introduction:** This study compared real versus sham acupuncture in early-stage breast cancer patients who developed CIPN during taxane therapy. • **Methodology:** Eighty patients on paclitaxel or nab-paclitaxel (with allowed co-therapies) were randomized 1:1 to real (RA) or sham acupuncture (SA) weekly for ≥4 sessions. Primary endpoint was Neuropathic Pain Scale (NPS) change at 4 weeks; relative dose intensity (RDI) was a secondary endpoint. • **Results:** Both RA and SA significantly reduced NPS at 4 weeks (RA −6.07; SA −6.98) and 12 weeks (RA −12.68; SA −10.52). No between-group differences were observed. ≥85% RDI was maintained in >80% of both arms. More RA patients met ≥30% pain reduction, but not significantly. • **Conclusions:** Real and sham acupuncture both improved CIPN symptoms without significant differences, suggesting nonspecific or placebo effects. Findings warrant further investigation into supportive interventions for CIPN despite cryotherapy.

Notable Presentations At SABCS 2025
Supportive Care, QoL, Toxicity, Lifestyle, Psychosocial (2/7)

Date	Title	Author	Summary
10 Dec 2025	Efficacy of cryotherapy using frozen gloves and socks to prevent docetaxel-induced onycholysis in early breast cancer patients undergoing sequential (neo)adjuvant (F)EC and docetaxel treatment: The Banquise randomized controlled trial.	Laurent Mathiot	• **Introduction:** Docetaxel commonly causes nail toxicity in early breast cancer (eBC), impairing quality of life and sometimes forcing dose modifications. Cryotherapy is used to mitigate toxicity, but evidence at standard cumulative doses remains limited. • **Methodology:** The randomized BANQUISE trial enrolled 280 eBC patients receiving three (neo)adjuvant docetaxel cycles after (F)EC. Patients were assigned to frozen gloves/socks or no cryotherapy. Primary endpoint was grade ≥2 nail toxicity; secondary endpoints included blinded dermatologist-assessed DNT scores, tolerability, and PROs. • **Results:** Cryotherapy significantly reduced grade ≥2 nail toxicity (18% vs 37%, p<0.001) across hands and feet, and lowered DNT scores at weeks 8 and 24. Nearly all patients completed at least one session, though ~40% reported discomfort. No PRO differences were observed. • **Conclusions:** Cryotherapy meaningfully reduces docetaxel-induced nail toxicity and represents an effective, scalable supportive-care strategy despite tolerability limitations.
10 Dec 2025	Preventing Chemotherapy-Induced Peripheral Neuropathy with Acupuncture: Preliminary Results of a Pooled Analysis of Three Parallel Randomized Trials	Weidong Lu	• **Introduction:** Chemotherapy-induced peripheral neuropathy (CIPN) is a major toxicity of taxanes, reducing quality of life and compromising treatment delivery. Acupuncture is widely studied for symptom relief, but its preventive efficacy remains uncertain. • **Methodology:** A pooled ITT analysis of three coordinated RCTs (USA, China, South Korea) randomized stage I–III breast cancer patients 1:1 to 14 acupuncture sessions vs. relaxation-video control over 12 weeks during taxane therapy. Primary endpoint was change in EORTC CIPN-20 sensory score at week 12; secondary endpoints included CIPN incidence, pain, and QoL through week 24. • **Results:** Among 127 analyzed patients (63 acupuncture, 64 control), baseline characteristics were similar. Both groups experienced significant CIPN worsening by week 12, but with no between-group differences at week 12 or 24. No acupuncture-related serious AEs occurred. • **Conclusions:** Acupuncture was safe and feasible but did not prevent CIPN progression versus control. Further analyses are ongoing.

Notable Presentations At SABCS 2025
Supportive Care, QoL, Toxicity, Lifestyle, Psychosocial (3/7)

Date	Title	Author	Summary
10 Dec 2025	Comparing Functional Measures and Their Associations with Toxicity and Survival in Older Adults with Early Breast Cancer: Results from the Prospective Multicenter HOPE Study	Yuliya Zektser	• **Introduction:** Geriatric assessment identifies vulnerability in older adults with early breast cancer better than clinician-rated Karnofsky Performance Status (cKPS). Whether patient-reported KPS (pKPS) can serve as a practical alternative is unclear. • **Methodology:** HOPE enrolled 499 women >65 years with stage I–III breast cancer starting (neo)adjuvant chemotherapy. Baseline frailty (DAFI), cKPS, and pKPS were categorized using standard cutoffs. Primary endpoint was grade ≥3 toxicity; secondary endpoints included treatment modifications and non–breast cancer–specific survival. Multivariable models adjusted for clinical factors. • **Results:** Prefrailty/frailty occurred in 21%, low cKPS in 4%, and low pKPS in 10%. Agreement between cKPS and pKPS was weak (κ=0.16). Frailty was consistently associated with toxicity, treatment modification, and non-BCSS. cKPS had limited associations; pKPS had none. • **Conclusions:** Patient-reported KPS did not predict outcomes and cannot substitute for geriatric assessment, which remains the strongest predictor of chemotherapy risk in older women.
10 Dec 2025	Effectiveness of post-discharge management program of breast cancer patients based on Smart Cancer Care 2.0 using patient reported outcome, a preliminary analysis of a randomized clinical trial	Su-Jin Koh	• **Introduction:** Smart Cancer Care 2.0 is a Korean digital platform using patient-reported outcomes to monitor post-treatment symptoms and unmet needs. This randomized trial assessed its effectiveness in breast cancer patients after discharge. • **Methodology:** Patients undergoing surgery, radiation, or chemotherapy were randomized to Smart Cancer Care–based management (A) or usual care (B). The intervention monitored symptoms and provided rehabilitation and health-behavior support for 3 months. Outcomes—EORTC QLQ-C30 quality of life and unplanned medical visits—were followed for 6 months. • **Results:** Among 169 analyzed patients, QoL did not differ at 1 month (A: 65.4 vs B: 65.2). Significant improvements emerged at 3 months (73.8 vs 64.7; p=0.017) and persisted at 6 months (75.7 vs 64.6; p=0.027). • **Conclusions:** Smart Cancer Care 2.0 post-discharge management significantly improved medium-term quality of life in breast cancer patients.

Notable Presentations At SABCS 2025
Supportive Care, QoL, Toxicity, Lifestyle, Psychosocial (4/7)

Date	Title	Author	Summary
10 Dec 2025	Exploratory Study on the Efficacy and Safety of Combined Scalp Cooling and HairRepro MEDIα for Chemotherapy-Induced Alopecia in Japanese Breast Cancer Patients	Emi Kanaya	• **Introduction:** This study explored its combined use with the PAXMAN cooling system. • **Methodology:** This retrospective analysis included 22 Japanese breast cancer patients (2022–2024) receiving standard adjuvant regimens. HairRepro MEDI α was applied twice daily from 6 days pre-chemotherapy to 90 days post-treatment. PAXMAN cooling was used at each cycle. Hair loss was evaluated photographically; safety was monitored • **Results:** Median hair loss at final chemotherapy was 45%; 50% achieved Grade ≤1 alopecia. No treatment-related adverse events occurred. Alopecia onset appeared delayed versus historical PAXMAN-only cohorts. All patients showed complete scalp hair regrowth by 3 months post-chemotherapy. • **Conclusions:** The combination of HairRepro MEDI α and PAXMAN scalp cooling showed encouraging prevention and accelerated regrowth of CIA, with outcomes appearing superior to scalp cooling alone. Findings support further randomized studies to validate efficacy and optimize CIA management.
10 Dec 2025	Secondary prevention of cancer therapy-induced thrombocytopenia with hetrombopag in breast cancer: a prospective,multi-center,self-controlled exploratory trial	Min Yan	• **Introduction:** Cancer therapy–induced thrombocytopenia (CTIT) disrupts treatment and increases bleeding risk. Hetrombopag, an oral TPO receptor agonist, may prevent CTIT in breast cancer patients. • **Methodology:** In this multicenter exploratory trial (NCT05394285), patients with platelet counts ≥100×10⁹/L after one CTIT episode (TTP) continued the same regimen in Cycle 2 and received prophylactic hetrombopag 7.5 mg/day for 14 days (SPP). The primary endpoint was SPP response: no platelet transfusion, no treatment modification, and no severe thrombocytopenia before Cycle 3. • **Results:** Among 66 evaluable patients, 77% received ADC monotherapy. Sixty patients completed both phases. The SPP response rate was 85% (51/60). During TTP, response rates were 86.7% with hetrombopag and 80% with rhTPO. No severe treatment-related adverse events occurred. • **Conclusions:** Hetrombopag showed promising efficacy and good tolerability for secondary CTIT prevention in breast cancer, supporting further confirmatory trials.

Notable Presentations At SABCS 2025
Supportive Care, QoL, Toxicity, Lifestyle, Psychosocial (5/7)

Date	Title	Author	Summary
10 Dec 2025	Incidence of relationship breakups during endocrine therapy for breast cancer: preliminary results of the ReBreCa trial	Mariana Carolina Vilas Boas Carvalho	• **Introduction:** Endocrine therapy (ET) can impair libido, body image, and communication, potentially destabilizing relationships. This study examined relationship breakups (RBr) during ET. • **Methodology:** Women ≥18 years with HR+ breast cancer on ET ≥6 months completed an online survey. Only those in relationships at ET start were analyzed. Associations used chi-square/Fisher tests. • **Results:** Of 201 respondents, 162 were in relationships. Median age was 44; most were premenopausal and on aromatase inhibitors. RBr occurred in 38%; 35% attributed it to cancer treatment and 27% to ET. Decisions were patient-driven (48%), partner-driven (37%), or mutual (15%). Drivers included low libido (27%), sexual dissatisfaction (19%), poor body image (22%), and communication issues (21%). Axillary dissection predicted higher RBr (52% vs 33%; p=0.04). Most who ended relationships anticipated future stable partnerships. Only 14% of those staying in relationships were dissatisfied; affection was the main reason for stability (73%). • **Conclusions:** Relationship breakups are frequent during ET and often linked to treatment-related sexual and emotional changes, stressing the need for proactive psychosocial support.
10 Dec 2025	Integrating Mental Health in Oncology: A Review of Psychiatric Symptom Monitoring in Recent Breast Cancer Trials	Fatma Nihan Akkoc Mustafayev	• **Introduction:** This study assessed how frequently psychiatric symptoms were monitored and reported in Phase III trials of FDA-approved BC therapies. • **Methodology:** From FDA archives, 21 BC treatments approved in the past decade were identified. Phase III trials initiated after 2015 with posted results (n=38; 26,298 participants) were reviewed for psychiatric symptom reporting. Protocols were examined for monitoring tools, criteria, and timing. Adverse events followed CTCAE guidelines. • **Results:** Of 38 trials, 97% reported at least one psychiatric symptom. Insomnia was most common (9.7%; 2,563 patients); nervousness was least reported (1 case). Other symptoms included anxiety, depression, stress, confusional states, and rare suicidal behaviors. Tools most often used were EORTC-QLQ-C30, EQ-5D-5L, NCI-PRO-CTCAE, and FACT-B, though application varied widely. Psychiatric monitoring was primarily confined to the treatment period, with minimal long-term follow-up. • **Conclusions:** Despite frequent reporting of psychiatric symptoms, monitoring remains inconsistent and largely short-term. Underrecognition and limited follow-up may compromise patient well-being, adherence, and outcomes.

Notable Presentations At SABCS 2025
Supportive Care, QoL, Toxicity, Lifestyle, Psychosocial (6/7)

Date	Title	Author	Summary
10 Dec 2025	Effects of Acupuncture vs Sham Acupuncture and Usual Care on Cancer-Related Cognitive Difficulties Among Breast Cancer Survivors: The ENHANCE Randomized Clinical Trial	Jun Mao	• **Introduction:** This analysis evaluated whether SETER/PR predicts benefit from extended letrozole therapy (ELT) in NSABP B-42, which randomized HR+ postmenopausal patients after 5 years of prior ET to ELT or placebo. • **Methodology:** SETER/PR was measured using the QuantiGene Plex assay on HER2-negative samples. Pre-specified cut points included the interquartile range (1.10–2.10) and mean value (≥1.50). Primary endpoint was breast cancer-free interval (BCFI). Stratified Cox models estimated hazard ratios (HRs). • **Results:** Of 1,556 eligible cases, 1,489 (96%) passed QC. ELT reduced 10-yr BCFI events by 4.2% (HR 0.69). SETER/PR distribution: 59% within 1.10–2.10; 42% ≥1.50. No differential ELT effect was observed using the interquartile cut point. However, patients with SETER/PR ≥1.50 derived significant benefit (HR 0.53) vs those <1.50 (HR 0.82). Absolute 10-yr benefit: 7.1% for ≥1.50 vs 2.1% for <1.50. Node-positive, high-index patients had the largest gain (10.5% absolute reduction). Increasing SETER/PR as a continuous variable correlated with greater benefit (interaction HR 0.71). • **Conclusions:** SETER/PR ≥1.50 enriches for patients most likely to benefit from extended letrozole, supporting its role as a predictive marker of endocrine sensitivity.
10 Dec 2025	Multimodal Exercise in Breast Cancer: Health Impact and Efficacy of Online Modalities. RCT	Soraya Casla	• **Introduction:** This RCT evaluated a 16-week multimodal exercise program delivered online or onsite for breast cancer survivors (stage IA–IIIB). • **Methodology:** Eighty-three participants were randomized to intervention (online or onsite) or control. Sessions combined aerobic, strength, and flexibility training. Primary outcomes were CRF (Bruce test) and body composition (bioimpedance). Secondary outcomes included functional capacity (sit-to-stand, 6-minute walk) and QoL. • **Results:** The intervention group showed a 22.4% CRF increase versus a 4.96% decline in controls. Functional capacity improved significantly in both online and onsite arms. Lean mass increased by 5.24% and fat mass decreased by 10%. Adherence was 95.3% overall and 100% online. • **Conclusions:** Online and onsite multimodal exercise produced equivalent gains in CRF, functional capacity, and body composition, demonstrating strong feasibility and high engagement. Remote programs offer a scalable, accessible option for survivorship care.

Notable Presentations At SABCS 2025
Supportive Care, QoL, Toxicity, Lifestyle, Psychosocial (7/7)

Date	Title	Author	Summary
10 Dec 2025	Efbemalenograstim alfa significantly reduces incidence of incidence of severe chemotherapy-induced neutropenia in later cycles: Results of a meta analysis	John A. Glasby	• **Introduction:** Efbemalenograstim alfa, a non-PEGylated long-acting G-CSF, was noninferior to pegfilgrastim in reducing severe neutropenia duration in a phase III breast cancer trial. Notably, later-cycle reductions in grade 4 severe neutropenia (ISN) were observed. This analysis examined whether similar later-cycle benefits occurred across prior trials and chemotherapy regimens. • **Methodology:** ISN rates across four cycles were reviewed from three phase III trials using TC, EC, or highly myelotoxic TA regimens, comparing efbemalenograstim alfa with pegfilgrastim or filgrastim (historical comparators for TA). • **Results:** Across TC, EC, and TA regimens, efbemalenograstim alfa showed comparable ISN rates in cycle 1 but consistently lower rates in later cycles. Examples include:TC: Cycle 4 ISN 1.6% vs 5.3% (p=0.05), EC: Cycle 3 ISN 0% vs 3.9% (p=0.048), TA: Cycle 2 ISN 15% vs 45–57% (pegfilgrastim) and 54–55% (filgrastim). • **Conclusions:** Across chemotherapy types, efbemalenograstim alfa provides equal first-cycle protection and superior multi-cycle prevention of grade 4 neutropenia. Its sustained later-cycle benefit may offer improved safety for breast cancer patients receiving prolonged chemotherapy.
12 Dec 2025	Quality of life in women after breast biopsy with a benign result	Hans-Christian Kolberg	• **Introduction:** This study evaluated quality of life (QoL) after benign biopsy outcomes. • **Methodology:** Women undergoing benign ultrasound-guided core biopsies (2021–2023) were invited to complete the SF-36v2 QoL survey. Returned questionnaires with consent were analyzed and compared with 2009 U.S. population norms. • **Results:** Of 241 eligible patients, 70 participated. Across all eight SF-36v2 domains, scores were comparable or better than population norms: physical functioning (84%), physical role (76%), pain (73%), general health (74%), vitality (71%), social functioning (67%), emotional role (67%), and mental health (61%). • **Conclusions:** Benign breast biopsy results did not negatively affect QoL. Findings suggest reassurance and may help reduce patient anxiety when biopsy is indicated, though prospective validation is warranted.

Notable Presentations At SABCS 2025
Screening, Prevention, Genetics, Disparities, Trial Enrollment (1/8)

Date	Title	Author	Summary
10 Dec 2025	Impact of Polygenic Risk Scores on Breast Cancer Risk Assessment and Clinical Decision Making in Carriers of Germline Pathogenic Variants in ATM, BRCA1, BRCA2, CHEK2, and PALB2: Results from the Prospective Multisite GENRE-2 Clinical Trial	Siddhartha Yadav	• **Introduction:** Polygenic risk scores (PRS) may refine breast cancer (BC) risk estimation, but their clinical utility in germline pathogenic variant (PV) carriers remains unclear. • **Methodology:** GENRE-2 prospectively integrated a 313-PRS into CanRisk models in ATM, BRCA1, BRCA2, CHEK2, and PALB2 carriers. Women were re-categorized into average, moderate, or high lifetime-risk groups, and changes in prevention/screening intentions pre- vs post-PRS were evaluated. • **Results:** PRS altered lifetime-risk categories in 29.2% of ATM and 16.7% of CHEK2 carriers, but <5% of BRCA1/BRCA2. Higher post-PRS risk correlated with greater preventive-action intent (41.4% vs 20.0%). • **Conclusions:** PRS meaningfully refines risk estimates for moderate-penetrance genes (ATM, CHEK2) but adds limited value for high-risk BRCA1/2 carriers, supporting gene-specific integration into risk counseling.
10 Dec 2025	Association between age at diagnosis and survival among young BRCA carriers with breast cancer: results from an international multicenter hospital-based cohort study	Matteo Lambertini	• **Introduction:** Young age worsens prognosis in general breast cancer, but its impact in BRCA1/2 carriers diagnosed ≤40 years is unclear. • **Methodology:** The BRCA BCY Collaboration analyzed 5,350 BRCA1/2 carriers diagnosed at ≤40 years across 109 centers (2000–2020). Outcomes were compared for ages ≤30, 31–35, and 36–40. DFS was primary; OS secondary. Multivariable Cox models adjusted for RRM/RRSO and key tumor factors. • **Results:** Despite more high-grade, TNBC, and larger tumors in ≤30-year patients, 8-year DFS rates were nearly identical (65.0%, 64.7%, 65.8%). Age was not associated with DFS (aHR 1.03 and 1.00) or OS (aHR 1.10 and 1.11). No subgroup showed age-related differences. • **Conclusions:** Among young BRCA carriers, very early age at diagnosis does not confer worse prognosis. With appropriate therapy, age ≤30 should not be viewed as an adverse prognostic factor.

Notable Presentations At SABCS 2025
Screening, Prevention, Genetics, Disparities, Trial Enrollment (2/8)

Date	Title	Author	Summary
10 Dec 2025	Tamoxifen use increases endometrial cancer risk in premenopausal breast cancer patients	Zoë Molinari	• **Introduction:** Tamoxifen-associated endometrial cancer (ECa) risk is established in postmenopausal women, but its impact in younger breast cancer patients remains unclear. • **Methodology:** A nationwide Belgian retrospective cohort (2008–2020) evaluated ECa incidence after tamoxifen initiation in 38,857 women aged 18–53 with early breast cancer. Cox models adjusted for metabolic, tumor, and treatment covariates assessed risk. • **Results:** ECa occurred in 0.41% of tamoxifen users vs 0.17% of non-users. Tamoxifen significantly increased ECa risk (HR 2.05; adjusted HR 1.93, 95% CI 1.14–3.28). Risk elevation persisted after accounting for diabetes, cardiovascular factors, tumor grade/stage, and systemic therapy. • **Conclusions:** Tamoxifen use in women <54 significantly increases ECa risk, independent of confounders, underscoring the need for vigilant monitoring in this population.
10 Dec 2025	Real-world patient (pt) and caregiver experiences with breast cancer (BC) risk of recurrence (ROR) in the US: Results of an Online Survey and Social Media Analysis	Hope S. Rugo	• **Introduction:** Recurrence risk (ROR) is a major concern in HR+/HER2− early breast cancer, yet patient understanding and support remain poorly characterized. • **Methodology:** An online US survey (Carenity, 2021–2022) and social-media analysis (Sprinklr, 2023–2025) evaluated patient and caregiver perceptions of ROR, unmet informational needs, and quality-of-life impacts. • **Results:** Among HR+/HER2− respondents, 29% recurred as metastatic. Most wished they had received clearer survival/ROR information (32%) or emotional-support guidance (26%); many reported receiving none. SMA (1622 relevant posts) showed persistent anxiety over late recurrence, inadequate monitoring, and limited support. Reducing metastasis risk was a top treatment priority, yet HR+/HER2− patients reported fewer services than HER2+ or TNBC groups. • **Conclusions:** Patients lack essential ROR education despite prioritizing recurrence prevention. Clearer communication and structured support are critical from diagnosis onward to improve decision-making and QoL.

Notable Presentations At SABCS 2025
Screening, Prevention, Genetics, Disparities, Trial Enrollment (3/8)

Date	Title	Author	Summary
11 Dec 2025	Predictive Value of Breast-Specific Gamma Imaging for Pathologic Response and Prognosis in Early Breast Cancer After Neoadjuvant Therapy: A Prospective Trial	Tianyi Qian	• **Introduction:** Residual metabolic activity after NAC is difficult to quantify with MRI. Breast-specific gamma imaging (BSGI) offers functional assessment via the tumor-to-normal ratio (TNR), but prospective validation of its prognostic value has been lacking. • **Methodology:** A single-center prospective trial (N=137, 2014–2023; NCT02556684) assessed post-NAC TNR using 99mTc-sestamibi BSGI. Primary endpoints were pCR and 3-year DFS, analyzed using χ^2 tests, Kaplan–Meier estimates, and multivariable Cox regression adjusting for key clinicopathologic factors. • **Results:** TNR-low patients had higher pCR (34.8% vs 14.7%) and significantly improved DFS (HR=0.33 overall). Benefits persisted across HR+/HER2−, HER2+, pCR and non-pCR subgroups. TNR remained independently prognostic (adjusted HR=0.43) and outperformed pCR alone: TNR-low/pCR patients had no events, while TNR-low/non-pCR patients had markedly reduced recurrence risk. • **Conclusions:** TNR is a strong, prospectively validated metabolic biomarker that enhances post-NAC risk stratification. BSGI may enable de-escalation in TNR-low/pCR patients and targeted escalation for TNR-high/non-pCR individuals.
11 Dec 2025	Effects of a physical exercise protocol via telehealth on the quality of life and stress of women undergoing chemotherapy: a randomized clinical trial	Giuliano Tavares Tosello	• **Introduction:** Chemotherapy-related physical and psychological stress can impair quality of life (QoL). Telehealth-delivered exercise may provide accessible supportive care for women undergoing treatment. • **Methodology:** In this randomized trial (N=44), women receiving chemotherapy were assigned to supervised telehealth exercise (IG) or minimal intervention (MIG). QoL (EORTC QLQ-C30) was analyzed using adjusted ANOVA; stress was assessed with Lipp's inventory. Smallest Worthwhile Change (SWC) quantified clinically meaningful effects. • **Results:** No statistically significant QoL differences were detected, but SWC showed IG patients more often improved or maintained global health and functional domains despite expected chemotherapy-related decline. Stress symptoms rose in both groups, yet IG demonstrated more favorable clinical changes—especially in the resistance phase—than MIG. • **Conclusions:** Telehealth exercise helped preserve QoL and reduce stress early during chemotherapy, supporting its integration into supportive care programs.

Notable Presentations At SABCS 2025
Screening, Prevention, Genetics, Disparities, Trial Enrollment (4/8)

Date	Title	Author	Summary
11 Dec 2025	Making informed choices on incorporating chemoprevention into care (MiCHOICE): Cluster randomized controlled trial of decision support for breast cancer chemoprevention, SWOG 1904	Katherine D. Crew	• **Introduction:** Chemoprevention with SERMs/AIs effectively reduces breast cancer (BC) risk but remains underused. Enhancing patient and provider understanding may improve informed decision-making among women with AH or LCIS. • **Methodology:** In this cluster-randomized trial (31 U.S. sites; N=412 patients, 210 providers), sites received either standard materials or additional web-based decision support (RealRisks + BNAV). The primary endpoint was chemoprevention informed choice at 6 months; secondary endpoints included risk perception, knowledge, worry, decision conflict, and uptake. • **Results:** Among 288 evaluable patients, informed choice was 35% vs 27% (OR 1.44; p=0.19). Decision support improved accurate BC risk perception (OR 1.80) and chemoprevention knowledge (OR 1.62), but not worry, conflict, or uptake. Chemoprevention use was high in both arms (~50%). • **Conclusions:** Decision support improved key knowledge-based antecedents but did not significantly increase informed choice or behavior. High chemoprevention uptake reflected specialized care settings, suggesting limited incremental impact of decision tools in already engaged high-risk populations.
11 Dec 2025	Impact of COVID-19 on neoadjuvant chemotherapy efficacy in patients with breast cancer: an ambidirectional cohort study and Mendelian randomization analysis	Yali Wang	• **Introduction:** COVID-19 may alter treatment responses in breast cancer, yet its impact on neoadjuvant chemotherapy (NAC) efficacy and potential shared genetic mechanisms with cancer remain unclear. • **Methodology:** In an 856-patient ambidirectional cohort, NAC response was assessed in patients with/without COVID-19 using multivariable regression and three matching approaches. Multi-omic analyses—single-cell and bulk transcriptomics plus Mendelian randomization—were applied to identify causal genes and shared pathways. • **Results:** COVID-19 was associated with poorer NAC response, particularly reduced ORR and lower RCB 0–I rates in HR+/HER2+ disease (OR 0.46; interaction p=0.024). Matching models confirmed consistency. Integrated genomic analyses revealed significant genetic correlations and implicated ABLIM1 and GZMM as drivers of NAC resistance. • **Conclusions:** SARS-CoV-2 infection during NAC may compromise treatment efficacy in breast cancer. ABLIM1 and GZMM emerge as potential mechanistic links and biomarkers for COVID-associated NAC resistance.

Notable Presentations At SABCS 2025
Screening, Prevention, Genetics, Disparities, Trial Enrollment (5/8)

Date	Title	Author	Summary
11 Dec 2025	Recruitment Strategy Success and Challenges in WISDOM 1.0: A Nationwide Risk-Based Breast Cancer Screening Trial	Allison Stover Fiscalini	• **Introduction:** WISDOM 1.0 evaluated personalized breast cancer screening and required recruitment of a large, diverse U.S. cohort. Understanding which outreach strategies worked best is essential for designing scalable, equitable screening trials. • **Methodology:** Recruitment data from 2016–2023 were analyzed using participant-reported "How You Heard" sources. Strategies were categorized and examined by geography and race/ethnicity to assess yield and diversity impact. • **Results:** Among 46,289 enrolled participants, medical-center emails/MyChart/physician outreach generated the largest share (40%). Family/friend referrals (10%) and VA partnership emails (6%) added substantial diversity—VA outreach drove 25% of enrollments during activation and contributed 26% of Black and 10% of Hispanic participants. Social media (2.5%), insurance plans (4%), and media coverage (4.5%) played smaller but complementary roles. Diversity increased markedly, with White non-Hispanic enrollment declining from 83% to 60% after expanded community-engagement strategies. • **Conclusions:** Multi-modal, trusted-channel recruitment—including physician outreach, VA partnerships, and community-informed approaches—effectively built a diverse national cohort. These findings inform optimized, culturally responsive strategies for WISDOM 2.0.
11 Dec 2025	Primary Care Provider Input On Personalized Breast Cancer Screening Recommendations in WISDOM 1.0: A Nationwide Risk-Based Breast Cancer Screening Trial	Arash Naeim	• **Introduction:** WISDOM 1.0 evaluates personalized vs annual breast cancer screening. Understanding how women and primary care providers (PCPs) discuss and perceive individualized screening recommendations is critical for real-world implementation. • **Methodology:** Survey data from the first 15,000 WISDOM participants were analyzed at baseline, recommendation disclosure, and annual follow-up. Outcomes included patient–PCP discussion rates and PCP agreement across randomized arms and assigned screening intervals. • **Results:** Discussion rates were higher in the risk-based arm (35.6%) vs annual screening (19.0%; $p<0.001$). PCP agreement was 75.7% in the annual arm and 58.6% in the risk-based arm, with disagreement higher for reduced-frequency recommendations (Delayed: 24.2%; Two-Year: 16.1%). Discussion was most frequent for more intensive recommendations (6-month MRI: 71.1%). • **Conclusions:** Risk-based screening prompts greater PCP engagement, but reduced-frequency recommendations face lower provider agreement. Enhancing PCP education may improve adoption of personalized screening strategies.

Notable Presentations At SABCS 2025
Screening, Prevention, Genetics, Disparities, Trial Enrollment (6/8)

Date	Title	Author	Summary
11 Dec 2025	Completion Rates of Risk Counseling Consultations For Women at High-Risk for Breast Cancer within the WISDOM 1.0 Pragmatic Screening Trial	Jackelyn Moya	• **Introduction:** WISDOM 1.0 integrates risk-based breast cancer screening and offers Breast Health Specialist (BHS) consultations to women in the highest 2.5% risk tier. Early findings revealed underrepresentation of racial and ethnic minorities, prompting efforts to diversify enrollment and evaluate consultation completion patterns. • **Methodology:** Among 2,883 high-risk participants (2015–2023), completion of BHS consultations was analyzed across age groups, race/ethnicity, and U.S. geographic regions using proportional comparisons. • **Results:** Completion varied by subgroup. By age, rates were 52–71%, lowest in women 70–79 (52%). By race/ethnicity: Other/Mixed Race 77%, White 68%, Hispanic 62%, Asian 54%, Black 41%. Regional completion ranged from Midwest 84% to South 51%. Most participants were White (84%) and from the West (66%). • **Conclusions:** Substantial disparities exist in consultation completion by race, geography, and age. WISDOM 2.0 will address structural barriers through redesigned workflows, expanded clinician availability, tailored outreach, and enhanced community engagement to ensure equitable delivery of risk counseling.
11 Dec 2025	Listening to the Community: Barriers and Beliefs About Clinical Trials Among Black Women with Breast Cancer	Sabrina Mayhew	• **Introduction:** African American women face disproportionately aggressive breast cancer yet remain underrepresented in clinical trials. To understand barriers and inform culturally responsive solutions, BreastCancerTrials.org and Sisters Network® Inc. surveyed African American survivors nationwide. • **Methodology:** Sisters Network® Inc. distributed a detailed survey to >100 African American breast cancer survivors, collecting data on demographics, cancer characteristics, clinical trial familiarity, provider communication, participation barriers, and interest in trial navigation support. • **Results:** Over 65% were familiar with trials, and 44% would join if recommended by their clinician. Thirty percent had discussed trials with their care team mostly provider-initiated (67%). Key barriers included determining eligibility, difficulty finding trials, and limited understanding of trial processes. More than half expressed interest in clinical trial navigation. • **Conclusions:** Findings highlight persistent structural and informational barriers to trial participation among African American women. Strong interest in navigation services underscores the need for culturally competent, personalized trial support.

Notable Presentations At SABCS 2025
Screening, Prevention, Genetics, Disparities, Trial Enrollment (7/8)

Date	Title	Author	Summary
11 Dec 2025	Racial and Ethnic Disparities in Enrollment to Breast Cancer Clinical Trials from 2000 to 2025	Fatma Nihan Akkoc Mustafayev	• **Introduction:** Breast cancer remains the most common cancer in women, yet equitable clinical trial (CT) access has not kept pace with therapeutic advances. Racial and ethnic disparities—especially underrepresentation of Black and Hispanic women—limit generalizability and perpetuate outcome gaps. • **Methodology:** Phase III–IV BC CTs completed between 2000–2025 on ClinicalTrials.gov was analysed. Of 283 eligible trials, race and ethnicity reporting, enrollment proportions, and 5-year temporal trends were evaluated. • **Results:** Only 42% of trials reported race and 22% reported ethnicity. White participants dominated enrollment (75%), while Black patients represented just 3.4%. White enrollment decreased from 88.9% to 66.7%, and Asian enrollment rose from 4.5% to 21.5%. Hispanic representation modestly improved but remained limited. Many trials reflected single-race cohorts due to geographic clustering. • **Conclusions:** Despite incremental gains, Black and Hispanic women remain markedly underrepresented in BC trials. Standardized demographic reporting and targeted diversification efforts are urgently needed..
11 Dec 2025	Evaluating Underrepresentation in Breast Cancer Clinical Trial Enrollment at Yale Cancer Center: A Retrospective Demographic Study	Jessica Liu	• **Introduction:** Representative breast cancer trial enrollment remains limited for minorities, young adults, Medicaid-insured, and non-English speakers. Yale Cancer Center implemented a machine-learning Clinical Trial Patient Matching (CTPM) system to improve identification of eligible patients. • **Methodology:** Demographics from 2013–2024 were compared across the full YCC population, manually identified trial candidates, and CTPM-identified patients. Pre- and post-CTPM periods were analyzed by age, race/ethnicity, language, insurance, and geography. • **Results:** Among 45,380 patients, underrepresented groups were historically low. Post-2022, diversity modestly increased. Manual review captured limited diversity, while CTPM identified 662 eligible patients and 99 consented, improving representation among young adults, racial/ethnic minorities, and Medicaid-insured patients. Most eligible patients still declined enrollment. • **Conclusions:** CTPM improves identification of diverse, trial-eligible patients but does not overcome enrollment barriers. Additional navigation and engagement strategies are needed to achieve equitable participation.

Notable Presentations At SABCS 2025
Screening, Prevention, Genetics, Disparities, Trial Enrollment (8/8)

Date	Title	Author	Summary
11 Dec 2025	Global disparities in breast cancer clinical trials and their impact on clinical evidence, driven by underrepresentation of low- and middle-income countries.	Varsha Gupta	• **Introduction:** Breast cancer clinical trials remain concentrated in high-income countries (HICs), limiting global generalizability. Patients in low-/middle-income countries (LMICs) face distinct biological, resource, and care-access challenges, yet their representation in evidence generating guidelines remains low. • **Methodology:** Using ClinicalTrials.gov, 5,518 breast cancer trials (2000–2023) were analyzed by country income level and geographic region. Trial phase, funding, design, LMIC site participation, and contribution to NCCN guideline citations were evaluated using World Bank classifications and chi-square testing. • **Results:** Only 29.5% of trials included any LMIC site versus 81.6% in HICs. LMIC representation was lowest in phase 1 (19.7%) and phase 2 (27.2%) trials and modest in phase 3 (50.7%) (all $p<0.01$). LMIC trials relied more on industry funding (55.4% vs. 35.2%) and were more often randomized (55.6% vs. 36.9%). Regional growth was driven almost entirely by East Asia Pacific (2.4%→39.1%); minimal change occurred in South Asia, Sub-Saharan Africa, or Latin America. Of 148 NCCN-referenced trials since 2000, only 64 (69.5%) involved an LMIC site versus 86 (93.5%) in HICs. NCCN-impacting trials were predominantly phase 3 (84.8%) and randomized (90.2%). • **Conclusions:** Despite modest gains, LMICs remain substantially underrepresented in breast cancer clinical trials and undercontribute to guideline-shaping evidence. Ensuring fair geographic and economic representation is essential for equitable, globally relevant treatment recommendations.

Key Industry Sponsored Sessions Information

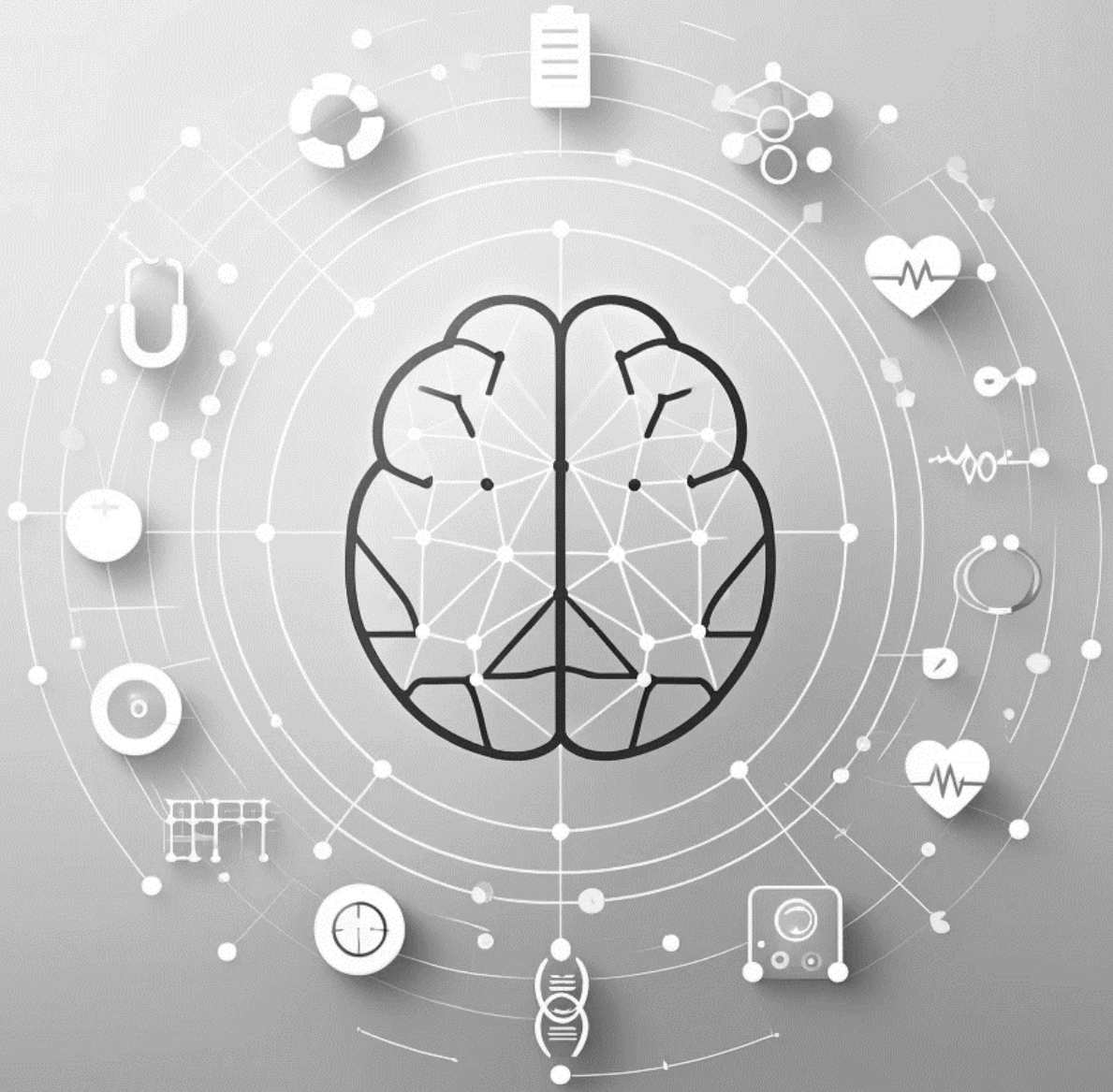
SABCS 2025 Key Industry Sponsored Sessions Information (1/2)

Date	Sponsor	Title
08 Dec 2025	Pfizer	Show Me the Data™: Personalizing First-Line and Maintenance Therapy in HER2+ Metastatic Breast Cancer to Extend Survival and Elevate Quality of Life
08 Dec 2025	AstraZeneca and Genentech	Medical Crossfire® From Frontline to Heavily Pretreated HR+/HER2- Metastatic Breast Cancer: Expert Perspectives on Optimizing the Expanding Treatment Armamentarium
09 Dec 2025	Gilead	Cases from the Community—Investigators Discuss the Role of Antibody-Drug Conjugates in the Management of Triple-Negative and HR-Positive Metastatic Breast Cancer
09 Dec 2025	AstraZeneca & MSD	Medical Crossfire® – Mastering the Nuances of Early-Stage HR+/HER2- Breast Cancer: Expert Perspectives on Applying Modern Treatment Paradigms
09 Dec 2025	AstraZeneca, Roche Group, and Lilly,	Dialing Up Precision in HR+, HER2- MBC With New Endocrine Agents, Targeted Therapies, and Combinations
09 Dec 2025	Celcuity	Extending Efficacy: New Approaches for Endocrine-Resistant HR+/HER2- Advanced Breast Cancer
10 Dec 2025	Pfizer	Key Steps to Success with CDK4/6 Inhibition in Early Through Metastatic HR+, HER2- Breast Cancer: Stratification, Selection, Sequencing, and Specialty Management

SABCS 2025 Key Industry Sponsored Sessions Information (2/2)

Date	Sponsor	Title
10 Dec 2025	Novartis and Lilly	Key Steps to Success with CDK4/6 Inhibition in Early Through Metastatic HR+, HER2- Breast Cancer: Stratification, Selection, Sequencing, and Specialty Management
10 Dec 2025	AstraZeneca, Daiichi Sankyo and MSD	Medical Crossfire®: The Who, When, and How of TROP2-Targeting, ADCs, ICIs, and PARP Inhibition in Triple-Negative Breast Cancer
10 Dec 2025	AstraZeneca and Daiichi Sankyo	Cases from the Community: Investigators Discuss the Optimal Management of HER2-Positive Breast Cancer
11 Dec 2025	AstraZeneca and Daiichi Sankyo	Forging New Paths With Earlier Use of ADCs in Breast Cancer: From Clinical Breakthroughs to Improved Outcomes
11 Dec 2025	Pfizer	Medical Crossfire™: Navigating the Expanding Arsenal of Endocrine Therapies for HR+/HER2- Metastatic Breast Cancer—How Can PROTAC ER Degradation Shift the Standard?
11 Dec 2025	Roche , Lilly, and Stemline Therapeutics	Cases from the Community: Investigators Discuss the Optimal Role of Endocrine-Based Therapy in the Management of Breast Cancer

Noteworthy AI / ML presentations at SABCS 2025



Themes from key AI / ML presentations at SABCS 2025 (1/4)

- **AI and ML will significantly enhance breast cancer management at SABCS 2025, focusing on improving risk prediction, personalized treatment strategies, and early detection through advanced tools like AI-driven imaging, digital pathology, and predictive models. These innovations will aim to streamline treatment decisions and improve patient outcomes, especially in resource-limited settings**
- Check out the key AI / ML themes at SABCS 2025 below:
- **AI-based Mammography Analysis for BC Risk Prediction:**
  - AI models will likely enhance breast cancer risk prediction in patients with benign breast disease, focusing on using AI to improve predictive accuracy and early detection beyond traditional models
- **AI-Enabled Digital Pathology in HER2-Positive BC:**
  - AI-driven tools will be used to improve the quantification and spatial assessment of immune cell infiltration (sTILs) in HER2-positive early breast cancer, helping guide targeted treatment decisions, such as pertuzumab therapy
- **Generative AI for Early Detection of Dense Breast Cancer:**
  - Generative AI models will be utilized to analyze tumor-derived oncRNAs for non-invasive screening of breast cancer in women with dense breast tissue, offering a potential early detection tool

Themes from key AI / ML presentations at SABCS 2025 (2/4)

- **FES-PET Imaging and AI Integration for Endocrine Response Prediction:**
  - AI-augmented FES-PET imaging will be explored to predict responses to endocrine therapy in ER+/HER2– metastatic breast cancer, combining imaging and clinical data for personalized treatment decisions
- **AI-Driven Morphologic Analysis for HR+/HER2- IBC Prognostication:**
  - AI will analyze H&E slides for prognostic stratification in early-stage HR+/HER2– inflammatory breast cancer, combining morphologic features with clinical data for better treatment planning
- **Digital Twin AI for Predicting pCR in TNBC:**
  - Multi-modal AI "digital twins" will be used to predict treatment responses in TNBC patients undergoing neoadjuvant therapy, enhancing personalized treatment and reducing unnecessary toxicity
- **AI-Enhanced Histology and TME Profiling in Invasive Lobular Carcinoma (ILC):**
  - AI will assist in profiling the tumor microenvironment in ILC, offering new insights into late-stage recurrence risks and supporting extended endocrine therapy decisions for patients at higher risk.

Themes from key AI / ML presentations at SABCS 2025 (3/4)

- **Machine Learning for Distant Metastasis Prediction in Early HR+ BC:**
  - AI models like MMAI will be tested to predict distant metastasis in HR+ early breast cancer patients, providing a low-cost alternative to genomic assays and aiding chemotherapy decision-making
- **AI for Non-Invasive Risk Stratification in HR+/HER2– Early BC:**
  - AI-driven models like RlapsRisk BC (RR) will offer an alternative to expensive genomic assays for HR+/HER2– early breast cancer risk stratification, enhancing treatment decision-making
- **Synthetic Datasets and AI for Early Detection and Prevention:**
  - AI-generated synthetic datasets enriched with modifiable risk factors will enable more accurate early detection and prevention simulations, focusing on the development of AI/ML models for breast cancer risk assessment
- **Enhanced Early Detection:**
  - AI models are expected to improve early detection, particularly for patients with dense breast tissue, using generative AI to analyze oncRNAs and non-invasive biomarkers

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

- **AI for Personalized Treatment:**
  - AI-driven tools will refine personalized treatment plans by predicting responses to therapies such as endocrine and immunotherapy, with a focus on HER2-positive and TNBC breast cancer subtypes
- **Cost-Effective AI Solutions:**
  - AI models like TRINITY AI and MMAI will provide low-cost alternatives to genomic assays, making breast cancer prognosis and treatment decisions more accessible, especially in resource-limited environments
- **Improved Prognostic Accuracy:**
  - AI-enhanced morphologic analysis will outperform traditional methods in predicting recurrence risk and survival, offering more precise prognostic tools for early and metastatic breast cancer
- **AI for Clinical Decision Support:**
  - AI will support real-time, evidence-based clinical decision-making by integrating and analyzing complex clinical, imaging, and genomic data, providing actionable insights for clinicians

Noteworthy AI / ML presentations at SABCS 2025

Notable Presentations At SABCS 2025
AI / ML (1/20)

Date	Title	Author	Summary
10 Dec 2025	An AI algorithm for breast cancer detection improves future BC risk prediction among women with benign breast disease	Celine M Vachon	• **Introduction**: AI-based mammography analysis may enhance future breast cancer (BC) risk prediction, particularly in women with benign breast disease (BBD), where traditional models perform poorly. • **Methodology:** A retrospective Mayo Clinic cohort (n=3,125; median follow-up 12.9 years) evaluated Transpara AI malignancy scores (1–10) and Volpara volumetric density. Cox models, C-statistics, likelihood-ratio tests, and bootstrapping assessed independent predictive value beyond BBD severity and density. • **Results:** AI score predicted incident BC (HR=1.16/unit), performing comparably to BBD + VPD models (C=0.626 vs 0.627). When combined, AI remained independently significant (HR=1.14) but yielded only marginal discrimination improvement (ΔC=0.024). • **Conclusions:** AI provides meaningful, independent BC-risk information but adds limited incremental predictive accuracy over established factors.
10 Dec 2025	Prognostic and predictive associations of manual, digital and AI-derived tumor infiltrating lymphocytes-scoring: A retrospective analysis from the Phase III APHINITY trial	Roberto Salgado	• **Introduction**: sTILs guide prognosis and pertuzumab benefit in HER2-positive early breast cancer. AI-enabled digital pathology may enhance quantification and spatial immune assessment. • **Methodology:** APHINITY included 4,306 evaluable H&E slides. Manual, digital, and zero-shot AI scoring (Case45) were compared using ICC, percentile-based high-TIL thresholds, Cox models for iDFS/OS, and treatment-interaction analyses. AI spatial metrics assessed lymphocyte proximity and immune hotspots. • **Results:** Manual reproducibility was high (ICC 0.87). Concordance across methods was modest (ICC 0.37–0.62). All approaches showed strong prognostic value (HR per 10% sTIL: manual 0.93; digital 0.92; AI 0.87). AI hotspots were most prognostic (HR 0.41). High-TIL groups derived substantial pertuzumab benefit; AI identified 10% more responsive node-positive patients. • **Conclusions:** AI equals or modestly surpasses manual sTIL performance and expands identification of pertuzumab-benefiting patients. Combining AI spatial and quantitative metrics strengthens individualized HER2-targeted therapy.

Notable Presentations At SABCS 2025
AI / ML (2/20)

Date	Title	Author	Summary
10 Dec 2025	Early-stage breast cancer detection with a plasma cell-free RNA and AI-based liquid biopsy platform	Lee S. Schwartzberg	• **Introduction**: Mammography underperforms in dense breasts. Tumor-derived oncRNAs, amplified through active transcription, offer a biologically enriched signal for early detection. Generative AI can leverage these cfRNA features for non-invasive screening. • **Methodology:** Pan-cancer oncRNAs were identified using TCGA data. A plasma cohort (n=745 BC; n=258 controls) trained a generative AI classifier; an independent cohort (n=92 BC; n=98 controls) served as validation. cfRNA was extracted from 1 mL plasma and sequenced (~53M reads). Five-fold CV assessed performance. • **Results:** AUCs were 0.88 (CV) and 0.89 (test). At 90% specificity, sensitivity was ~72% overall and 63% for stage I across both sets. • **Conclusions:** The oncRNA-AI assay shows robust early-stage performance and strong potential as an adjunct screening tool for women with dense breasts.
10 Dec 2025	Deep learning model for predicting hormonal therapy response using FES-PET in ER+ HER2− metastatic breast cancer	Mohyeldin S Abdelhalim	• **Introduction**: Endocrine resistance in ER+/HER2− metastatic breast cancer demands better predictive tools. FES-PET captures whole-body ER availability, and deep learning can integrate nuanced imaging–clinical patterns for response prediction. • **Methodology:** A retrospective cohort (n=60) underwent baseline FES-PET before endocrine therapy. Images were standardized (128^3 voxels) and fused with four clinical variables. A 3D ResNet-18 (MedicalNet-initialized) was fine-tuned using focal loss. Data were split 48/12 for training/testing, with performance tracked via accuracy, sensitivity, specificity, and AUC. • **Results:** Optimal performance occurred at epoch 2: 91.7% accuracy, 100% sensitivity, 67% specificity, AUC 0.83. Clinical-imaging fusion improved balanced classification. • **Conclusions:** This pilot demonstrates strong feasibility of AI-augmented FES-PET for predicting endocrine response, though larger multi-site validation is essential.

Notable Presentations At SABCS 2025
AI / ML (3/20)

Date	Title	Author	Summary
10 Dec 2025	Clinical validation of an Artificial Intelligence digital pathology-based prognostic test to predict risk of recurrence using biopsy specimens from patients with invasive breast cancer	Michael Donovan	• **Introduction**: Early HR+/HER2– IBC requires biopsy-based prognostic tools to guide neoadjuvant and adjuvant decisions. AI-enabled morphologic analysis may enhance recurrence-risk prediction beyond age alone. • **Methodology:** From 1,788 patients, 60/40 surgical-training and biopsy-validation cohorts were created. H&E slides were digitized, deconstructed into eight AI-quantified morphologic features, and combined with age to generate the PDxBRBx risk score. Validation used C-index, HRs, Se/Sp, NPV/PPV, and concordance with excision-based testing. • **Results:** PDxBRBx achieved C-indices of 0.72–0.73, outperforming age and AI-grade alone. A risk cut-off of 73 yielded HR 4.49 and NPV 0.93. Biopsy–excision agreement was substantial (κ 0.57). • **Conclusions:** PDxBRBx provides validated, early prognostic stratification, supporting more precise treatment planning.
10 Dec 2025	Personalised Therapy in Triple Negative breast cancer (TNBC), evaluating predictive performance of Bayesian AI Digital Twins.	Uzma S Asghar	• **Introduction**: TNBC lacks reliable predictive biomarkers, and ~40% of stage 2–3 patients die despite intensive therapy. Multi-modal AI "digital twins" may improve treatment-response prediction and reduce ineffective exposure. • **Methodology:** VISION (n=200) evaluated FarrSight®-Twin using clinico-pathologic variables plus WES/RNA-seq from diagnostic FFPE biopsies. Digital twins were generated per patient; pCR and survival predictions were benchmarked against real outcomes using leave-one-out validation. • **Results:** Among 94 analyzable patients (34 pCR; 60 non-pCR), pCR varied by regimen (50% with platinum-IO; 31–35% with standard/platinum). One-year survival was 95%, declining to 73% over follow-up. FarrSight®-Twin showed early accuracy for pCR classification across integrated inputs. • **Conclusions:** Digital-twin AI shows promise for identifying TNBC patients unlikely to achieve pCR, supporting individualized neoadjuvant therapy and toxicity-sparing decisions.

Notable Presentations At SABCS 2025
AI / ML (4/20)

Date	Title	Author	Summary
10 Dec 2025	Clinical outcomes of invasive lobular carcinoma (ILC) versus non-lobular breast cancer (NLC) assessed by expert pathologists, an artificial intelligence (AI) CDH1 classifier, and AI-derived tumor microenvironment (TME) biomarkers in TAILORx	Roberto Salgado	• **Introduction**: ILC comprises ~15% of breast cancers and differs biologically from NLC, yet long-term prognostic tools remain limited. AI-enabled digital pathology offers scalable histology and TME assessment beyond manual review. • **Methodology:** In TAILORx (n=8,422), 16 pathologists reviewed H&E WSIs for grade, TILs, and histology; AI tools included a CDH1-based ILC classifier and a zero-shot TME model generating abundance/spatial fibroblast–immune metrics. Multivariable Cox models adjusted for clinicopathologic factors and 21-gene RS. • **Results:** ILC showed higher late (5–15y) recurrence risk and 4.9% lower OS at 15y. Manual TILs were modestly prognostic (HR10-pt=1.06). AI-TME score strongly stratified DRFI (HR/SD=1.27; adjusted HR=1.14). • **Conclusions:** AI and manual pathology confirm ILC's higher late-recurrence risk and demonstrate TME biomarkers' additive prognostic value beyond 21-gene RS, supporting extended endocrine therapy considerations.
10 Dec 2025	Evaluation of a digital pathology based multimodal artificial intelligence model for prognosis and prediction of chemotherapy benefit in node-negative, hormone receptor-positive breast cancer patients: analysis of the NSABP B-20 trial.	Charles E Geyer	• **Introduction**: Risk stratification for distant metastasis in HR+ N0 early breast cancer is essential, but genomic assays remain costly. The MMAI multimodal model integrates H&E images and clinical data as a scalable alternative. • **Methodology:** In NSABP B-20 (n=1,763; median follow-up 14.6y), locked MMAI scores assigned low/intermediate/high-risk groups. Prognostic value was tested in the tamoxifen arm using Fine-Gray models. Predictive interactions with chemotherapy were evaluated overall and stratified by age ≥50 vs <50. • **Results:** MMAI strongly predicted DM (high vs low sHR 3.97). No overall chemo–risk interaction emerged, but in patients ≥50, high/intermediate-risk achieved a 52% 10-year DM reduction with CMF (10% vs 21%). • **Conclusions:** MMAI is a robust prognostic tool and may guide chemotherapy decisions in older HR+ N0 patients as a lower-cost alternative to genomic testing.

Notable Presentations At SABCS 2025
AI / ML (5/20)

Date	Title	Author	Summary
10 Dec 2025	A Multimodal-Multitask Deep Learning Model Trained in NSABP B-42 and Validated in TAILORx for Late Distant Recurrence Risk in HR+ Early Breast Cancer	Eleftherios Mamounas	• **Introduction**: Clarity BCR is a multimodal deep-learning model integrating H&E WSIs and clinical data to estimate late distant-recurrence (DR) risk and guide extended endocrine therapy (EET) decisions in HR+ breast cancer. • **Methodology:** TAILORx validation included 6,516 patients with digitized WSIs; 4,469 disease-free at 5 years formed the late-DR cohort. Prespecified thresholds generated high/low-risk groups. DRFI was assessed using uni- and multivariable Cox models adjusting for clinicopathologic and Oncotype DX variables. • **Results:** High-risk patients showed significantly worse late DR (HR 1.88) with 15-year DRFI 86.4% vs 93.0%. Clarity BCR remained independently prognostic (HR 1.54) and outperformed Oncotype DX for late-DR discrimination (C-index 0.59 vs 0.54). • **Conclusions:** Clarity BCR consistently stratifies long-term DR risk across trials, supporting its utility in informing EET decisions in HR+ early breast cancer.
10 Dec 2025	Prognostic Value of a Machine Learning Tool for Recurrence Risk Stratification in HR+/HER2- Early Breast Cancer: A Brazilian Cohort Analysis	Rubem Moreira	• **Introduction**: Brazil lacks access to genomic assays for HR+/HER2– early breast cancer, necessitating low-cost prognostic alternatives. ML models predicting 21-gene–equivalent risk from quantitative IHC may address this gap. • **Methodology:** A retrospective INCA cohort (n=299; stage I–III, ≤3 nodes) was analyzed using an established ML tool integrating age, grade, subtype, ER/PR levels, and Ki-67. A predefined threshold (90% sensitivity for RS>25) stratified patients as low vs high risk. Prognosis was assessed via DFI, OS, and multivariable Cox models. • **Results:** Only 15.4% were low risk, yet their recurrence rate was 2.2% vs 19.4% in high risk. Five-year DFI was 97.4% vs 81.8% (p=0.0054). Chemotherapy conferred no observable DFI benefit, especially in low-risk patients. • **Conclusions:** The ML tool reliably identified a low-risk group with excellent outcomes, supporting chemotherapy de-escalation where genomic testing is unavailable.

Notable Presentations At SABCS 2025
AI / ML (6/20)

Date	Title	Author	Summary
10 Dec 2025	Pathologist- and artificial intelligence-based TILs assessment in patients with early triple-negative breast cancer treated with neoadjuvant chemo-immunotherapy: real-world evidence from a nationwide cohort	Ioannis Zerdes	• **Introduction**: Pre-treatment sTILs predict pCR in TNBC receiving neoadjuvant chemo-immunotherapy. AI-enabled digital pathology may standardize quantification and enhance response discrimination. • **Methodology:** A nationwide Swedish KEYNOTE-522–treated TNBC cohort (n=337) underwent manual sTILs scoring and AI-TILs quantification using HoverNet. Concordance and association with pCR were evaluated via Spearman correlation and univariate logistic regression; subgroup analyses focused on non-LPBC. • **Results:** pCR occurred in 51.5%. sTILs ≥30% strongly associated with higher pCR ($p<0.0001$). sTILs and AI-TILs correlated moderately (rho=0.59). Both predicted pCR (OR≈1.07 per unit). In non-LPBC, high AI-TILs markedly enriched for pCR (OR 4.1). • **Conclusions:** AI-TILs match manual performance and improve response stratification in non-LPBC, supporting broader validation for clinical integration.
10 Dec 2025	Evaluation of spatial collagen morphometry in TNBC versus non-TNBC biopsies: a cross-sectional SHG/TPE and AI-based analysis of tumor and non-tumor regions	Kutbuddin Akbary	• **Introduction**: TNBC exhibits aggressive biology, yet its region-specific stromal collagen architecture is poorly characterized. SHG/TPE imaging with AI-enabled morphometrics offers high-resolution fibrosis profiling beyond routine pathology. • **Methodology:** Unstained biopsies (n=266) underwent SHG/TPE microscopy and AI collagen quantification across four regions: tumor, lobule/duct, stroma-fat, stroma-fibrosis. TNBC (n=21) and non-TNBC (n=245) were compared using parameter-normalized median differences and Wilcoxon tests. • **Results:** Tumor-region collagen showed no significant subtype differences. Lobule/duct regions revealed multiple significant morphometric alterations in TNBC—higher collagen string abundance, greater string aggregation, and elevated fibre-distribution metrics. Stroma-fibrosis differences were numerical but nonsignificant. • **Conclusions:** TNBC displays a distinct desmoplastic signature localized to lobule/duct compartments, highlighting potential spatial collagen biomarkers and insights into subtype-specific stromal remodeling.

Notable Presentations At SABCS 2025
AI / ML (7/20)

Date	Title	Author	Summary
10 Dec 2025	Breast Cancer Mutation Detection via Liquid Biopsy Using cfDNA from 50 mL Urine Samples	Nafiseh Jafari	• **Introduction**: Urine cfDNA represents a non-invasive alternative for breast cancer genotyping, but stability, yield, and preservative compatibility remain limiting factors. • **Methodology:** Fifty-milliliter pooled urine samples were spiked with four actionable mutations and preserved using Streck, UAS, or TE buffer. Samples were processed at day 0 and day 3 using the nRichDX Max 50 kit. cfDNA quantity, integrity, and qPCR mutation detection were assessed across replicates. • **Results:** All preservatives enabled stable cfDNA recovery with intact fragment profiles. Yields differed (Streck 88%, UAS 75%, TE 62%), but mutation detection remained robust, with unchanged Ct values and low variability (CV <5%). • **Conclusions:** Large-volume preserved urine provides reliable mutation detection after 3-day ambient storage, supporting its utility for scalable breast cancer liquid biopsy workflows.
11 Dec 2025	Prediction of pathologic complete response from histopathology images of HER2+ breast cancer using an AI foundation model	Reva Basho	• **Introduction**: HER2+/HR+ tumors achieve lower pCR rates despite standard neoadjuvant chemo-anti-HER2 therapy. AI-enabled digital pathology may reveal morphological predictors of therapy sensitivity unavailable from routine parameters. • **Methodology:** Baseline H&E WSIs from 231 HER2+ cases (119 HR+, 112 HR–) were processed using the CanvOI foundation model. Tile/slide embeddings informed logistic regression–based pCR classifiers per HR subgroup. Performance was assessed with repeated 4×4 cross-validation; multivariable models included grade and HER2 IHC. Class imbalance was mitigated by sample trimming. • **Results:** pCR rates were 40.4% (HR+) and 64.1% (HR–). The AI model predicted pCR with AUC 0.69 (HR+) and 0.65 (HR–), improving to 0.70 and 0.67 after balancing. Model outputs remained independently predictive beyond grade and HER2 status. • **Conclusions:** Digital pathology–based AI provides meaningful, independent pCR prediction in HER2+ disease—particularly valuable for HR+ patients with low response rates—supporting future integration into neoadjuvant treatment selection.

Notable Presentations At SABCS 2025
AI / ML (8/20)

Date	Title	Author	Summary
11 Dec 2025	A Novel Non-invasive Machine Learning Model for Predicting Tertiary Lymphoid Structures and Treatment Response to Neoadjuvant Therapy in Triple-Negative Breast Cancer: A Multicenter Retrospective Study	Yidan Lin	• **Introduction**: TNBC lacks non-invasive biomarkers predicting tertiary lymphoid structures (TLSs), despite their strong association with NAT response. Radiomics-based ML may enable early TLS detection and response forecasting. • **Methodology:** DCE-MRI radiomics (4,788 features) were extracted from 698 patients across multicenter cohorts. Five ML classifiers were trained to predict TLSs; XGBoost was selected and validated across three NAT cohorts. Performance metrics included AUC, accuracy, and prognostic associations. SHAP interpretation and CellProfiler-based pathomics assessed biological correlates. • **Results:** XGBoost achieved AUCs of 0.922 (training), 0.852 (TLS validation), and 0.724–0.919 across NAT cohorts. Low rTLS scores correlated with superior DFS, and the score remained independently prognostic. Pathology confirmed TLS enrichment and remission in high-score cases. • **Conclusions:** The rTLS model reliably predicts TLS presence and NAT response, supporting integration into personalized TNBC treatment planning.
11 Dec 2025	Using a Real-Time Artificial Intelligence Ultrasound System with Computer-Aided Detection and Diagnosis to Distinguish Ductal Carcinoma In Situ and Invasive Ductal Carcinoma	Joon Suk Moon	• **Introduction**: Real-time AI-CAD for ultrasound offers lesion-level malignancy probabilities that may help distinguish DCIS from IDC, a clinically relevant differentiation rarely achievable sonographically. • **Methodology:** Thirty-four biopsy-proven cases (DCIS = 12; IDC = 22) were retrospectively analyzed using CadAI-B. Probability of malignancy (POM) and BI-RADS assignments were compared across key ultrasound features, identifying those with significant DCIS–IDC separation. • **Results:** IDC showed markedly higher POM than DCIS (0.365 vs 0.126; $p<0.001$). Irregular shape, indistinct/microlobulated margins, hypoechogenicity, and parallel orientation produced significant POM differentials. IDC clustered in BI-RADS 4B–5 with high POM, whereas DCIS maintained low POM despite similar categories. • **Conclusions:** CadAI-B enhances real-time DCIS–IDC discrimination and may support more consistent ultrasound-based triage, warranting broader validation.

Notable Presentations At SABCS 2025
AI / ML (9/20)

Date	Title	Author	Summary
11 Dec 2025	Development and Validation of a Living Decision Support Tool (Living-DST) in Oncology Using Agentic AI-Augmented Systematic Literature Review (SLR)	Rozee Liu	• **Introduction**: Rapidly expanding oncology evidence burdens clinicians. A living AI-augmented decision-support tool (DST) can streamline synthesis of trials, guidelines, and regulatory updates to deliver real-time, patient-specific insights. • **Methodology:** An agentic AI system (GPT-4.1, o3, Claude Sonnet-4) emulating Cochrane-compliant SLRs was trained on 29,236 manually annotated abstracts using a 36-variable framework. Accuracy was benchmarked against 1,997 human annotations and compared with major AI chatbots across 8 breast-cancer clinical scenarios. • **Results:** Accuracy reached 95–97% for review variables and >90% for all extraction variables, with 50% >95%. The system annotated 1,997 studies in 7.25 hours (99% time savings). It outperformed ChatGPT, Perplexity, and Consensus, capturing 23% additional pivotal evidence. • **Conclusions:** The Living-DST reliably delivers comprehensive, guideline-linked, real-time evidence, supporting more precise breast-cancer decision-making.
11 Dec 2025	Artificial intelligence (AI) as a decision support tool for practicing oncologists: breast cancer cases	Mohammad Jahanzeb	• **Introduction**: Second opinions and MDR reviews improve cancer care, but access is uneven. Modern foundation models may help bridge expertise gaps if their recommendations match expert consensus. • **Methodology:** Fifty complex breast cancer cases previously adjudicated by MDR panels were evaluated using ChatGPT-4.5, Claude Opus 4, and Gemini Ultra. Outputs were scored (1–5) for completeness, reasoning, clarity, options, recency, and relevance, benchmarked against MDR recommendations and NCCN guidelines. • **Results:** All models showed high concordance with MDR decisions, with differences limited to minor, non–management-altering nuances. AI excelled in clarity and reasoning, with slightly lower performance in relevance and breadth of options. • **Conclusions:** Leading AI models demonstrate expert-level alignment in complex breast cancer scenarios, supporting their use as decision-support tools—provided human oversight ensures safe, individualized care.

Notable Presentations At SABCS 2025
AI / ML (10/20)

Date	Title	Author	Summary
11 Dec 2025	Merlin: dissecting therapeutically relevant elements of the oncogenic microenvironment using multi-modal deep learning	Albert E Kim	• **Introduction**: MERLIN aims to move DL beyond prediction toward therapeutic discovery by inferring TME phenotypes directly from routine H&E and clinical data, overcoming incomplete biological characterization in current decision-making. • **Methodology:** MERLIN was trained on 3,111 TCGA H&E WSIs with matched clinico-genomic data using attention-based multiple-instance learning and multimodal fusion. Bulk RNA-seq–derived GSEA signatures served as ground truth. Validation included expert review of attention maps and application to 232 TNBC biopsies. • **Results:** MERLIN accurately recovered TME programs, with attention maps highlighting phenotype-specific lymphocyte and tumor-cell patterns verified by pathology. In TNBC, higher MERLIN-derived T-cell cytotoxicity correlated with pCR to Keynote-522 (p=0.017). • **Conclusions:** MERLIN effectively extracts therapeutically relevant TME signatures from standard pathology, supporting its potential to uncover resistance mechanisms and guide treatment in future large-scale applications.
11 Dec 2025	Deep Learning Classification of Inflammatory Breast Cancer Using Multiparametric MRI: A Multi-Sequence Analysis	Saleh Ramezani	• **Introduction**: IBC diagnosis is subjective and error-prone. mpMRI captures hallmark features, but interpretation varies. Automated deep learning could standardize and accelerate IBC detection. • **Methodology:** DenseNet121 models were trained on 791–267 mpMRI scans (T1, DWI, DCE, T2c). Ipsilateral and bilateral inputs were tested. Data were stage-stratified (80/20 split), normalized, augmented, and evaluated via 5-fold cross-validated ensembles. AUC-ROC measured performance. • **Results:** DWI and T2c achieved highest discrimination (AUC=0.96). Accuracy was 92–97% for early stages and 94–95% for classic IBC. Differentiating cT4b vs cT4d remained poor (40–42%). Ensembles outperformed individual folds; bilateral imaging added no benefit. • **Conclusions:** mpMRI-based deep learning enables high-accuracy IBC detection, with strongest performance on DWI. Challenges persist for borderline cT4b presentations, supporting future multimodal and uncertainty-aware modeling.

Notable Presentations At SABCS 2025
AI / ML (11/20)

Date	Title	Author	Summary
11 Dec 2025	Health Economic Evaluation of an Artificial Intelligence assisted Breast Cancer Multi Disciplinary Team Meeting/Tumour Board: Preliminary results from a UK Single Centre Simulation Trial	Pritika Garodia	• **Introduction**: UK breast MDTMs improve care but impose substantial labour and financial burden. AI-assisted automation may streamline preparation and reduce system-wide costs. • **Methodology:** Two prospective MDTMs (10 matched cases each) compared standard manual preparation versus OncoFlow™, a UKCA-registered AI CoPilot. Manual preparation required 1.5 hours from 10 MDT members; OncoFlow required only its £25,000 annual licence. Costs were modelled per case and annualized for 1,560–2,080 yearly MDT cases. ICER quantified cost per clinician-hour saved. • **Results:** Manual prep cost £37.80/case; OncoFlow cost £12.02–£16.03/case, saving £21.77–£25.78. Annual savings reached £34k–£54k. Preparation time fell from 13.5 to ~0.01 hours, yielding an ICER of £1.91/hour saved. • **Conclusions:** OncoFlow markedly reduces MDT workload and cost, supporting scalable NHS adoption to modernize cancer pathways.
11 Dec 2025	Artificial intelligence (AI)-generated electronic medical record summarization in breast oncology	Ko Un Park	• **Introduction**: Oncology pre-charting is labor-intensive and error-prone. A GPT-4o/RAG-based summarization agent may standardize breast-cancer record review and reduce clinician workload. • **Methodology:** An AI agent processed radiology, pathology, and consultation reports to generate HPIs. For 50 consecutive patients, AI summaries were compared with PA-generated HPIs. Two breast surgeons scored clarity and relevance (1–5 scale) and evaluated accuracy/completeness across age, imaging, pathology, medical history, and pending workup. • **Results:** AI achieved high clarity (4.01) and relevance (3.87). Accuracy was strong for age (94%), histology (97.6%), grade (95%), and receptor status (89.8%). Imaging completeness varied—MRI lowest (44.4%). Biopsy modality was often nonspecific (39.8% missing). Pending workup was captured in 41.7%. • **Conclusions:** GPT-4o/RAG provides reliable, clinician-ready breast-cancer pre-chart summaries, supporting workflow integration with continued human oversight.

Notable Presentations At SABCS 2025
AI / ML (12/20)

Date	Title	Author	Summary
11 Dec 2025	Artificial intelligence (AI) based image analysis of PD-L1, TIL, immune signature and ctDNA for prediction of response to neoadjuvant chemotherapy in breast cancer	Eun Young Kim	• **Introduction**: TILs are prognostic in breast cancer but limited by variability; ctDNA offers minimally invasive response monitoring. Integrating AI-based TIL quantification with ctDNA may enhance NAC response assessment. • **Methodology:** Pre-treatment H&Es from 101 patients were analyzed using Lunit SCOPE IO to classify immune phenotypes. PD-L1 was assessed by 22C3. ctDNA was sequenced at baseline and pre-surgery using 47-gene and 157-mutation targeted panels, with ddPCR validation. Logistic regression evaluated clinical and molecular predictors. • **Results:** TP53 and PIK3CA dominated FFPE and ctDNA profiles. TNBC showed strongest ctDNA detectability (OR 209.5). Inflamed TIL phenotype plus ctDNA clearance corresponded to higher pCR (38.5% vs 11.1%). • **Conclusions:** AI-TILs combined with ctDNA dynamics provides a feasible, sensitive framework for NAC response monitoring and stratification in early breast cancer.
11 Dec 2025	Espwa: a deep learning-enabled computational pathology tool that facilitates precision oncology for haitian breast cancer patients	Albert E Kim	• **Introduction**: Haiti's extreme pathology workforce shortage prevents ER testing, forcing universal endocrine therapy. ESPWA leverages DL on H&E WSIs to deliver low-cost ER assessment and enable precision treatment. • **Methodology:** Using 3,448 ZL slides plus TCGA data, weakly supervised attention-based MIL models were trained for ER classification and regression. Datasets were split 70/15/15, with extensive augmentation. Cross-validation and bootstrapping assessed robustness, and performance was compared to an expert pathologist. • **Results:** A TCGA-trained model failed under domain shift (AUROC 0.846→0.671 on ZL). ZL-trained ESPWA achieved AUROC 0.790 and ICC 0.524, with weaker performance in ER-low and poorly differentiated tumors. ESPWA outperformed an expert pathologist (accuracy 0.726 vs 0.639). • **Conclusions:** ESPWA shows strong feasibility for scalable ER assessment in Haiti and is advancing to clinical trials to support precision endocrine therapy access.

Notable Presentations At SABCS 2025
AI / ML (13/20)

Date	Title	Author	Summary
11 Dec 2025	Machine Learning predicts early tumor progression in Hormone Receptor-positive, Human Epidermal growth factor Receptor 2-negative (HR+/HER2-) advanced breast cancer (aBC) patients treated with first-line endocrine therapy (ET) plus Cyclin Dependent Kinase 4/6 inhibitors (CDK4/6i)	Leonardo Provenzano	• **Introduction**: Although CDK4/6i + ET is standard first-line therapy for HR+/HER2– advanced breast cancer, ~13% experience early progression (<6 months), with markedly poor outcomes. ML may enable proactive identification of these high-risk patients. • **Methodology:** In PALMARES-2 (n=4,104), 73 clinical, pathological, and laboratory variables were modeled using glmnet, RF, XGBoost, and neural networks. missForest imputation and undersampling addressed missingness and imbalance. Ten-fold CV optimized hyperparameters; performance was confirmed in a 20% test set and an external Milan cohort. • **Results:** Early progressors (12.7%) had dramatically worse rwTTC (5.3 vs 43.4 mo) and rwOS (21.4 vs 73.0 mo). Risk factors included low ER/PR, high Ki-67, endocrine resistance, ECOG deterioration, and liver metastases. All ML models showed consistent predictive accuracy and external generalizability. • **Conclusions:** This first ML framework for early CDK4/6i progression identifies patients needing alternative first-line strategies, supporting future prospective validation.
11 Dec 2025	Prospective Evaluation of "PreciseBreast" AI Tool in Early-Stage Invasive Breast Cancer Risk Stratification	Talar Telvizian	• **Introduction**: Multigene assays like Oncotype DX guide therapy in early HR+ breast cancer but are costly and slow. PDxBR, an AI-driven digital-pathology assay, offers rapid, morphology-based recurrence-risk stratification. • **Methodology:** A prospective correlational study enrolled 32 eligible early-stage HR+ IDC patients. PDxBR scores—derived from nuclear pleomorphism, mitoses, tubule formation, and TILs—were compared with ODX and RSClin classifications using McNemar and symmetry tests. Turnaround time and costs were assessed. • **Results:** ODX low-risk patients (n=6) were all classified high-risk by PDxBR; the single ODX high-risk case was PDxBR low-risk. PDxBR strongly aligned with RSClin ($p<0.0001$). Turnaround time was markedly shorter (2.0 vs 6.3 days), and cost substantially lower ($1,500 vs $4,620). • **Conclusions:** PDxBR delivers rapid, lower-cost risk assessment with strong RSClin concordance, supporting further validation as a scalable complement or alternative to genomic assays.

Notable Presentations At SABCS 2025
AI / ML (14/20)

Date	Title	Author	Summary
11 Dec 2025	A Novel Agent-Based AI System to Unlock Unstructured Data in Synoptic Reports for Advanced Population Health Analysis in Breast Cancer	Steven N Hart	• **Introduction**: Synoptic reports standardize breast cancer data, but key biomarker and procedural insights remain buried in free text, limiting population-scale analytics. An agent-based AI extraction pipeline can unlock this information. • **Methodology:** A modular multi-LLM system sequentially parsed synoptic fields, extracted/normalized tumor and biomarker details, and produced structured outputs. A synthetic data generator provided ground-truth training and testing across models (Gemini, Llama3.3, Phi4, DeepSeek-r1, Gemma3). Accuracy, sensitivity, specificity, and F1-scores were assessed. • **Results:** Gemini-1.5-pro achieved 96.9% accuracy (F1 97.0%); Llama3.3:70B reached 98.7% accuracy (F1 98.8%). Smaller models (Phi4, DeepSeek-r1) outperformed Gemma3:27B (F1 66.2%). Error analysis refined agent logic ahead of large-scale real-world deployment. • **Conclusions:** This agent-based AI system reliably converts unstructured breast-cancer text into computable data, enabling real-time population analytics and supporting more informed clinical and research decisions.
11 Dec 2025	Prognostic performance analysis of artificial intelligence test and 21-gene assay in premenopausal node-positive HR+ HER2- breast cancer patients	Jailan Elayoubi	• **Introduction**: In premenopausal HR+/HER2– node-positive breast cancer, ODX provides limited risk-adapted guidance. ATX, a multimodal AI test integrating H&E-derived morphology and clinical data, may improve prognostication. • **Methodology:** Four cohorts (n=150) were analyzed using a locked ATX model; 43 patients also had ODX. Prognostic accuracy for DFI was assessed via HR per 0.1 ATX increase and Harrell's C-index. Results were pooled using random-effects meta-analysis and examined in multivariable models. • **Results:** ATX significantly predicted DFI (HR 2.77; C-index 0.78), outperforming ODX (HR 1.05; C-index 0.46). ATX remained the only independent predictor after adjustment. Five-year recurrence was 9.1% vs 25.7% for lowest vs highest ATX quartiles. • **Conclusions:** ATX shows strong, independent prognostic value in premenopausal N+ disease, warranting larger validation studies.

Notable Presentations At SABCS 2025
AI / ML (15/20)

Date	Title	Author	Summary
11 Dec 2025	Artificial Intelligence Predicts OncotypeDX Recurrence Scores Directly from H&E-Stained Whole Slide Images of ER+/HER2-Node-Negative Breast Cancer Surgical Sections	Savitri Krishnamurthy	• **Introduction**: Oncotype DX guides adjuvant therapy in early ER+/HER2– N0 breast cancer but is costly and slow. AI prediction of ODX scores directly from H&E WSIs could offer a scalable alternative. • **Methodology:** A two-step framework used a pan-cancer Phenotype Atlas to extract morphological phenotypes and weakly supervised learning to map them to RNA-seq–estimated ODX scores. External validation used 300 real-world cases with true ODX and >10-year follow-up. Performance was assessed using AUC and outcome concordance. • **Results:** The model achieved AUC 0.82, improving to 0.86 with clinical variables and 0.91 in premenopausal patients. AI-predicted risk aligned with ODX-based distant-metastasis stratification (p=0.9). • **Conclusions:** AI-derived ODX estimates from H&E show strong accuracy and clinical concordance, supporting use as a rapid, low-cost alternative for treatment decision-making.
11 Dec 2025	Simulating Personalized Patient Journeys for Early Cancer Detection Using Artificial Intelligence Synthetic Data	Oge Marques	• **Introduction**: Early-detection AI development is constrained by limited real-world data and privacy concerns. Synthetic datasets enriched with modifiable risk factors (MRFs) may enable safe, scalable model training and prevention-focused simulations. • **Methodology:** A synthetic cohort was generated by adapting NVIDIA Nemotron-Personas for demographic diversity and augmenting them with Synthea-based longitudinal EHRs, including a breast-cancer module. Personas incorporated detailed lifestyle, environmental, and behavioral MRFs, enabling future "what-if" scenario modeling. • **Results:** The resulting dataset provides high-fidelity, privacy-preserving longitudinal personas with realistic breast-cancer–relevant trajectories suitable for AI/ML early-detection research and simulation testing. • **Conclusions:** This framework establishes the foundation for dynamic MRF-driven prevention simulations, supporting precision-prevention strategies and accelerating early-detection model development.

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Date	Title	Author	Summary
11 Dec 2025	Deep Learning to Predict Pathological Complete Response in Patients Receiving NAC using Pre-treatment Clinical and Imaging Features	Ryan Gifford	• **Introduction**: pCR prediction from pre-treatment MRI alone is clinically valuable but underperforms compared with models requiring post-treatment imaging. A new architecture aims to close this gap by predicting post-treatment radiomics from baseline scans. • **Methodology:** Using I-SPY2, a two-CNN pipeline was trained: CNN-1 learned radiomic changes associated with pCR from paired pre/post MRIs; CNN-2 predicted post-treatment radiomic features from pre-treatment MRI alone. Predicted features were substituted into CNN-1, enabling pCR prediction without post-treatment data. Clinical variables were optionally added • **Results:** Pre-MRI CNN AUC was 0.53; paired-timepoint CNN 0.71. The proposed model achieved 0.62 (87% of full-model accuracy). Adding subtype and age increased AUC from 0.70 to 0.73, narrowing the gap to the 0.78 paired model. • **Conclusions:** This architecture substantially improves pre-treatment pCR prediction and approaches post-treatment performance, supporting earlier, less invasive decision-making.
11 Dec 2025	Machine Learning Prediction of High Oncotype DX® RS based on Clinicopathologic features: Results from the GBECAM 0520 Multicenter Retrospective Study	Julio araujo	• **Introduction**: High Oncotype DX® (ODX) scores guide chemotherapy use in ER+/HER2– early breast cancer, but cost limits access. This study tested whether routine clinicopathologic variables can predict high-risk (RS ≥25) disease using machine learning (ML). • **Methodology:** A retrospective multicenter cohort (n=897) with complete pathology and ODX results was analyzed. Ki-67, PR status, and histologic grade were selected as top predictors and entered into a ridge-regression ML model. Performance was evaluated using AUC and leave-one-center-out cross-validation. • **Results:** Eighteen percent had RS ≥25. The model achieved AUC 0.78 ± 0.03 for high-risk detection and Pearson correlation 0.50 ± 0.03 with continuous scores. Ki-67 and grade strongly predicted higher RS, while PR inversely correlated. Performance was stable across menopausal groups. • **Conclusions:** A minimal-variable ML model reliably identifies high-risk ODX profiles, offering a low-cost triage tool for resource-limited settings. Prospective validation is warranted.

Notable Presentations At SABCS 2025
AI / ML (17/20)

Date	Title	Author	Summary
11 Dec 2025	Machine learning-enhanced ultra-deep sequencing for low-abundance circulating tumor DNA (ctDNA) in breast cancer	Yuwei Ni	• **Introduction**: Breast cancer management increasingly relies on ctDNA for minimally invasive monitoring, treatment selection (e.g., ESR1-guided therapy), and relapse risk prediction. Sensitive detection is essential in low–tumor-burden settings. • **Methodology:** Plasma cfDNA (20–60 ng) and matched WBC DNA underwent UMI-tagged targeted sequencing of 168 cancer-genes (NovaSeq6000; 35,000× raw, ~4,000× unique depth). A consensus-building pipeline, ML-based noise modeling, and WBC-filtering removed PCR/sequencing errors and clonal hematopoiesis variants. Analytical performance was assessed using reference standards, dilution series, LoD/LoB testing, and 44 clinical samples. • **Results:** Median SNV LoD: 0.25% (20 ng) → 0.15% (50 ng); indel LoD: 0.25% → 0.14%. LoB was extremely low (4.88×10^{-7}). Clinical validation showed PPA 83% (SNVs), 85.7% (indels) and NPA 99.9%. • **Conclusions:** Ultra-deep, ML-enhanced ctDNA sequencing enables highly accurate mutation profiling at very low allele fractions, supporting precise, non-invasive monitoring in breast cancer.
11 Dec 2025	Machine learning based inference of real-time HER2 activity from gene expression profiling in breast cancer to inform HER2 targeted therapy selection	Saumya D. Sisoudiya	• **Introduction**: HER2-low and ultra-low tumors expand eligibility for HER2-directed ADCs, yet IHC alone incompletely reflects true HER2 pathway activity. Gene-expression–based ML may refine patient selection. • **Methodology:** FoundationOne®RNA profiles (1,517 genes) from 477 breast cancers were analyzed. DEGs between IHC 0 and IHC 2+/3+ (FDR<0.01, $\log_2$FC>1) guided lasso-regression model training using 70:30 splits, with held-out samples for evaluation. Fifty iterations estimated the proportion of predicted "high HER2 activity" across IHC categories. • **Results:** Forty-four DEGs—including ERBB2, GRB7, TTYH1—formed the model. Predicted high-activity rates increased with IHC score: 3+ (87%), 2+ (58%), 1+ (41%), 0 (22%). IHC 3+ tumors predicted as low-activity had markedly reduced ERBB2 expression (4.8k vs 34k TPM) and lacked amplification (OR 14.2). • **Conclusions:** A multi-gene ML signature more accurately captures HER2 pathway activity than IHC alone and may better identify HER2-responsive patients, particularly within HER2-low disease. Independent validation is forthcoming.

Notable Presentations At SABCS 2025
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Date	Title	Author	Summary
11 Dec 2025	A novel approach for phenotyping triple negative breast cancer using an Artificial Intelligence digital pathology-based prognostic test to assess recurrence risk and response to therapy	Michael Donovan	• **Introduction**: TNBC prognosis depends heavily on spatial immune-tumor interactions, yet reliable risk-stratification tools remain limited. AI-enhanced morphologic profiling (PDxBR) may capture microarchitectural features linked to recurrence risk. • **Methodology:** UCLA TNBC surgical H&Es (2008–2017) were digitized and analyzed using PDxBR, integrating eight AI-derived morphologic features with four clinical variables. An optimized TNBC-specific threshold (≤50 vs >50) generated high/low-risk groups. Performance was compared against the AI-grade model alone. • **Results:** Among 77 patients (18% events), PDxBR identified 39% high-risk vs 83% by AI-grade. PDxBR was the only significant prognostic model (HR 3.72; p=0.017), with Se 0.57, Sp 0.65, NPV 0.87. It captured 8/14 events, including DM, LR, SP, D. Key predictive morphologic signatures included mitotic "hot-spot" density and architectural differentiation. • **Conclusions:** PDxBR demonstrates independent prognostic value in TNBC, outperforming morphology-only models and enabling refined risk stratification. AI-driven digital pathology may enhance chemotherapy/IO decision-making and clinical-trial patient selection.
12 Dec 2025	Artificial Intelligence for Tumor-Infiltrating Lymphocytes in Early-Stage TNBC: Results of a Collaborative Prospective TIL Validation Challenge	Julia R Dixon-Douglas	• **Introduction**: TILs are powerful prognostic markers in TNBC, but manual scoring faces variability. The CATALINA challenge tested whether computational TIL (cTIL) methods can match or surpass expert sTIL assessment. • **Methodology:** Five cTIL scores from two independent AI models were evaluated on 220 blinded WSIs for concordance with sTIL, then validated in 1,356 early-stage TNBC cases across seven trials. Prognostic endpoints (IDFS, DDFS, OS) were assessed using multivariable Cox models adjusting for clinicopathologic factors. High/low groups used sTIL≥30% and cTIL≥75th percentile. • **Results:** cTIL–sTIL correlation was moderate (ρ=0.37–0.47). All cTIL scores predicted outcomes, but after adjusting for sTIL, only one (percentage_lymphocyte) remained significant, while sTIL retained strong prognostic power. Discordant categories aligned more closely with sTIL-derived risk (e.g., 5-yr DDFS: high/high 0.82; low/low 0.66; cTIL-high/sTIL-low 0.67; cTIL-low/sTIL-high 0.78). • **Conclusions:** cTIL algorithms show prognostic value but cannot substitute for expert sTIL. sTIL remains the more robust biomarker, highlighting the need for rigorous benchmarking of AI pathology tools before clinical adoption.

Notable Presentations At SABCS 2025
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Date	Title	Author	Summary
12 Dec 2025	Development of a Multi-Modal Artificial Intelligence (MMAI) Model for Predicting Distant Metastasis in HR+ Early-Stage Invasive Breast Cancer	Charles E. Geyer Jr.	• **Introduction**: Risk prediction for distant metastasis (DM) in HR+ early-stage breast cancer remains limited by reliance on narrow clinical or genomic inputs. A multimodal AI (MMAI) model integrating pathology and clinical factors was developed to address this gap. • **Methodology:** Using digitized biopsy/surgical slides and clinical variables from six Phase III trials, a locked MMAI score predicted DM. Performance assessed via 10-year time-dependent AUC, Cox models, and Kaplan–Meier estimates versus a clinical comparator (age, tumor size, nodal status). Pre-specified subgroup analyses and optimized cut points were applied • **Results:** MMAI outperformed the clinical model in B14 (tdAUC 0.71 vs 0.65) and B39 (0.72 vs 0.69). DM risk was strongly associated with MMAI score (B14 HR 2.06; B39 HR 2.31), remaining significant after adjustment. Risk groups showed distinct 10-year DM-free rates: low 95.5%, intermediate 89.5%, high 83.6%. Performance was consistent across nodal and menopausal subgroups. • **Conclusions:** The MMAI model provides robust, independent prognostic value for DM across multiple randomized trials. Its rapid, nondestructive workflow supports real-world adoption and personalized management in HR+ early breast cancer.
12 Dec 2025	Comparative performance of an AI-based digital pathology tool and genomic signatures in early ER+/HER2- breast cancer	Victor Aubert	• **Introduction**: Risk-stratifying ER+/HER2- early breast cancer remains challenging, especially for treatment de-escalation. AI applied to H&E slides offers a scalable alternative to genomic assays. RlapsRisk BC (RR) was evaluated against EndoPredict (EP) and Oncotype DX (ODX) using 5-year distant recurrence-free survival. • **Methodology:** Retrospective analysis included two cohorts: Gustave Roussy EP-tested patients (n=381) and MD Anderson ODX-tested node-negative patients on endocrine therapy alone (n=154). Digitized resection H&E slides were analyzed with RR. Discriminative performance was compared via AUC and 5-year dRFS across risk groups. • **Results:** RR outperformed EPclin (AUC 0.73 vs 0.57) and ODX (0.78 vs 0.58). RR low-risk patients had excellent outcomes (EP: 99.6% dRFS; ODX: 95.3%), outperforming genomic tools. RR high-risk classification captured most events (EP: 6/7; ODX: 35/42). RR classified fewer high-risk patients than EPclin, more than ODX, with closer alignment to observed recurrence. • **Conclusions:** RR provides superior prognostic accuracy and may safely expand de-escalation candidates while improving identification of true high-risk patients. As a tissue-efficient, cost-effective AI tool, RR shows strong potential as an alternative to genomic testing in ER+/HER2- early breast cancer.

Notable Presentations At SABCS 2025
AI / ML (20/20)

Date	Title	Author	Summary
12 Dec 2025	The St. Gallen AI Consensus – Should AI have a vote?	Anton Oseledchyk	• **Introduction**: Expert panels provide consensus, but AI may offer unbiased, data-driven guidance. This study provides the first systematic comparison of AI-generated recommendations versus St. Gallen 2025 expert consensus. • **Methodology:** 80 clinical scenarios across surgery, radiation, systemic therapy, elderly care, and recurrence were posed to four LLMs (ChatGPT-4o, Gemini 2.5, DeepSeek-V3, Claude Sonnet 4). Agreement with expert voting was assessed. Discordant responses were re-evaluated after unblinding LLMs to expert choices. • **Results:** Agreement rates were modest: ChatGPT 60%, Gemini 57.5%, DeepSeek 48.8%, Claude 26.3%. Concordance varied widely—highest for endocrine therapy (70.8%) and lowest for radiation (25%). After seeing expert votes, LLMs revised 50–100% of discordant answers, yet 19–50% remained unchanged, reflecting persistent reasoning gaps. • **Conclusions:** AI systems show limited alignment with expert consensus in early breast cancer management, highlighting current constraints in complex clinical reasoning. Nonetheless, AI provides unbiased, comprehensive evidence synthesis and may serve as a valuable complementary perspective for expert panels.
12 Dec 2025	Multimodal Deep Learning for Recurrence Stratification for Early-Stage Breast Cancer in Resource-Constrained Environments	Mohan Uttarwar	• **Introduction**: Genomic assays guide adjuvant chemotherapy in early-stage breast cancer but remain expensive and inaccessible. H&E slides, universally available, contain latent prognostic biology that AI can unlock. This study validates TRINITY AI, a multimodal model integrating morphology, clinicopathologic factors, and AI-inferred transcriptomics to predict recurrence risk. • **Methodology:** Trained on 1,219 TCGA/CPTAC cases, TRINITY AI uses a self-supervised transformer to infer transcriptomics from WSIs and fuse these with morphology and clinical variables in a shared latent space. External validation used 166 cases with matched Oncotype DX; prognostic analyses used 1,051 TCGA cases with ≥5-year DRFI. • **Results:** Across pooled external cohorts, TRINITY AI achieved AUC 0.88, specificity 95%, NPV 92%, outperforming clinicopathologic models and approximating Oncotype DX. Cohort-specific NPVs remained >87%. High-risk calls predicted a 3.8-fold higher DRFI hazard (C-index 0.698) independent of size, grade, nodes, and subtype. • **Conclusions:** TRINITY AI delivers genomics-level recurrence risk directly from routine H&E slides, offering fast, low-cost, and scalable precision oncology—particularly valuable in resource-limited settings. Its strong prognostic independence supports its role as a practical alternative to current genomic assays.

Strategic Insights and Strategy Development is our focus