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2025 São Paulo Breast Symposium Guidelines: luminal breast cancer and axillary surgery

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ABSTRACT

Introduction: This study aims to disseminate evidence-based expert consensus statements derived from the 2025 International Symposium on Breast Diseases of Inland São Paulo (SIMIP), addressing four critical areas in breast cancer management: (1) initial treatment strategies for luminal breast cancer with imaging-positive (iN1) and clinically positive axilla (cN1); (2) therapeutic approaches for estrogen receptor–low (ER-low) breast cancer; (3) optimal duration of adjuvant endocrine therapy (ET) in luminal tumors; and (4) criteria for omitting axillary surgery in early breast cancer. **Methods:** The 2025 São Paulo Breast Diseases Symposium was a two-day event held in São Paulo, Brazil, involving 110 panelists, including 99 mastologists (90%) and 11 professionals from related fields (pathology, breast imaging, radiotherapy, and clinical oncology). Panelists were selected based on recognized expertise, defined by at least 10 years of clinical experience or significant academic contribution. Four priority thematic axes were identified through a pre-symposium survey of Brazilian and South American specialists. Each topic was introduced by a 10-minute evidence-based lecture followed by a 50-minute technical debate. Anonymous electronic voting was conducted via a secure online platform during hybrid sessions, with consensus defined as agreement by ≥75% of participants. **Results:** For patients with imaging-positive axilla (iN1), 52% of panelists preferred upfront surgery, without reaching consensus. In clinically positive axilla (cN1), treatment choice between upfront surgery and neoadjuvant chemotherapy varied according to age and menopausal status, supported by 57% of voters, also without consensus. A consensus of 84% was achieved to manage ER-low breast cancer similarly to triple-negative disease, using chemotherapy combined with endocrine therapy. Regarding endocrine therapy duration, consensus was reached for 7–10 years in high-risk Luminal B tumors (97%) and for 5 years in low-risk Luminal A tumors (95%). Omission of axillary surgery was supported by 85% of panelists in patients with tumors ≤2 cm, clinically node-negative disease (cT1N0), hormone receptor-positive/HER2-negative tumors, and negative axillary ultrasound findings. **Conclusions:** These expert consensus statements support personalized, multidisciplinary strategies to optimize oncologic outcomes while minimizing morbidity. Consensus favors extended endocrine therapy for high-risk luminal disease, shorter therapy for low-risk tumors, combined chemotherapy and endocrine therapy for ER-low disease, and omission of axillary surgery in carefully selected early breast cancer cases. Management of iN1 and cN1 disease should remain individualized based on clinical and biological factors, particularly in Brazil, where late-stage presentation remains frequent.

Keywords: breast neoplasms; luminal breast cancer; estrogen receptors; endocrine therapy; axillary surgery; neoadjuvant therapy.

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INTRODUCTION

The 2025 São Paulo Breast Diseases Symposium addressed key controversies in contemporary breast cancer management through a structured expert consensus process. Given the heterogeneity of breast cancer biology and the evolving role of systemic therapy, imaging, and surgical de-escalation, several clinical scenarios remain debated in daily practice, particularly within the Brazilian context.

This consensus document focuses on four priority areas identified as highly relevant for clinical decision-making:

1. Initial treatment strategies for luminal breast cancer with imaging-positive axilla (iN1) or clinically positive axilla (cN1);
2. Management of estrogen receptor–low (ER-low) breast cancer;
3. Optimal duration of adjuvant endocrine therapy in luminal tumors; and
4. Criteria for omitting axillary surgery in early-stage breast cancer.

The objective is to synthesize evidence, expert discussion, and voting results to support individualized, multidisciplinary care.

METHODS

The 2025 São Paulo Breast Diseases Symposium was a two-day event held in São Paulo, Brazil, with 110 panelists, including 99 mastologists (90%) and 11 professionals involved in the diagnosis and treatment of breast cancer (pathologists, breast imaging specialists, radiotherapists, and clinical oncologists) (10%). Panelists were selected based on expertise, with a minimum of 10 years of clinical experience or significant academic contributions (e.g., peer-reviewed publications or leadership in national breast cancer societies).

The event's multidisciplinary composition aimed to foster collaboration and address gaps in the literature relevant to Brazilian clinical practice. Four priority thematic axes were selected through a pre-symposium survey of Brazilian and South American breast cancer specialists, focusing on regional clinical challenges.

Each topic was introduced with a 10-minute evidence-based lecture, followed by a 50-minute technical debate among panelists, discussants, and speakers. Anonymous electronic voting was conducted by all 110 panelists via a secure online platform during hybrid (in-person and virtual) presentations, with consensus defined as ≥75% agreement. Results were tabulated descriptively and drafted as expert consensus statements to ensure transparency, reproducibility, and alignment with regional healthcare needs.

RESULTS

Initial treatment of luminal disease with imaging-positive axilla (in1) and clinically positive axilla (cn1)

INTRODUCTION

Initial management of luminal breast cancer with axillary involvement — either clinically positive (cN1) or detected by imaging (iN1) — requires a personalized approach balancing oncologic efficacy and morbidity minimization. The choice between upfront surgery or neoadjuvant systemic treatment (chemotherapy [NAC] or endocrine therapy [NET]) should consider factors such as tumor biology, nodal burden, patient age, menopausal status, and genomic profile. During SIMIP 2025, experts reviewed the latest evidence and voted on optimal approaches. Consensus was defined as ≥75% agreement among panelists.

Rationale and evidence

Luminal disease with iN1 (imaging-positive axilla)

Diagnostic evaluation

Axillary ultrasound (AxUS), combined with fine-needle aspiration or core needle biopsy, is essential to confirm nodal involvement. Physical examination alone has high false-negative (40–65%) and false-positive (17–53%) rates[1,2]. Histopathologic confirmation is critical to avoid overtreatment[3].

Therapeutic considerations

In patients with cT1–2 and iN1, upfront surgery with sentinel lymph node biopsy (SLNB) is preferred when breast-conserving surgery (BCS) is feasible. Studies show that 33–74% of iN1 cases have ≤2 positive lymph nodes on SLNB, allowing for avoidance of axillary lymph node dissection (ALND)[4,5]. NAC or NET can achieve breast and axillary downstaging, with axillary pathologic complete response (pCR) rates ranging from 13% (Luminal A-like) to 35% (Luminal B-like)[6]. The RxPONDER and MINDACT trials demonstrate that in postmenopausal women with 1–3 positive lymph nodes and low genomic risk (recurrence score [RS] ≤25 or low-risk MammaPrint signature), the benefit of adjuvant chemotherapy is marginal (<2% gain in disease-free survival)[7,8].

Luminal disease with cN1 (clinically positive axilla)

Clinical evaluation

The presence of clinically palpable lymph nodes (cN1) suggests a higher tumor burden. However, the accuracy of physical examination alone is limited (false-negative 40–65%; false-positive 17–53%)[1,2]. AxUS with biopsy confirms nodal status with greater precision[3].

Therapeutic considerations

For cT3-4 and cN1 or extensive iN1, NAC is standard, as it enables BCS and reduces the extent of axillary surgery[3]. In cT1-2 cN1, the choice between upfront surgery and NAC should consider genomic risk and patient clinical profile. Postmenopausal women with low RS (≤25) can be managed with upfront surgery if BCS is feasible[7,8]. Premenopausal women with cT1-2 cN1 benefit more from NAC, although axillary pCR rates remain modest (13–35%)[6-9]. In cases achieving axillary pCR after NAC (ypN0), SLNB is sufficient[10-18]

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However, residual disease (ypN+) still warrants ALND, pending results from ongoing trials[3,10-18]. In patients >50 years or postmenopausal, with low-risk luminal tumors and when BCS is not feasible, NET may be considered[3].

Voting results

During SIMIP 2025, all 110 panelists voted anonymously on the best initial treatment strategies:

1. cN1:
   - Upfront surgery: 19%
   - NAC: 24%
   - Individualized decision (age/menopause): 57%
2. iN1:
   - Upfront surgery: 52%
   - NAC: 10%
   - Individualized decision (age/menopause): 38%

Practical recommendations

Criteria for iN1:

- Initial surgery preferred for cT1–2 iN1 with feasible BCS.
- NAC/NET considered for cT3–4 iN1 or non-feasible BCS.

Criteria for cN1:

- Premenopausal: recommend NAC for cT1–2 cN1.
- Postmenopausal: considered upfront surgery if RS ≤25.
- NAC: standard for cT3–4 cN1.

Estrogen receptor-low breast cancer

INTRODUCTION

Breast cancer with low estrogen receptor expression (ER-low), defined as 1–10% positivity, represents a biologically heterogeneous subtype sharing features with triple-negative breast cancer, while retaining partial sensitivity to endocrine therapy.

Rationale and evidence

Definition and biological profile

Per the American Society of Clinical Oncology and College of American Pathologists (ASCO/CAP) 2020 update, ER-low is defined as 1–10% ER positivity, distinguishing it from ER-negative (<1%) and classic ER-positive (>10%) tumors. Concerns exist regarding the reproducibility of ER expression in this range and its therapeutic implications, with retrospective data showing variability and limited prospective validation[18]. These tumors are typically high-grade (grade 3), with elevated Ki-67 marker (>20%) and low progesterone receptor expression (PgR) <1%[19-21]. Molecular studies show a predominant basal-like profile, similar to TNBC[21-24].

Treatment response and prognosis

ER-low tumors exhibit good sensitivity to chemotherapy, with pCR rates comparable to TNBC[23]. However, their response to ET is limited, though not absent. A study presented at ASCO 2024 showed that omitting adjuvant ET led to worse overall survival (hazard ratio [HR] 1.25; 95% confidence interval [CI] 1.05–1.48; p=0.01)[25]. Adding immunotherapy (pembrolizumab) to NAC has shown benefit in high-risk ER-low tumors, similar to TNBC[26]. The lack of prospective validation for ER-low treatment strategies underscores the need for further research.

Molecular perspective and current guidelines

Reduced ER1 expression and increased TP53 mutation frequency limit ET efficacy[21]. Genomic signatures like Oncotype DX are not fully validated for ER-low but may aid decision-making in low clinical risk cases[23]. The National Comprehensive Cancer Network (NCCN) version 3.2025 guidelines classify ER-low as ER-positive but recommend an individualized approach, acknowledging its similarity to TNBC in aggressiveness[3]. The European Society for Medical Oncology (ESMO) 2024 suggests chemotherapy based on aggressive tumor biology, combined with maintenance of adjuvant ET in cases with residual ER positivity[27].

Voting results

- Treat as TNBC, maintaining ET: 84%
- Treat as TNBC, omitting ET: 11%
- Do not treat as TNBC: 5%

Practical recommendations

Based on voting and literature analysis, the following was recommended:

- High-risk clinical and/or pathologic ER-low:
  - Treat as TNBC, using intensive NAC (with or without immunotherapy, as eligible).
  - Maintain adjuvant ET, even with ER-low (1–10%).
- Low-risk ER-low (small tumors, grade 1, low Ki-67):
  - Evaluate individually based on age, comorbidities, and patient preferences.
  - ET may be maintained, despite limited evidence of benefit in highly indolent subgroups.

Duration of adjuvant endocrine therapy in luminal breast cancer

INTRODUCTION

Adjuvant ET is the cornerstone of treatment for hormone receptor-positive (HR+) luminal breast cancer, significantly reducing the risk of local, regional, and distant recurrence. However, the optimal duration of ET — 5 years versus extension to 7–10 years — remains a critical question, determined by the risk of late recurrence, integrating clinical variables (age, stage, histologic grade, nodal status) and genomic factors (molecular signatures and risk scores). Adherence to long-term ET is often suboptimal in real-world settings, necessitating monitoring strategies and shared

decision-making to optimize outcomes. During SIMIP 2025, experts deliberated on two distinct clinical scenarios (high and low risk) and established approaches based on ≥75% panelist consensus.

Rationale and evidence

Adjuvant ET has evolved over decades. Initially limited to 2 years of tamoxifen, it was extended to 5 years by the mid-1990s. The introduction of aromatase inhibitors in the 2000s expanded strategies for postmenopausal women[28]. The MA.17 trial was pivotal, demonstrating that extending ET with letrozole after 5 years of tamoxifen significantly improves disease-free survival[28]. A recent meta-analysis (n=29,497) confirmed that extended ET (>5 years) reduces recurrence (HR 0.81; 95%CI 0.72–0.92), improves overall survival (HR 0.88; 95%CI 0.82–0.95), and reduces distant metastases (HR 0.82; 95%CI 0.69–0.97), particularly in node-positive patients[29]. The risk of late recurrence depends heavily on stage and tumor biology. The Early Breast Cancer Clinical Trialists' Collaborative Group (EBCTCG) reported an annual recurrence risk after 5 years of ET of 0.50–0.80% for T1a/bN0 and 0.80–1.20% for T1cN0[30]. Tools like the Clinical Treatment Score at 5 years (CTS5) and molecular tests like the Breast Cancer Index (BCI) aid in estimating late recurrence risk and deciding on extended ET[31,32]. Genomic signatures such as Oncotype DX, EndoPredict, and MammaPrint help identify ultralow-risk subgroups where ET extension can be safely avoided[33]. Prolonged ET adverse effects (osteoporosis, thromboembolic events, vasomotor symptoms, and arthralgias) must be weighed, especially in elderly patients with comorbidities. Adherence challenges can be addressed through patient education, regular follow-up, and shared decision-making to balance benefits and risks.

Voting results

- High-risk: ET 7–10 years (97%).
- Low-risk: ET 5 years (95%).

Practical recommendations

High-risk patients:

- Indication: ET for 7–10 years.
- Criteria: Age ≤50 years, pN1 or higher, grade 3, Ki-67 >20%, Luminal B subtype, or high-risk genomic signature[3,29].
- Adherence: Monitor adherence through regular follow-up and patient education to address side effects and improve compliance.
- Low-risk patients:
- Indication: ET for 5 years.
- Criteria: Postmenopausal, pT1a/bN0 tumors, grade 1 or 2, ER+/PR+, HER2-, Ki-67 <10%, no lymphovascular invasion. Includes special histologic subtypes (papillary, mucinous, tubular)[3,30].
- Adherence: Use shared decision-making to discuss benefits and risks, particularly in elderly patients with comorbidities.

A summary of the panel-based recommendations for endocrine therapy duration is presented in Table 1.

Omission of axillary surgery in early breast cancer

INTRODUCTION

Omission of axillary surgery — both SLNB and ALND — has emerged as a safe strategy in well-selected early breast cancer cases, aiming to reduce morbidity without compromising oncologic control. Complications avoided include lymphedema, neuropathic pain, functional limitation, and infectious events. Advances in imaging, such as AxUS, combined with the efficacy of systemic therapy and radiotherapy (RT), enable surgical de-escalation in low-risk patients. During SIMIP 2025, experts evaluated criteria for omitting axillary surgery based on the latest evidence, emphasizing its applicability in routine clinical practice while noting caution in Brazil due to high rates of late-stage diagnosis.

Rationale and evidence

Historical evolution of axillary management

In the 1970s–1980s, ALND was standard even in clinically node-negative (cN0) patients, as shown in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-04 trial[31]. From 2000, SLNB replaced ALND in cN0, significantly reducing morbidity, as demonstrated in NSABP B-32[31]. Subsequent trials like the American College of Surgeons Oncology Group (ACOSOG) Z0011, After Mapping of the Axilla: Radiotherapy Or Surgery (AMAROS), and Optimal Treatment Of the Axilla - Surgery Or Radiotherapy (OTOASOR) showed that patients with 1–2 positive sentinel nodes undergoing BCS and adjuvant RT can forgo ALND without loss of locoregional control[31]. Recent studies, such as Sentinel Node vs. Observation After Axillary Ultrasound in Breast Cancer (SOUND (2012–2021) and Intergroup Sentinel Mamma (INSEMA) (2015–2024), validated omitting even SLNB in tumor ≤2 cm, no lymph node involvement (cT1N0) patients with negative AxUS, ushering in a new era of axillary

Table 1. Endocrine therapy duration recommendations.

Risk level	Patient profile	ET duration (years)	Consensus (%)	Adherence atrategies
High	Age ≤50, pN1+, grade 3, Luminal B	7–10	97	Regular follow-up, patient education
Low	Postmenopausal, pT1a/bN0, grade 1–2, Luminal A	5	95	Shared decision-making, monitor comorbidities

ET: endocrine therapy.

de-escalation[34-39]. ASCO 2025 endorses this approach in patients ≥50 years, hormone receptor-positive/human epidermal growth factor receptor-type 2-negative (HR+/HER2-), tumors ≤2 cm, negative AxUS, and candidates for BCS[40]. In Brazil, where late-stage diagnoses are common, careful patient selection is critical to ensure safety[41].

Key clinical trials

- ACOSOG Z0011: In 856 cT1–2N0 patients with up to 2 positive sentinel nodes, no significant difference in axillary recurrence was observed between groups with and without ALND after 9 years (0.5% vs. 1.1%). ALND identified additional positive nodes in 27.3% of cases, with no survival impact[31].
- AMAROS and OTOASOR: Demonstrated equivalence between SLNB with RT and ALND in patients with up to 2 positive nodes (axillary recurrence 1–1.8% vs. 0.4–2%), despite 32.8–38.5% additional node involvement in ALND[31].
- SOUND: In 1,405 cT1N0 patients (negative AxUS), distant disease-free survival was similar between groups with or without SLNB after 5.7 years. SLNB showed 13% node positivity, with <1% axillary recurrence[35].
- INSEMA: In 5,504 cT1–2N0 patients, invasive disease-free survival was non-inferior without SLNB after 62 months. Lymphedema was significantly lower (1.8% vs. 5.7%), and 5-year overall survival was comparable (96.6% vs. 95.6%)[36].

Imaging evaluation and patient selection

AxUS is the standard tool for confirming nodal status in cN0/iN0[37]. Absence of suspicious disease on imaging correlates with low SLNB positivity (13–15%)[35,36]. Eligibility criteria for omitting axillary surgery include:

- Women ≥60 years, HR+/HER2-, cT1N0 (≤2 cm), grade 1–2, Ki-67 ≤20%, no lymphovascular invasion, indicated for BCS + RT[35,36,39].
- Patients ≥70 years, cT1N0, HR+, treated with endocrine therapy alone are also eligible, as shown in Cancer and Leukemia Group B (CALGB 9343[3], HER2+ and triple-negative tumors require caution due to aggressive biology and limited robust data[36,39]. In Brazil, high rates of late-stage diagnosis necessitate stringent adherence to these criteria.

Voting results

- Omission in selected luminal tumors: 85%.
- HER2+/TNBC: 5%.
- Maintain SLNB in all: 10%.

Practical recommendations

- Criteria for omitting axillary surgery:
  - Omit SLNB and ALND in routine clinical practice for patients:
- Postmenopausal, ≥60 years, cT1N0 (tumor ≤2 cm), HR+/HER2-, grade 1–2, Ki-67 ≤20%, negative AxUS, candidates for BCS with RT (whole-breast irradiation or partial breast irradiation)[35,36,39].
- ≥70 years, cT1N0, HR+, treated with ET alone[3,39].
  - Caution in Brazil: Due to high rates of late-stage diagnosis, strict adherence to eligibility criteria is essential to ensure oncologic safety.

DISCUSSION

Across all four thematic axes, panel opinions largely aligned with contemporary evidence but frequently did not reach the predefined ≥75% consensus threshold. These findings highlight areas of ongoing uncertainty, particularly regarding axillary management, ER-low tumors, endocrine therapy duration, and treatment de-escalation strategies. The Brazilian context, characterized by heterogeneous access to diagnostic resources and higher rates of advanced disease at presentation, reinforces the importance of cautious patient selection and multidisciplinary decision-making. To facilitate clinical interpretation of the panel discussions on axillary management, a pragmatic decision algorithm derived from the voting results is presented in Table 2.

CONCLUSIONS

This expert consensus from the 2025 São Paulo Breast Diseases Symposium provides practical, evidence-informed recommendations for complex clinical scenarios in breast cancer management. The statements reflect majority expert opinion and are intended to support individualized clinical reasoning rather than define

Table 2. Decision algorithm: omission of axillary surgery.

Patient criteria	AxUS result	Recommendation	Consensus (%)
≥60 years, cT1N0, HR+/HER2-, grade 1–2, Ki-67 ≤20%, BCS + RT	Negative	Omit SLNB/ALND	85
≥70 years, cT1N0, HR+, ET alone	Negative	Omit SLNB/ALND	85
HER2+ or TNBC, cT1N0	Negative	Maintain SLNB	5

AxUS: axillary ultrasound; cT1N0: tumor ≤2cm no lymph node involvement; HR+/HER2-: hormone receptor-positive / human epidermal growth factor receptor-type 2-negative: BCS: breast-conserving surgery; RT: radiotherapy; ET: endocrine therapy; TNBC: triple-negative breast cancer; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection.

mandatory treatment protocols. Further prospective studies are required to refine and validate these strategies.

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AUTHORS' CONTRIBUTION

ECP: Conceptualization, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. FB: Conceptualization, methodology, investigation, writing – review & editing. MM: Conceptualization, Methodology, Writing – review & editing. JTAN: Methodology, Investigation, Project administration, Writing – review & editing. GMT: Methodology, Resources, Writing – review & editing. FB: Methodology, Investigation, Resources, Writing – review & editing. BBG: Data curation, Validation, Visualization, Writing – review & editing. DAB: Methodology, Supervision, Validation, Writing – review & editing. FZ: Formal analysis, Investigation, Writing – review & editing. MA: Methodology, Resources, Investigation, Writing – review & editing. DLG: Formal analysis, Data curation, Writing – original draft. SEB: Methodology, Supervision, Validation, Writing – review & editing. ATH: Supervision, Validation, Writing – review & editing.

REFERENCES

1. Navarro DTSM, Aguiar MG, Galvão MFO, Germano TCO, Lajus TBP, Oliveira TCA. Clinical andhistopathological axillary assessment. Mastology. 2018;28(1):7-10. https://doi.org/10.29289/Z2594539420180000255
2. Specht MC, Fey JV, Borgen PI, Hiram 3rd SC. Is the clinically positive axilla in breast cancer really a contraindication to sentinel lymph node biopsy? J Am Coll Surg. 2005;200(1):10-4. https://doi.org/10.1016/j.jamcollsurg.2004.09.010
3. Gradishar WJ, Moran MS, Abraham J, Abramson V, Aft R, Agnese D, et al. NCCN Guidelines® insights: breast cancer, version 5.2025. JNCCN. 2025;23(11):426-36. https://doi.org/10.6004/jnccn.2025.0053
4. Matar-Ujvary R, Sevilimedu V, Morrow M. Are clinically node-negative patients with a positive preoperative axillary lymph node biopsy appropriate candidates for sentinel lymph node biopsy? Ann Surg Oncol. 2025;32(1):92-7. https://doi.org/10.1245/s10434-024-16321-6
5. Liberale V, Rosso R, Arisio R, D'Alonzo M, Villasco A, Fuso L, et al. Axillary dissection in patients with preoperative positive nodal cytology: Genuine need or overtreatment? Breast J. 2020;26(2):168-75. https://doi.org/10.1111/tbj.13479
6. Samiei S, Simons JM, Engelen SME, Beets-Tan RGH, Classe JM, Smidt ML, et al. Axillary pathologic complete response after neoadjuvant systemic therapy by breast

cancer subtype in patients with initially clinically node-positive disease: a systematic review and meta-analysis. JAMA Surg. 2021;156(6):e210891. https://doi.org/10.1001/jamasurg.2021.0891

7. Loibl S, André F, Bachelot T, Barrios CH, Bergh J, Burstein HJ, et al. Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2024;35(2):159-82. https://doi.org/10.1016/j.annonc.2023.11.016
8. Kalinsky K, Barlow WE, Gralow JR, Meric-Bernstam F, Albain KS, Hayes DF, et al. 21-gene assay to inform chemotherapy benefit in node-positive breast cancer. N Engl J Med. 2021;385(25):2336-47. https://doi.org/10.1056/NEJMoa2108873
9. Cardoso F, van't Veer L, Bogaerts J, Slaets L, Viale G, Delaloge S, et al. 70-gene signature as an aid to treatment decisions in early-stage breast cancer. N Engl J Med. 2016;375(8):717-29. https://doi.org/10.1056/NEJMoa1602253
10. Ordonez L, Tornillo G, Kendrick H, Hay T, Smalley MJ. NOTCH and AKT signalling interact to drive mammary tumour heterogeneity. Cancers (Basel). 2023;15(17):4324. https://doi.org/10.3390/cancers15174324
11. Almahariq MF, Levitin R, Quinn TJ, Chen PY, Dekhne N, Kiran S, et al. Omission of axillary lymph node dissection is associated with inferior survival in breast cancer patients with residual n1 nodal disease following neoadjuvant chemotherapy. Ann Surg Oncol. 2021;28(2):930-40. https://doi.org/10.1245/s10434-020-08928-2
12. Albuainain RY, Althawadi R, Eid R, Abdulla HA. Oncological outcomes of omitting axillary surgery in early breast cancer: a systematic review and meta-analysis. ***J Surg Oncol.*** 2026;131(2):130-40. https://doi.org/10.1002/jso.70145
13. Limberg JN, Jones T, Thomas SM, Ntowe KW, Dalton JC, van den Bruele AB, et al. Omission of axillary lymph node dissection in patients with residual nodal disease after neoadjuvant chemotherapy. Ann Surg Oncol. 2024;31(13):8813-20. https://doi,org/10.1245/s10434-024-16143-6
14. Khan AJ, Montagna G. Contextual framework for understanding treatment de-escalation in patients with breast cancer. JCO Oncol Pract. 2025;21(3):278-80. https://doi.org/10.1200/OP-24-00870
15. Skarping I, Bendahl PO, Szulkin R, Alkner S, Andersson Y, Bergkvist L, et al. Prediction of high nodal burden in patients with sentinel node-positive luminal ERBB2-negative breast cancer. JAMA Surg. 2024;159(12):1393-403. https://doi.org/10.1001/jamasurg.2024.3944
16. Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, et al. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the acosog z0011 (alliance) randomized clinical trial. JAMA. 2017;318(9):918-26. https://doi.org/10.1001/jama.2017.11470
17. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA. 2011;305(6):569-75. https://doi.org/10.1001/jama.2011.90
18. Allison KH, Hammond MEH, Dowsett M, McKernin SE, Carey LA, Fitzgibbons PL, et al. Estrogen and progesterone receptor testing in breast cancer: ASCO/CAP guideline update. J Clin Oncol. 2020;38(12):1346-66. https://doi.org/10.1200/JCO.19.02309
19. Perou CM, Sørlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature. 2000;406(6797):747-52. https://doi.org/10.1038/35021093
20. Yi M, Huo L, Koenig KB, Mittendorf EA, Meric-Bernstam F, Kuerer HM, et al. Which threshold for ER positivity? a retrospective study based on 9639 patients. Ann Oncol. 2014;25(5):1004-11. https://doi.org/10.1093/annonc/mdu053
21. Fusco N, Viale G. The "lows": update on ER-low and HER2-low breast cancer. Breast. 2024;78:103831. https://doi.org/10.1016/j.breast.2024.103831
22. Poon IK, Tsang JY, Li J, Chan SK, Shea KH, Tse GM. The significance of highlighting the oestrogen receptor low category in breast cancer. Br J Cancer. 2020;123(8):1223-7. https://doi.org/10.1038/s41416-020-1009-1
23. Villegas SL, Nekljudova V, Pfarr N, Engel J, Untch M, Schrodi S, et al. Therapy response and prognosis of patients with early breast cancer with low positivity for hormone receptors - An analysis of 2765 patients from neoadjuvant clinical trials. Eur J Cancer. 2021:148:159-70. https://doi.org/10.1016/j.ejca.2021.02.020
24. Choong GM, Hoskin TL, Boughey JC, Ingle JN, Goetz MP. Endocrine therapy omission in estrogen receptor-low (1%-10%) early-stage breast cancer. ***J Clin Oncol.*** 2025;43(16):1875-85. https://doi.org/10.1200/JCO-24-02263
25. Choong GM, Nanda R, Carey LA. Adjuvant endocrine therapy improves survival in ER-low tumors. In: ASCO Annual Meeting Abstracts. Chicago; 2024.
26. Schmid P, Cortes J, Pusztai L, McArthur H, Kümmel S, Bergh J, et al. Pembrolizumab for Early Triple-Negative Breast Cancer. N Engl J Med. 2020;382(9):810-21. https://doi.org/10.1056/NEJMoa1910549
27. Loibl S, André F, Bachelot T, Barrios CH, Bergh J, Burstein HJ, et al. Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2024;35(2):159-82. https://doi.org/10.1016/j.annonc.2023.11.016
28. Goss PE. Letrozole in the extended adjuvant setting: MA.17. Breast Cancer Res Treat. 2007;105 Suppl 1(Suppl 1):45-53. https://doi.org/10.1007/s10549-007-9698-1
29. Xie M, Zhong Y, Yang Y, Shen F, Nie Y. Extended adjuvant endocrine therapy for women with hormone receptor-positive early breast cancer: a meta-analysis with trial sequential analysis of randomized controlled trials. ***Front Oncol.*** 2022;12:1015690. https://doi.org/10.3389/fonc.2022.1039320
30. Francis PA, Pagani O, Fleming GF, Walley BA, Colleoni M, Láng I, et al. Tailoring adjuvant endocrine therapy in premenopausal breast cancer. N Engl J Med. 2018;379(2):122-37. https://doi.org/10.1056/NEJMoa1803164
31. Pan H, Gray R, Braybrooke J, Davies C, Taylor C, McGale P, et al. 20-year risks of breast-cancer recurrence after stopping endocrine therapy at 5 years. N Engl J Med. 2017;377:1836-46. https://doi.org/10.1056/NEJMoa1701830
32. Hughes KS, Schnaper LA, Bellon JR, Cirrincione CT, Berry DA, McCormick B, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. J Clin Oncol. 2013;31(19):2382-7. https://doi.org/10.1200/JCO.2012.45.2615
33. Richman J, Ring A, Dowsett M, Sestak I· Clinical validity of clinical treatment score 5 (CTS5) for estimating risk of late recurrence in unselected, non-trial patients with early oestrogen receptor-positive breast cancer. Breast Cancer Res Treat. 2021186(1):115-23. https://doi.org/10.1007/s10549-020-06013-6
34. Liefers GJ, van de Velde CJH, Rutgers EJT. Predicting late recurrence using BCI and CTS5. In: San Antonio Breast Cancer Symposium; 2022. Abstract GS5-10.

35. Howell A, Cuzick J, Baum M, Buzdar A, Dowsett M, Forbes JF, et al. Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. Lancet. 2005;365(9453):60-2. https://doi.org/10.1016/S0140-6736(04)17666-6

36. Gentilini OD, Botteri E, Sangalli C, Galimberti V, Porpiglia M, Agresti R, et al. Sentinel lymph node biopsy vs no axillary surgery in patients with small breast cancer and negative results on ultrasonography of axillary lymph nodes: the SOUND randomized clinical trial. JAMA Oncol. 2023;9(11):1557-64. https://doi.org/10.1001/jamaoncol.2023.3759

37. Li X, Wang L, Wang Y, Ma L, Zheng R, Ding J, et al. Omission of sentinel lymph node biopsy in patients with clinically axillary lymph node-negative early breast cancer (OMSLNB): protocol for a prospective, non-inferiority, single-arm, phase II clinical trial in China. BMJ Open. 2024;14(9):e087700. https://doi.org/10.1136/bmjopen-2024-087700

38. Pilewskie M, Jochelson M, Gooch JC, Patil S, Stempel M, Morrow M. Is preoperative axillary imaging beneficial in identifying clinically node-negative patients requiring axillary lymph node dissection? J Am Coll Surg. 2016;222(2):138-45. https://doi.org/10.1016/j.jamcollsurg.2015.11.013

39. Giannakou A, Kantor O, Park KU, Waks A, Punglia R, Dominici L, et al. Real-world implications of the SOUND trial. Ann Surg Oncol. 2024;31(13):8776-85. https://doi.org/10.1245/s10434-024-16354-x

40. Park KU, Somerfield MR, Anne N, Brackstone M, Conlin AK, Couto HL, et al. Sentinel lymph node biopsy in early-stage breast cancer: ASCO Guideline update. J Clin Oncol. 2025;43(14):1720-41. https://doi.org/10.1200/JCO-25-00099

41. Almeida RJ, Luizaga CTM, Eluf-Neto J, Nunes HRC, Pessoa EC, Murta-Nascimento C. Impact of educational level and travel burden on breast cancer stage at diagnosis in the state of São Paulo, Brazil. Sci Rep. 2022;12(1):8357. https://doi.org/10.1038/s41598-022-12487-9