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Advances in Screening, Surgical Management, and Therapeutics of Breast Cancer: Expert Insights from SABCS 2025

The 2025 San Antonio Breast Cancer Symposium (SABCS) gathered leading international experts in clinical, translational, and basic breast cancer research to discuss breakthrough advancements in surgical and therapeutic management of breast cancer.

This Key Opinions in Medicine highlights expert (medical oncologists and surgeons) insights on key clinical trial outcomes presented at the SABCS 2025 symposium, emphasising their relevance to advancing clinical practice and improving breast cancer care.

Coming out of SABCS 2025, the following advances in breast cancer were noteworthy

New screening method for breast cancer risk

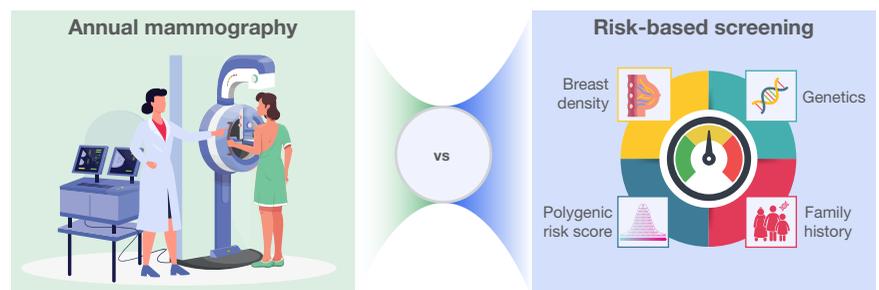
Breast cancer risk of an individual not only helps guide screening frequency and preventive measures but also allows allocation of resources to high-risk patients.

Dr. Sherene Loi: Risk-based assessments improve awareness and motivate women at high risk to make lifestyle changes at the initial assessment, while presenting the opportunity for chemoprevention. The **WISDOM study**¹ compared risk-based breast cancer screening to standard annual mammography in over 28,000 women in the United States, aged between 40 and 74 years. The risk-based cancer screening

assessed individual risk of breast cancer based on genetics, family history, polygenic risk score, and breast density. The primary objective was to assess the feasibility of implementation and safety that was successfully demonstrated.

However, the screening method did not reduce the number of biopsies or the frequency of mammography/magnetic resonance imaging. Interestingly, adherence to the screening schedule was very poor in the long-term, suggesting that even in a trial cohort motivated to do screening, the screening behaviour is difficult to change. This is concerning when considering the real-world acceptance of newer risk-based assessments for screening. However, the benefit of these types of risk-based assessments is that people are aware about their risk and are perhaps more motivated to make lifestyle changes. Overall, this study can revolutionise breast cancer screening in women.

Figure 1: Screening of breast cancer





Surgical de-escalation strategies

Surgical de-escalation in breast cancer treatment, particularly for early-stage patients is a vital decision in breast cancer management.

Dr. Han-Byoel Lee: De-escalation in the surgical management of early breast cancer (EBC) is the current approach. The **SOUND²** and **INSEMA³** trials show that axillary staging surgery can be avoided in hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative postmenopausal women with no clinical node-positive disease, further confirmed by the **BOOG 2013-08 trial⁴**. In the upfront surgery setting, recent BOOG trial compared sentinel lymph node biopsy (SLNB) versus no SLNB, showing non-inferiority of omitting SLNB. There was no difference in regional recurrence with < 0.5% in the SLNB arm and only about 1.2% in patients with no SLNB. There was no difference in disease-free survival (DFS) and overall survival (OS), confirming that staging operation can be safely omitted in HR-positive HER2-negative postmenopausal, older women. Interestingly, in this trial, no endocrine therapy (ET) was given in both arms and the importance of axillary lymph node (ALN) biopsy staging is very low. Further, these observations/findings will be confirmed by acquiring valuable information from the 40% of premenopausal patients enrolled in the Korean NAUTILUS trial.

Dr. Wendy Chan: Multiple studies have shown that breast-conserving therapy with radiotherapy offers outcomes comparable

with mastectomy. Further, the Z0011 trial showed that omitting complete ALN dissection after a positive SLNB can reduce mobility complications, particularly lymphoedema, without compromising survival, especially when combined with nodal irradiation.

The second randomisation study from the **INSEMA trial** addresses whether complete lymph node dissection can be safely omitted in patients with one to three micro SLN metastases. In this study, patients were randomised to either SLNB alone or complete ALN dissection. In the protocol analysis, non-inferiority of SLNB alone was not demonstrated, given the hazard ratio of 1.69. Five-year invasive DFS (iDFS) was 86.6% in SLNB group versus 93.8% in the ALN dissection. However, in the intention-to-treat analysis, the difference was smaller. Importantly, OS and regional recurrence rates were similar between the two groups suggesting that while SLNB alone may be reasonable for selected patients, the evidence is not yet strong enough to replace ALN dissection in this group and a longer follow-up is essential.

The INSEMA study also compared the radiotherapy patterns within the trial. All patients received whole breast irradiation, with no major differences in technique between the two groups. About half of all the patients received incidental axillary coverage of radiotherapy of at least 85% of the prescribed dose, whereas patients who underwent SLNB received slightly high incidental doses and more frequent regional nodal irradiation. Among the small group of patients who did not receive post-operative radiotherapy, iDFS did not differ significantly

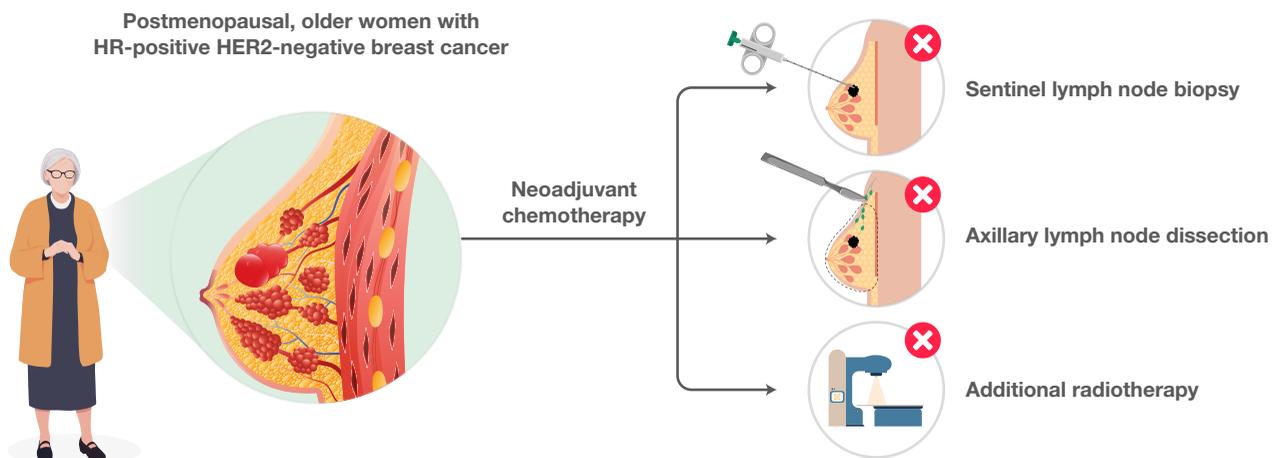
between the two arms. The key message is that omitting SLNB does not require compensatory escalation of radiotherapy, either dose or field, supporting the safety of a true surgical de-escalation.

Dr. Han-Byoel Lee: The approach for ductal carcinoma *in situ* is controversial as the LORETTA trial reported negative results compared to COMET trial, which was positive. The **AXSANA EUBREAST 03 trial** study in the neoadjuvant setting showed that ALN dissection was unnecessary in clinical node-positive disease that converted to clinically node negative after neoadjuvant systemic therapy.

Dr. Wendy Chan: The **AXSANA study** showed no differences in the 3-year axillary recurrence-free survival (RFS) between the ALN dissection group (99.2%) and the less extensive procedures like SLNB, targeted axillary dissection, or targeted lymph node biopsy (98.8%). These early results support the safety of less intensive axillary surgery in patients who respond well to neoadjuvant therapy, aligning the approach with the global trend towards minimising surgical mobility.

Dr. Han-Byoel Lee: In the context of de-escalation, it is important to mention the **MARRES trial** from Korea, a multicentre prospective cohort study comparing minimal invasive surgery, including robotic and endoscopic mastectomies versus conventional nipple-sparing mastectomies. Notably, fewer serious complications were reported, by the Clavien-Dindo scale, in the minimally invasive surgery cohort.

Figure 2: Surgical de-escalation strategies





Antibody drug conjugates (ADCs) in breast cancer therapeutics

ADCs, combining monoclonal antibodies with a cytotoxic agent (payload) through a chemical linker, have revolutionised breast cancer therapy by enabling the targeted delivery of cytotoxic agents. ADCs include trastuzumab deruxtecan (T-DXd) and trastuzumab emtansine (T-DM1).

Dr. Wendy Chan: In the **DESTINY-Breast05⁵** study, T-DXd outperformed trastuzumab and T-DM1. In the HER2-positive population, iDFS was 53% better with T-DXd. The 3-year iDFS was 92.4% for T-DXd arm and 83.7% for the T-DM1 arm. Clinically meaningful improvement in central nervous system recurrence was noted with T-DXd, and updated results show that the benefits were consistent regardless of adjuvant chemotherapy used.

Low-grade ADC-induced interstitial lung disease (ILD) was seen in 10% of patients in the T-DXd arm. Only 0.2% of patients showed grade 5 ILD, and adjuvant radiation therapy given sequentially or concurrently did not impact the incidence or severity of ILD. Safety profile of TDXd was manageable with protocol specific interventions.

In **DESTINY-Breast11⁶**, T-DXd-paclitaxel, trastuzumab, and pertuzumab (THP) neo-adjuvant regimen demonstrated superiority over dose-dense doxorubicin + cyclophosphamide (ddAC)-THP with pathologic complete response (pCR) rates of 67.3% for TDXd-THP arm and 56.3% for the ddAC-THP arm. Safety outcomes were favourable for TDXd-THP with low rates of grade ≥ 3 adverse events, low incidence of

ILD, and fewer serious adverse events than anthracycline-based chemotherapy regimen.

The **ASCENT-07⁷** Phase III study evaluated sacituzumab govitecan (SG) versus physician choice chemotherapy as first-line ET in HR-positive/HER2-negative metastatic breast cancer (MBC). At the primary analysis, ASCENT-07 did not meet its primary endpoint. Median progression-free survival (PFS) by blinded independent central review was 8.3 months in both treatment arms, with a stratified hazard ratio of 0.85. However, median OS showed an early trend favouring SG with a hazard ratio of 0.72 ($p = 0.029$). Investigator assessment showed improved PFS and similar objective response rates (37% in SG arm versus 33% in chemotherapy arm). The median duration of response was longer with 12.1 months for SG compared with 9.3 months for chemotherapy. Safety profile of SG matched with its previously known profile with neutropenia being common, and comparable adverse events in both arms. Early survival advantage and longer duration of response with favourable safety, points to SG as a promising therapeutic agent.

Survival benefits of new maintenance therapy

Maintenance therapy aims to prolong the benefit of prior line treatment in terms of survival.

Dr. Sherene Loi: One of the significantly positive trials presented was the **HER2CLIMB-05 Phase III⁸** study evaluating maintenance therapy with the tyrosine kinase inhibitor, tucatinib, or placebo, following therapy with docetaxel, trastuzumab, and pertuzumab (as in the **CLEOPATRA study**).

The study met its primary endpoint, with tucatinib improving PFS in patients with HER2-positive MBC compared to placebo. With a hazard ratio of 0.641 and median PFS with tucatinib as 24.9 months versus 16.3 months in the placebo, the study reported clinically meaningful difference of 8.6 months.

Interestingly, tucatinib was more beneficial in the HR-negative population with a hazard ratio of 0.55 compared to 0.72 in the HR-positive population, and the median PFS was 25 months versus 18 months in the HR-positive population. Although effective, the toxicity was much higher with addition of tucatinib, with over 40% showing liver toxicity and 70% exhibiting all grade diarrhoea, reducing the quality of life in these patients.

Dr. Zola Chia-Chen Li: In Taiwan, therapy for HER2-positive MBC includes HER2-dual blockade plus taxane; however, patients often suffer from taxane-induced toxicities. Often, the chemotherapy is switched to the less toxic oral 5-fluorouracil but given the newly reported survival benefits of maintenance tucatinib in the HR-negative HER2-positive group, there is something new to offer to patients other than chemotherapy.

Dr. Han-Byoel Lee: An exploratory analysis of the **ALTTO study**, compared tamoxifen versus aromatase inhibitor (AI) for HER2-positive luminal type cancers. The analysis showed that in all settings including HER2-positive population, AI-based therapy was more beneficial in younger patients. However, patients do better to tamoxifen in terms of side effects and so tamoxifen is preferred for early-stage disease.

Table 1: Key clinical trials reporting effective breast cancer therapeutics

Clinical trial	Target breast cancer subtype	Therapeutic agent	Stage of intervention	Outcomes
HER2CLIMB-05	HER2-positive MBC	Tucatinib (tyrosine kinase inhibitor)	Maintenance therapy	Improved PFS
lidERA	ER-positive HER2-negative EBC	Giredestrant (oral SERD)	Adjuvant ET	Improved RFS and DFS
RJBC 1501	Early TNBC	Taxane ± carboplatin	Adjuvant therapy	Improved DFS and OS
DESTINY-Breast05	HER2-positive EBC	T-DXd	Post-neoadjuvant therapy	Improved 3-year iDFS
DESTINY-Breast11	HER2-positive EBC	T-DXd plus THP	Neoadjuvant therapy	Improved pCR rates
ASCENT-07	HR-positive/HER2-negative MBC	SG	First-line ET	Improved PFS



New adjuvant ET

Approximately 70% of all breast cancers are oestrogen receptor (ER)-positive, and up to a third of these patients experience disease recurrence despite adjuvant ET treatment. Treatment is often interrupted or discontinued due to safety or tolerability issues, highlighting the urgent need for more effective and tolerable therapies.

Dr. Sherene Loi: Another potentially practice-changing trial presented was the Phase III **lidERA⁹** study. This adjuvant study investigated an oral selective oestrogen receptor degrader (SERD), giredestrant, as an adjuvant ET for ER-positive HER2-negative EBC. Five years of upfront giredestrant was compared to standard-of-care therapy with AI. Premenopausal women received concurrent ovarian function suppression along with AI.

This global study was positive despite the largely endocrine-sensitive study cohort with nearly 40% being high risk, stage III patients. With an impressive hazard ratio of 0.7, giredestrant significantly improved RFS or DFS in these patients over a median follow-up of 33 months. The oral tablet of giredestrant is an advantage, and fewer discontinuations in the giredestrant arm makes it a significant future contender as favoured ET. This is hopefully the first of many trials offering a new type of ET for patients that is also better tolerated.

Dr. Zola Chia-Chen Li: In the MBC setting, patients with *oestrogen receptor 1 (ESR1)* mutation are known to benefit from SERD therapy. Hence, the recent **lidERA trial** result showing benefit also in EBC is really exciting. Given that *ESR1* mutations are acquired as a consequence of prior ET exposure, the **lidERA** results are surprising as the patient population had no prior exposure to therapy and are not expected to have acquired *ESR* mutations. Similar to the MonarchE trial, a prolonged follow-up may be necessary to determine the effect on long-term survival outcomes.

Dr. Han-Byoel Lee: The **lidERA study** is well designed and presents the first ET modality for the adjuvant setting in a long time after AI. Compared to tamoxifen or AI, oral SERD

are likely to be resistant to the presence of acquired mutations, hence potentially useful in overcoming therapy resistance.

Dr. Wendy Wing Lok Chan: Among the key updates focusing on EBC were the two studies highlighting the role of carboplatin in early-stage triple negative breast cancer (TNBC). In the first, pooled analysis¹⁰ of the **BrightNess, CALGB 40603**, and **GeparSixto** clinical trials, tested the impact of neoadjuvant carboplatin. Across the combined dataset, adjuvant chemotherapy with carboplatin, significantly improved pCR rates and event-free survival (EFS), though it did not improve OS. In patients with germline *BRCA* mutations, carboplatin improved EFS but not pCR or OS. Although many immune related gene signatures were prognostic, none were predictive of the benefit from carboplatin, underscoring the need for better biomarkers to guide carboplatin treatment in patients with stage II–III TNBC.

The **RJBC 1501 study**, a randomised phase III trial from China, evaluating adjuvant therapy with taxane with or without carboplatin in patients with node-positive or high-risk, gire-negative TNBC. In clinically node-positive patients who chose surgery followed by neoadjuvant chemotherapy, with a median follow-up for 4.5 years, the addition of carboplatin showed a significant improvement in DFS and OS. The 3-year DFS improved from 89.8% to 93.1%. However, carboplatin shows higher grade 3 to 4 toxicity, particularly in patients experiencing neutropenia and thrombocytopenia.

Dr. Sherene Loi: The SABCS featured many promising studies employing artificial intelligence tools for prognosis, pathology, and assessment of lymphocytic infiltration. There were also some great sessions on circulating liquid biopsies or circulating tumour DNA and their use in detecting minimal residual disease post-adjuvant therapy or for dynamic monitoring to escalate or de-escalate patients, allowing optimisation of not only the type of therapy but also the duration of therapy.

The exciting new findings from SABCS 2025 offered new surgical considerations and therapeutic options for improved management of EBC and MBC.

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