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SPECIAL ARTICLE

Understanding breast cancer complexity to improve patient outcomes: The St Gallen International Consensus Conference for the Primary Therapy of Individuals with Early Breast Cancer 2023

G. Curigliano[1,2*†], H. J. Burstein[3,4*†], M. Gnant[5,6], S. Loibl[7,8], D. Cameron[9], M. M. Regan[10], C. Denkert[11], P. Poortmans[12,13], W. P. Weber[14,15] & B. Thürlimann[16,17], St Gallen Consensus Conference Panelists 2023

[1]Division of New Drugs and Early Drug Development for Innovative Therapies, European Institute of Oncology, IRCCS, Milan; [2]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy; [3]Medical Oncology, Dana-Farber Cancer Institute, Boston; [4]Harvard Medical School, Boston, USA; [5]Comprehensive Cancer Center, Medical University of Vienna, Vienna; [6]Austrian Breast and Colorectal Cancer Study Group, Vienna, Austria; [7]Center for Hematology and Oncology Bethanien, Frankfurt; [8]German Breast Group, Neu-Isenburg, Germany; [9]Edinburgh Cancer Research Centre, University of Edinburgh and NHS Lothian, Edinburgh, UK; [10]International Breast Cancer Study Group Statistical Center, Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA; [11]Institut für Pathologie, Philipps-Universität Marburg und Universitätsklinikum Marburg, Marburg, Germany; [12]Department of Radiation Oncology, Iridium Netwerk, Wilrijk-Antwerp; [13]University of Antwerp, Faculty of Medicine and Health Sciences, Wilrijk-Antwerp, Belgium; [14]Department of Surgery, University Hospital Basel, Basel, Switzerland; [15]Faculty of Medicine, University of Basel, Basel, Switzerland; [16]SwissBreastCare, Bethanienspital, Zürich, Switzerland; [17]SONK Foundation, St. Gallen, Switzerland

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The 18th St Gallen International Breast Cancer Conference held in March 2023, in Vienna, Austria, assessed significant new findings for local and systemic therapies for early breast cancer with a focus on the evaluation of multimodal treatment options. The emergence of more effective, innovative agents in both the preoperative (primary or neoadjuvant) and post-operative (adjuvant) settings has underscored the pivotal role of a multidisciplinary approach in treatment decision making, particularly when selecting systemic therapy for an individual patient. The importance of multidisciplinary discussions regarding the clinical benefits of interventions was explicitly emphasized by the consensus panel as an integral part of developing an optimal treatment plan with the 'right' degree of intensity and duration. The panelists focused on controversies surrounding the management of common ductal/no special type and lobular breast cancer histology, which account for the vast majority of breast tumors. The expert opinion of the panelists was based on interpretations of available data, as well as current practices in their professional environments, personal and socioeconomic factors affecting patients, and cognizant of varying reimbursement and accessibility constraints around the world. The panelists strongly advocated patient participation in well-designed clinical studies whenever feasible. With these considerations in mind, the St Gallen Consensus Conference aims to offer guidance to clinicians regarding appropriate treatments for early-stage breast cancer and assist in balancing the realistic trade-offs between treatment benefit and toxicity, enabling patients and clinicians to make well-informed choices through a shared decision-making process.

Key words: early breast cancer, triple-negative breast cancer, HER2-positive breast cancer, ER-positive breast cancer surgery, radiation therapy

INTRODUCTION

Despite the vast literature on the biology and clinical management of early-stage breast cancer, not all clinical scenarios can be directly guided by data from randomized trials, or definitive treatment studies, owing to the moderate benefits of some treatment approaches, the variations in tumor biology and stage, and thus risk of recurrence, the side effects of therapy, and varying personal preferences. For those reasons, the approach to breast cancer is increasingly personalized, taking into account specific factors such as: clinical stage; biological features of the tumor including tumor subtype, and within subtype, additional

*Correspondence to: Prof. Giuseppe Curigliano, Istituto Europeo di Oncologia, IRCCS, University of Milano, Via Ripamonti 435, 20141 Milan, Italy. Tel.: +39 02 57489439

E-mail: giuseppe.curigliano@ieo.it (G. Curigliano).

*Prof. Harold J. Burstein, Dana-Farber Cancer Institute, 450 Brookline Avenue, Boston, MA 02215, USA. Tel.: +1 617 632 3800

E-mail: hal_burstein@dfci.harvard.edu (H. J. Burstein).

†Co-first authors.

pathological and genomic risk markers; patient age, health, and personal preferences; efficacy of systemic and local treatments; and in some instances, tumor response to preoperative therapy.

Breast cancer is the most frequently diagnosed cancer worldwide and the leading cause of cancer-related death among patients.[1,2] Recent data on breast cancer management reflect an improved understanding of the biology and treatment of early- and advanced-stage disease (Table 1). Significant disparities persist among and within nations for screening, high-quality treatment, and supportive care for breast cancer. Many essential services remain inaccessible, unaffordable, or beyond the capacity of local health care systems. As an international consensus panel, the St Gallen faculty recognizes the disparities in resources for detecting and treating early breast cancer and is committed to reducing these inequities. However, it should be noted that panelist recommendations are often influenced by the availability of specific techniques, imaging modalities, molecular diagnostic approaches, or treatment options, which can vary between countries or even within nations.[3]

The panel's objective was to provide clinical guidance on common situations encountered in early breast cancer, including detailed recommendations on local-regional and systemic therapy, building upon previous recommendations. This year, there was a particular focus on refining treatment thresholds, the utilization of genomic signatures, evolving practices in radiation oncology, the use of ovarian suppression, and decision making regarding surgery and systemic treatment following neoadjuvant therapy including immunotherapy. Additionally, for the first time, the panel addressed challenges in managing oligometastatic breast cancer, as in some situations, these patients are treated with a 'curative' intent. The integration of molecular diagnostics in the early setting was critically discussed. This year, the panel dedicated more discussion to breast cancer survivorship, acknowledging the millions of patients and men with personal histories of breast cancer, who are living with the socioeconomic, psychological, and physical side effects of their cancer treatments. The guidance provided is applicable to the 'majority' of patients with early breast cancer who are in reasonably good health and do not have medical, psychological, or social conditions that would preclude standard treatment. The consensus addresses common ductal/no special type and lobular histologies in generally healthy patients. However, special considerations may be necessary for breast cancer histological subtypes with unique characteristics, as well as for individual patients with significant health concerns. The panelists' votes reflect expert opinions they would recommend in clinical practice.

GENETIC TESTING AND MANAGEMENT OF PATIENTS WITH HEREDITARY BREAST CANCER AND SYNDROMES

Nearly 10% of breast cancers have a familial risk factor. Around 6% of breast cancer patients possess pathogenic variants (PVs) in hereditary breast cancer genes. Of these, roughly half (~3%) are attributed to high-risk genes such as *BRCA1*, *BRCA2*, and other genes like *PALB2*. The other half (~3%) are associated with moderate-risk genes like *ATM* and *CHEK2*.[4-6] The remaining 4% consists of unknown factors that may stem from genetic, environmental, or combined influences.[4]

The panel was divided on whether all patients with newly diagnosed breast cancer should undergo genetic testing; there was no consensus for universal germline testing for all patients younger than age 70. In general, Panelists favored genetic testing for younger patients, those with a family history of breast cancer or cancers linked to breast cancer through known genetic syndromes, or in those in whom genetic test results would affect treatment such as patients considering prophylactic ipsilateral or contralateral mastectomy, or those potentially eligible for poly (ADP-ribose) polymerase (PARP) inhibitor therapy. Patients who develop a second primary cancer in either the ipsilateral or contralateral breast should also be offered genetic testing.[7] In some instances, testing for moderate-penetrance genes may be offered to inform personal and family cancer risk. If a gene panel testing is chosen, the majority (67%) voted that the preferred panel should routinely include: *BRCA1, BRCA2, ATM, BARD1, BRIP1, CDH1, CHEK2, NBN, PALB2, PTEN, STK11, RAD51C* and *RAD51D*, and *TP53*.[7] Variants of unknown significance should not impact treatment decisions, and patients with such variants should be monitored for any reclassification of their variants.

The panel addressed the management of early-stage breast cancers associated with hereditary *BRCA1* or *BRCA2* PV. Elective bilateral risk-reducing mastectomy was favored by panelists for pre- and postmenopausal *BRCA1, BRCA2* PV carriers, and premenopausal *PALB2* PV carriers, but favored intensive screening over prophylactic surgery for postmenopausal *PALB2*, or for *ATM* or *CHEK2* PV carriers. The panelists (over 93%) strongly endorsed the use of 1 year of adjuvant olaparib for patients with stage II or III, human epidermal growth factor receptor 2 (HER2)-negative cancers with higher-risk tumors as outlined in the OlympiA study,[8] regardless of their estrogen receptor (ER) status, neoadjuvant or adjuvant chemotherapy (ChT) or prior treatment with platinum-based ChT. Consequently, the panel nearly unanimously (95%) recommended genetic testing for patients who are potential candidates for olaparib-based therapy. Despite evidence for activity in metastatic breast cancer patients with *PALB2* mutations,[9,10] there was no consensus in favoring the use of olaparib in patients with *PALB2* germinal PVs.

PATHOLOGY AND GENOMIC ASSAYS

The optimal ER threshold for initiating endocrine therapy (ET) remains controversial, with some studies indicating a less favorable prognosis for tumors with 1%-9% ER expression, and a non-luminal biology warranting ChT.[11,12] Previously, the panel had recommended that adjuvant treatment includes ET for tumors with >1% ER expression, an opinion panelists endorsed again (Figure 1), with at least 50% favoring initiation of ET for tumors with an ER of 1%. For tumors with 9% ER expression, nearly 80% of the panel

Table 1. New practice-changing studies in early breast cancer since St Gallen 2021

Area	Discovery/innovation	Reference
Genetics and hereditary breast cancer	Patients diagnosed with breast cancer and known to carry germline PVs in *BRCA1, BRCA2, CHEK2,* or *PALB2* are at substantially increased risk of contralateral breast cancer	83
	PVs in *BRCA1* and *BRCA2* are associated with a high risk of breast cancer, while PVs in *PALB2* are associated with a moderate risk	5
	The OlympiA trial demonstrates that adjuvant therapy with olaparib increases overall survival in patients with breast cancer harboring germline *BRCA1/2* mutation	84
Supportive care	After 8 years, adjuvant denosumab during adjuvant therapy with AI confirmed to markedly reduce treatment-induced clinical fractures	85
	Q-122 is an effective and well-tolerated non-hormonal oral treatment for vasomotor symptoms in patients taking oral adjuvant endocrine therapy after breast cancer	86
Radiation therapy	Omission of radiotherapy was associated with an increased incidence of local recurrence but had no detrimental effect on distant recurrence or survival among patients aged ≥65 years with low-risk, HR-positive early breast cancer who are taking ET	87
	External-beam partial breast irradiation for patients with low-risk breast cancer was non-inferior to whole breast irradiation in terms of breast induration	88
	Simultaneous integrated boost is a safe treatment with reduced patient visits and further escalation of booster dose does not appear advantageous	89
	Five-year local control after 26 or 27 Gy/five fractions is non-inferior to 40 Gy/15 fractions	90
DCIS	In patients with resected non-low-risk DCIS, a tumor bed boost after whole breast irradiation reduced local recurrence	63
	Tamoxifen 5 mg once daily for 3 years lowers risk of second breast cancers	64
Surgery	In patients with breast cancer up to 2 cm and a negative preoperative axillary ultrasound (most of them with luminal-like disease), the omission of SLNB does not affect distant disease-free survival	103
	In patients with cN1 disease rendered cN0 with neoadjuvant chemotherapy, with three or more negative SLNs with SLNB alone, nodal recurrence rates were low, without routine nodal clipping	91
	Early locoregional therapy for the primary site did not improve survival in patients presenting with metastatic breast cancer. Although it was associated with improved locoregional control, this had no overall impact on quality of life	79
	The ACOSOG Z11102 trial demonstrated the safety of breast-conserving surgery and radiation for patients with multiple ipsilateral breast cancers	92
Early-stage, ER-positive breast cancer: clinical	The MONARCH-E trial showed that adjuvant abemaciclib reduced invasive disease-free survival in high-risk, ER-positive breast cancer	21
	The NATALEE trial showed that adjuvant ribociclib reduced invasive disease-free survival in high-risk, ER-positive breast cancer	55
	After 13 years of follow-up of the SOFT and TEXT trials, the addition of OFS to adjuvant endocrine therapy confirmed a clinically significant OS benefit in high-risk premenopausal patients	93
	The RxPonder study shows that there is no benefit to chemotherapy in postmenopausal patients with lower genomic risk N1 tumors, but that chemotherapy can reduce the risk of recurrence in premenopausal patients, possibly due to chemo-induced amenorrhea	49
	After 11 years of follow-up, ET was confirmed as non-inferior to chemo-ET in patients with HR-positive, HER2-negative, node-negative early BC and an RS of 11-25	94
	In postmenopausal patients with stage I or II, HR-positive breast cancer who had received 5 years of adjuvant endocrine therapy, extending hormone therapy by 5 years provided no benefit over a 2-year extension but was associated with a greater risk of bone fracture	95
Survivorship	Among select patients with previous HR-positive early BC, temporary interruption of ET to attempt pregnancy did not confer a greater short-term risk of BC events, including distant recurrence, than that in the external control cohort	68
	Mindfulness meditation and survivorship education reduced depressive symptoms in younger breast cancer survivors	72
Early-stage, HER2-positive breast cancer	Long-term follow-up of the APHINITY trial shows IDFS benefit for pertuzumab in node-positive breast cancer	35
	After 10 years of follow-up, adjuvant paclitaxel and trastuzumab remained a reasonable treatment standard in patients with small, node-negative, HER2-positive breast cancer	56
	Similar 3-year EFS and OS estimates with or without anthracyclines as NAST in patients with stage II and III HER2-positive breast cancer	32
Early-stage, triple-negative breast cancer	The addition of carboplatin to neoadjuvant paclitaxel followed by AC improves event-free survival in stage II-III triple-negative breast cancer	37
	The addition of neoadjuvant pembrolizumab to paclitaxel plus carboplatin chemotherapy followed by EC/AC improves event-free survival in stage II-III triple-negative breast cancer	39
	In patients with triple-negative breast cancer and residual disease after neoadjuvant chemotherapy, platinum agents do not improve outcomes and are associated with more severe toxicity when compared with capecitabine	96
	Individual patient-level meta-analysis supporting the DFS and OS benefit of post-neoadjuvant capecitabine	97
Diagnostics	In patients with high-risk HR-positive breast cancer in the late adjuvant setting, ctDNA was identified a median of 1 year before all individuals developing distant metastases	98
	A clinically relevant breast cancer classification schema incorporating immune, DNA-repair deficiency, and luminal-like biological phenotypes with HER2 status could stratify patients for clinical therapy	99
	c-TRAK TN failed to demonstrate the clinical utility of minimal residual disease monitoring by ctDNA, since patients had a high rate of metastatic disease on ctDNA detection	100

Continued

Table 1. Continued

Area	Discovery/innovation	Reference
	The HER2DX combined prognostic score identifies patients with early-stage, HER2-positive breast cancer who might be candidates for escalated or de-escalated systemic treatment	101
	Chemotherapy-naïve, young patients with N0 triple-negative breast cancer with high sTILs (≥75%) have a 15-year cumulative incidence of a distant metastasis or death of 2.1%	102

AC, doxorubicin-cyclophosphamide; AI, aromatase inhibitor; BC, breast cancer; ctDNA, circulating tumor DNA; DCIS, ductal carcinoma *in situ*; DFS, disease-free survival; EC, epirubicin-cyclophosphamide; EFS, event-free survival; ER, estrogen receptor; ET, endocrine therapy; HR, human receptor; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease-free survival; NAST, neoadjuvant systemic therapy; OFS, ovarian function suppression; OS, overall survival; PVs, pathogenic variants; RS, recurrence score; SLN, sentinel lymph node; SLNB, sentinel lymph node biopsy; sTILs, stromal tumor-infiltrating lymphocytes.

favored adjuvant ET. In addition to receptor status, the heterogeneity of ER-positive early-stage breast cancers can be characterized by determining grade, proliferation (Ki67 labeling index, and Ki67 dynamics in the preoperative setting), progesterone status, and multigene assays such as the 70-gene signature test and 21-gene recurrence score.[13] These markers serve as prognostic indicators for recurrence risk and can classify ER-positive cancers into luminal A-like and luminal B-like subtypes. Genomic signatures can define the benefit of ChT in ER-positive, HER2-negative breast cancer, with mature data from prospective studies supporting their use in most individuals where the indication for ChT is considered uncertain. However, access to such testing is limited, making Ki67 assessment a necessary but less proven strategy for determining the role of adjuvant ChT in ER-positive breast cancer.[14-16] Prognostic markers such as tumor-infiltrating lymphocytes (TILs) and programmed death-ligand 1 (PD-L1) expression are being explored in the field of early triple-negative breast cancer (TNBC). While TILs are prognostic in early breast cancer, particularly TNBC, panelists did not endorse routine assessment of TILs due to the absence of predictive value for current practice. Based on available data, the panel specifically rejected the notion that a high TIL score should prompt the omission of ChT. The panel endorsed PD-L1 protein expression being a predictive marker for the benefit of checkpoint inhibitors only in advanced but not early-stage TNBC.

LOCAL-REGIONAL THERAPY

Surgery of breast

Breast-conserving surgery (BCS) is the surgical choice for the majority of breast cancer patients. When opting for BCS, which is usually followed by post-operative radiation therapy (RT), it is crucial to prioritize both oncological and cosmetic outcomes. To achieve this, the panelists recommended that breast surgeons collaborate with reconstructive surgeons and/or have training in oncoplastic approaches, and facilitate shared decision making by providing appropriate patient-oriented information tools.[17]

The margin status of the excised tissue should be reported, with the absence of tumor at the inked margin being required for invasive cancer, while a margin of >2 mm is preferred for purely *in situ* disease. To aid in the accurate planning of the RT, if indicated, it is beneficial to mark the tumor bed with clips. When primary breast conservation is not achievable, nipple-sparing mastectomy and skin-sparing mastectomy achieve acceptable oncological outcomes, and can improve cosmetic outcomes. For patients undergoing mastectomy, the panelists felt that immediate or delayed breast reconstruction should be offered as an option in most instances. However, in inflammatory breast cancer, mastectomy without immediate reconstruction is advised to avoid delays in initiating post-operative RT. Following mastectomy, autologous tissue-based reconstructive techniques generally have better cosmetic outcome after RT than implant-based reconstruction.

Surgery of the axilla

Regional lymph node (LN) status remains a significant prognostic factor in predicting long-term outcomes in early-stage breast cancer (EBC). Sentinel lymph node biopsy (SLNB) is the standard approach for staging the axilla when there are no clinical signs of axillary involvement at diagnosis or after neoadjuvant ChT. The presence of micrometastatic or isolated tumor cells (ITCs) in treatment-naive axillary lymph nodes is prognostically similar to N0 disease. Treatment decisions are based on other tumor- and patient-based factors, and routine immunohistochemistry (IHC) or PCR evaluation of SLNs in patients who have not received neoadjuvant ChT were not recommended by the panelists.

Recent data from the SOUND study suggest that patients with clinical stage I breast cancer and negative axillary ultrasound may not need axillary surgery, an important advancement if validated. However, SLNB remains the standard of care. The panel strongly endorsed (85%) clinical exam and ultrasound of the axilla as part of routine assessment before SLNB, and the majority readily favored SLNB at least up to age 70 years; for patients age >70 years with ER-positive breast cancers and a clinically negative axilla, most favored omission of SLNB.

Among individuals with macrometastatic spread to the SLN, the ACOSOG-Z0011 trial reported similar outcomes without axillary lymph node dissection (ALND) for patients with clinical T1-T2 cN0 invasive breast cancer who had 1-2 SLNs containing metastases without gross extracapsular extension.[18] These patients underwent BCS, tangential post-operative RT including part of the axilla, and adjuvant systemic therapy. ALND remains the standard of care for patients who do not meet these criteria or have more than

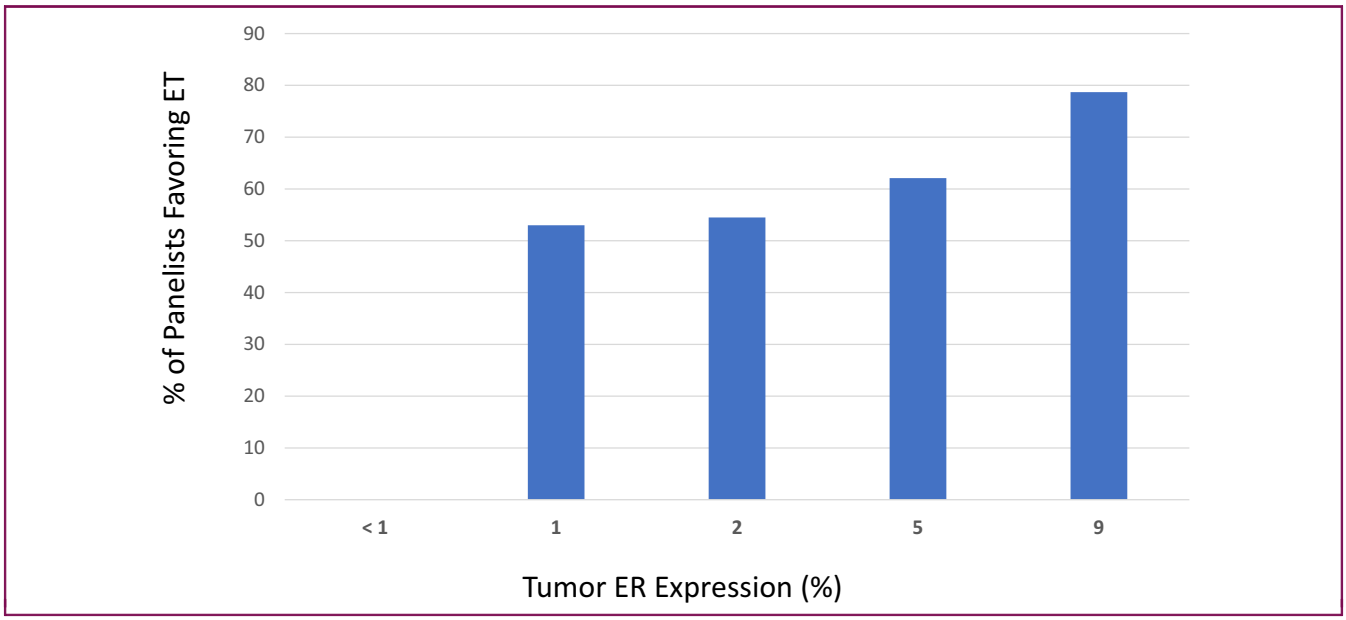

Figure 1. Percentage of panelists recommending ET by degree of tumor ER expression.
ER, estrogen receptor; ET, endocrine therapy.

two positive SLNs. Axillary RT is an option for cN0 patients with SLN metastases.[19,20]

Recent trials for use of additional targeted therapies such as PARP inhibitors or cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors have based eligibility on the number of affected lymph nodes.[8,21] The panel discussed the appropriateness of completion axillary dissection in patients with positive lymph nodes at SLNB in order to 'stage' more extensively the axilla to determine treatment suitability, especially in ER-positive tumors. While the panel acknowledged that nodal involvement-based indications for systemic therapy options (e.g. abemaciclib, olaparib) should be discussed by a multidisciplinary team and individualized to patients, it cautioned against routine completion axillary dissection in order to determine eligibility for such treatments. In the ACOSOG-Z0011 and AMAROS trials, the likelihood of four or more positive axillary nodes after a positive SLNB for a clinically negative axilla was comparably low (8%-14%),[20,22] and the panel believes that most often, the definitive treatment plan can be established based on tumor size, SLNB assessment, and biomarker data without resorting to completion ALND. The question of whether mastectomy patients with tumors <5 cm who will receive post-mastectomy radiation therapy (PMRT) can omit ALND after positive SLNB remained a subject of debate during the panel consensus. However, the panel favored proceeding to PMRT without additional axillary surgery.

Surgery after neoadjuvant chemotherapy

The extent of surgery may be tailored by the extent of residual tumor following neoadjuvant ChT. While not mandatory, magnetic resonance imaging before surgery is the most accurate method for gauging the extent of residual breast disease after neoadjuvant systemic treatment. In the post-neoadjuvant setting, breast surgery should adhere to the principles of ensuring oncological safety, minimizing morbidity, and achieving favorable cosmetic outcomes, similar to primary breast surgery. For patients with clinically and imaging-negative axilla, SLNB is the preferred method after neoadjuvant treatment. Among patients initially diagnosed with limited nodal involvement (cN1) who convert to biopsy-negative (ycN0) with neoadjuvant treatment, several trials such as SENTINA, ACOSOG Z1071, SN FNAC, and GANEA 2 have demonstrated the safe performance of SLNB.[23-26] Thus, patients with no evidence for residual cancer in the SLNB after neoadjuvant ChT do not require axillary dissection. The benefit of ALND in patients with micrometastatic and macrometastatic SLNs after neoadjuvant ChT is currently under investigation, and until randomized trials report outcomes, ALND is recommended for ypN0mic as well as any macrometastatic disease, regardless of other features. At present, there are no robust, multicenter data that such surgery can be safely omitted. There was some controversy at the extremes of low risk—for instance, an ER-positive cancer with ITCs in a single SN—as to whether an axillary dissection was required; however, in nearly all other scenarios, the panel strongly favored axillary dissection. In patients initially diagnosed with extensive nodal involvement (cN2-3) or inflammatory breast cancer, standard axillary surgery after neoadjuvant treatment remains an axillary LN dissection, regardless of clinical response.

LOCAL-REGIONAL THERAPY

Radiation therapy

Whole breast radiation therapy (WBRT) is a standard treatment after BCS. Based on longer follow-up from

multiple randomized trials,[27] the 2023 panel strongly reiterated its preference for moderately hypofractionated radiation treatment courses, consisting of 15 or 16 fractions, as standard therapy, irrespective of irradiated volume (breast with or without regional lymph nodes), tumor subtype, or patient age. Multiple studies have shown that omitting RT from lower-risk patients (older age, with low- or intermediate-grade, ER-positive, node-negative cancers) does not affect distance recurrence or overall survival (OS) but is associated with higher risks of in-breast recurrence. The panel was divided on whether older (age >65 years) patients with stage I, ER-positive breast cancer should routinely be offered RT in addition to ET, with 46% voting against routine RT, citing the lack of OS benefit, and 35% favoring RT, citing the reduction of in-breast recurrence. Emerging data for ultra-hypofractionated (5 fraction) treatment schedules are very encouraging. Panelists acknowledged that longer follow-up is needed to be confident that it is as effective in the long term. For selected patients with low-risk disease—typically older patients with small, lower-grade, ER-positive tumors—accelerated partial breast irradiation has shown results equivalent to WBRT.

PMRT was recommended by the panelists for patients at higher risk, including those with involved resection margins, four or more involved ALNs, and pT3-T4 tumors, regardless of the nodal status. There was controversy regarding PMRT for intermediate-risk patients, including those with stage IIB cancers (Figure 2), where panelists factored in the extent of nodal involvement, and the tumor subtype, when determining when to offer PMRT. For pT2 N1 tumors, the panel tended to favor PMRT when two or more LNs were involved, and to recommend against PMRT when there was only micrometastatic involvement. The panelists recommended regional RT for a positive SLNB without subsequent ALND. Decisions for T2 with one positive LN reflected tumor biomarker features—the panel favored PMRT for HER2-positive or triple negative tumors, broadly similar to presentations of stage pT3N0.

In patients who received neoadjuvant systemic therapy, the indications and target volumes for regional RT can be individualized based on the initial tumor stage and the tumor's response to treatment. The extent of regional radiation could be individualized by several risk factors, with the lowest-risk group (clinically node negative at baseline with no residual tumor in lymph nodes) requiring no regional field radiation, the intermediate-risk group (clinically N1 at baseline with no residual tumor in lymph nodes; without ALND; with low-genomic risk/luminal A-like, grade 1 or 2; without lymphovascular invasion or extranodal extension) receiving exclusive level 1-2 axillary RT, and the highest-risk group (clinically N+ at baseline with no residual tumor in lymph nodes and not intermediate risk; all those with residual nodal involvement after neoadjuvant treatment) receiving RT to level 1-3 axillary nodes excluding the surgically removed areas, and to supraclavicular and internal mammary nodes.[28] Reassuringly, with 15 years of follow-up, the 2023 Early Breast Cancer Trialists' Collaborative Group meta-analysis of regional nodal RT found benefit without an increased risk for non-breast cancer mortality in patients receiving effective systemic therapy.

NEOADJUVANT THERAPY AND POST-NEOADJUVANT SYSTEMIC THERAPY

For patients diagnosed with stage II or III breast cancer, the St Gallen 2023 panel again recommended preoperative systemic therapy as the preferred approach, particularly in those with HER2-positive or triple-negative subtypes, as such treatment provides effective systemic therapy, can improve surgical options in the breast and axilla, and allows for tailoring of adjuvant treatment based on the extent of tumor response. Neoadjuvant therapy is also the standard treatment for patients with inflammatory breast cancer or other inoperable, locally advanced tumors, who subsequently undergo mastectomy if deemed operable after induction treatment.[29]

Neoadjuvant ChT can effectively downstage HR-positive/HER2-negative cancers for surgical purposes, although achieving a pathologic complete response (pCR) is uncommon. The same considerations for selecting appropriate neoadjuvant treatments also apply to adjuvant therapy. If a neoadjuvant ET is selected (for tumors with low-risk genomic signature or otherwise low-risk features and/or in patients who require neoadjuvant treatment but are not candidates for ChT) the duration should be at least 6 months, or should continue until maximum response is achieved.[29]

HER2-positive breast cancer

Anthracycline-taxane-based combinations have traditionally been a mainstay of neoadjuvant ChT for HER2-positive disease.[30] However, they may have a low but potentially significant risk of cardiac toxicity and secondary acute myeloid leukemia.[31] Alternative anthracycline-free regimens, such as carboplatin with taxanes, show similar outcomes to anthracycline-containing regimens while improving cardiac safety.[32,33] For patients with stage II or III, HER2-positive breast cancer, the panelists strongly endorsed the use of neoadjuvant ChT combined with dual HER2 blockade (trastuzumab and pertuzumab; HP) (Table 2), which yields higher rates of pCR compared to trastuzumab alone, and lower risks of recurrence.[34] Patients who achieved a pCR after standard neoadjuvant systemic ChT with HP should continue anti-HER2 therapy for a total duration of 1 year; there was no consensus whether patients should continue with trastuzumab alone or with pertuzumab and trastuzumab.[35] However, the addition of pertuzumab to trastuzumab in the post-neoadjuvant treatment setting need not be routinely considered clinically node-negative tumors at baseline that achieve a pCR.[35] For patients with residual disease the panelists endorsed the use of T-DM1 (trastuzumab emtansine) for 14 courses.[36]

Triple-negative breast cancer

Neoadjuvant therapy is the standard approach for treating patients with stage II and III early TNBC (Table 2). Based on

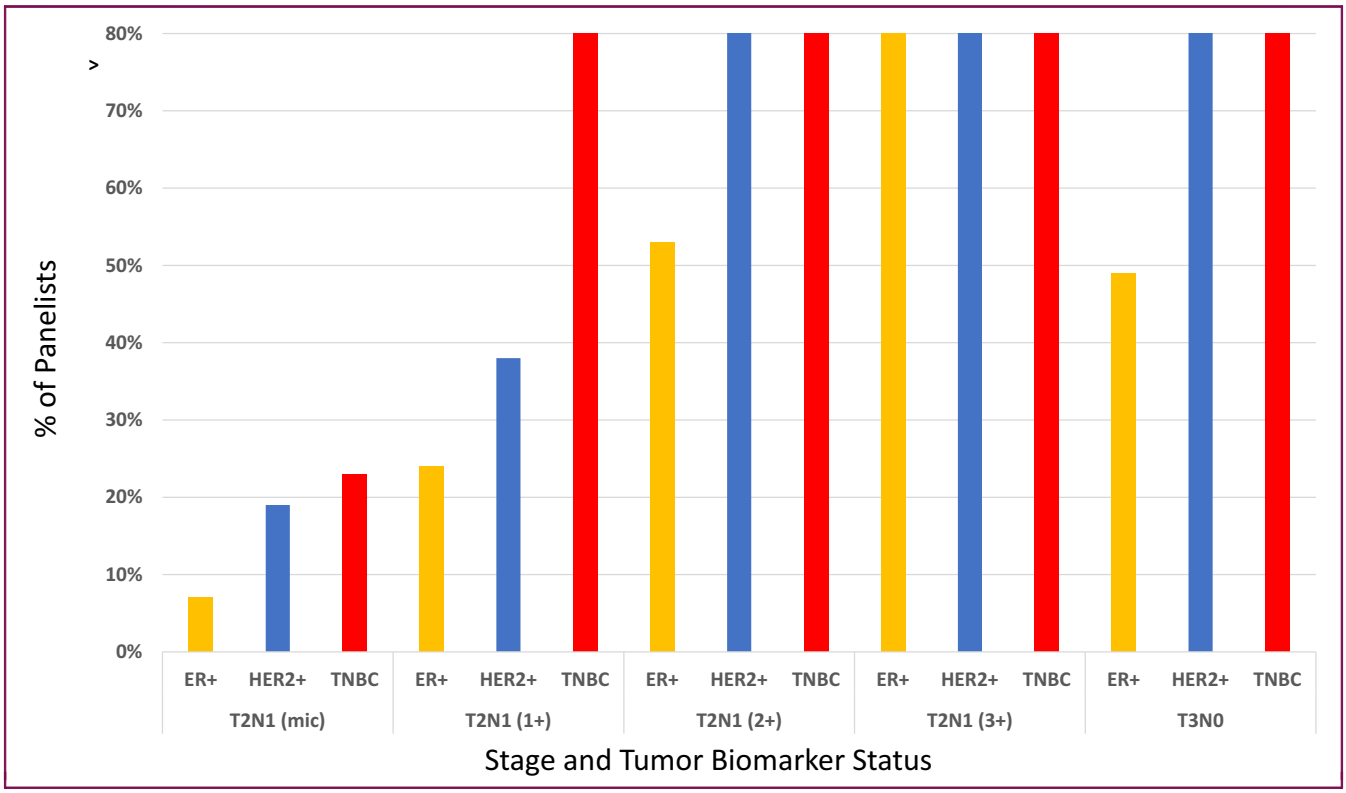

Figure 2. Percentage of panelists recommending post-mastectomy radiation therapy in stage IIB breast cancers by nodal status and tumor subtype.
ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer.

recent studies showing reduced risk of recurrence with regimens that incorporate carboplatin in addition to anthracycline-, taxane-, and alkylator- ChT, panelists recommended the inclusion of carboplatin as neoadjuvant treatment for stage II or III TNBC regardless of whether pembrolizumab is available/utilized.[37]

The preferred neoadjuvant regimen for stage II/III TNBC is that of KN522 trial: ChT with taxanes, carboplatin, anthracyclines, and cyclophosphamide, with concurrent pembrolizumab.[38,39] In the absence of access to pembrolizumab, evidence-based regimens involve sequential therapy, either anthracycline-based followed by taxanes, or taxanes combined with carboplatin in sequence with anthracycline-based therapy. The benefit from carboplatin is independent of germline *BRCA1/2* status. Standard anthracycline-based regimens include doxorubicin-cyclophosphamide (AC) or epirubicin-cyclophosphamide (EC) given for four cycles over 8 or 12 weeks, followed by a taxane given for four cycles or 8-12 weeks. Dose-dense therapies, such as fortnightly AC/EC/paclitaxel, or weekly paclitaxel, are standard.[40] pCR remains a strong prognostic factor regardless of *gBRCA1*/2 status.[37]

The panel was split as to whether dose-dense every-2-week AC/EC regimens or standard every 3-week schedule should be used with neoadjuvant pembrolizumab; 30% of the panelists supported the dose-dense, fortnightly combination, while 38% noted the lack of safety and efficacy data and were not inclined to use the dose-dense approach in this phase of therapy.

The majority of the panelists advised against neoadjuvant pembrolizumab-based regimen for stage I TNBC.[39] Regardless of the extent of response to neoadjuvant ChT plus pembrolizumab, panelists favored ongoing adjuvant pembrolizumab, though the clinical value of this adjuvant phase of therapy is not known. The benefit from pembrolizumab is independent of PD-L1 status.

Panelists were asked how residual cancer following neoadjuvant therapy should affect optimal therapy in the adjuvant setting. The CREATE-X trial demonstrated that adjuvant capecitabine improves invasive disease-free survival (iDFS) and OS, with the greatest benefit observed in TNBC tumors.[41] In patients with residual cancer not pretreated with pembrolizumab, panelists (70%) favored capecitabine alone for patients with residual cancer. The benefit of post-neoadjuvant capecitabine in patients receiving continued adjuvant pembrolizumab or adjuvant olaparib (indicated in carriers of a germline *BRCA* PV) is unknown.

ADJUVANT THERAPY

ER-positive/HER2-negative breast cancers

Treatments for patients with ER-positive/HER2-negative breast cancer are personalized based on factors such as tumor stage, subtype, menopausal status, and life expectancy (Table 3). Almost all patients with ER-positive tumors will be candidates for adjuvant ET (Figure 1).[42] The panelists agreed that while the relative benefits of ChT and ET may be

Table 2. Systemic therapy for HER2-positive or TNBCs

Stage		Tumor subtype	
		HER2 positive	TNBC
Stage I Typically as adjuvant therapy	T1a	TH—case by case (with ET therapy if HR positive)	Chemo—case by case
	T1b	TH	TC or AC/EC chemo
	T1c	TH	AC/T or TC chemo
Stage II Neoadjuvant therapy preferred		AC/TH or TCH, with addition of P if neoadjuvant and/or node-positive	AC/T chemo[a] (For cT2 cN0, consider addition of pembrolizumab[b])
Stage III Neoadjuvant therapy preferred		AC/THP or TCHP[c]	AC/T chemo[a] and pembrolizumab[d]
Residual invasive cancer after neoadjuvant therapy		Trastuzumab emtansine (T-DM1) for 14 cycles	Capecitabine every 3 weeks for six or eight cycles if gBRCA1/2-wt Olaparib for 1 year if gBRCA1/2-mut Pembrolizumab for nine courses (if given in the neoadjuvant setting)

A, anthracycline such as doxorubicin or epirubicin; C, cyclophosphamide; ET, Endocrine therapy; H, trastuzumab; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; P, pertuzumab; T, taxane; TC, Docetaxel and cyclophsphamide; TNBC, triple-negative breast cancer.

[a]Some panelists favor inclusion of carboplatin in neoadjuvant therapy for TNBC, particularly if used in node-positive cancers and in conjunction with pembrolizumab-based treatment.

[b]In KEYNOTE-522, patients cT2 cN0 were eligible to pembrolizumab.

[c]Consider addition of adjuvant neratinib after trastuzumab if tumor is ER-positive and four or more positive LN; however, the panel noted there are no data for use in patients also receiving pertuzumab or trastuzumab emtansine as is often standard for such patients.

[d]Consider adjuvant pembrolizumab regardless of extent of response.

similar across different subgroups, the absolute benefit depends on the risk of recurrence in each subgroup and dependent on competing risks of mortality from comorbidities. It is essential to consider the absolute benefit in conjunction with the potential side effects of each treatment, involving the patient in an informed decision-making process. Higher-risk hormone receptor (HR)-positive tumors typically require initial adjuvant treatment with aromatase inhibitor (AI)-based therapy, consideration of ChT, targeted treatments, and extended adjuvant ET, and, for premenopausal patients, ovarian function suppression (OFS).[43,44]

In the adjuvant care of postmenopausal patients, AIs used upfront, or sequentially following 2-3 years of tamoxifen and vice versa, offer a lower risk of recurrence compared to tamoxifen alone, especially in higher-stage cancers.[45,46] For premenopausal patients with higher-risk HR-positive cancers (usually meaning tumors with stage II or III and/or nodal involvement; grade 3 features; age $<$40 years), adjuvant OFS in combination with AI reduces recurrence and improves OS. For premenopausal patients receiving OFS, concurrent use of an AI provides more benefit than OFS/tamoxifen in young patients with high-risk clinicopathological features.

The historic standard duration of ET has been 5 years, but extended durations up to 7 or 10 years may further reduce recurrence risk and increase survival, particularly in higher-stage cancers.[47] The panel voted strongly that patient preferences along with clinicopathological features such as stage, grade, Ki67, and genomic assays associated with baseline recurrence risk should be used to inform the decision about the duration of therapy, but that there were insufficient data to rely on a genomic test alone to determine the duration of adjuvant ET. The panel favored adjuvant ET treatment duration of 5 years for stage I cancers, and 10 years for stage III cancers (Figure 3). For stage II tumors, especially those with nodal involvement, the panel endorsed 7 to 8 years, or up to 10 years, of treatment.

It has become commonplace to use genomic assays to determine whether patients with ER-positive, HER2-negative cancers warrant adjuvant ChT in addition to adjuvant ET. Three prospective trials—TAILORx, RxPonder, and MINDACT—have shown that adding ChT to ET does not improve outcomes in postmenopausal patients whose tumors have low-risk genomic scores.[48-51] The combination of low-grade and/or low Ki67 levels, strong ER/progesterone receptor expression, and endocrine response to a short preoperative ET can serve as indicators of favorable biology and outcome in situations where genomic testing is not available.[52,53]

An important controversy has been the use of genomic assays to guide the treatment of premenopausal patients. All three prospective studies showed benefit for ChT among younger patients whose tumors carry lower-risk genomic scores. Yet other trials have shown favorable outcomes for premenopausal patients with lower-risk cancers in the absence of ChT, and ChT -induced amenorrhea, not accounted for in the design of the genomic trials, is a strong prognostic factor.

The panel categorically rejected the notion that all premenopausal patients warrant adjuvant ChT. Instead, it favored a nuanced approach informed by tumor stage, the actual genomic score, and patient age. The panel explored decision making for a 47-year-old, premenopausal woman with a 1.6-cm, grade 2 breast cancer (Figure 4) as a function of clinical features and recurrence score. If the tumor was node negative, the panel largely recommended tamoxifen or ET plus OFS and not ChT. With single LN involvement, the panel was more likely to recommend ET plus OFS for lower recurrence scores ($<$20), and greater consideration of ChT as the recurrence score shifted closer to 25 (Figure 4). In a separate polling, the panel was progressively more likely to

Table 3. Systemic therapy for ER-positive HER2-negative breast cancer

Anatomic stage	TN	Type and duration of endocrine therapy[a]	Ovarian suppression	Chemotherapy[b]/abemaciclib		Olaparib
				Premenopausal	Postmenopausal	Premenopausal and postmenopausal
Stage I	T1ab N0	AI or Tam, 5 years[c]	No OFS	No	No	No
	T1c N0	AI or Tam, 5 years	Consider OFS and AI/Tam for higher risk, particularly those warranting chemotherapy, age <40 years, high grade, or intermediate genomic scores (e.g. recurrence score 16-25)	Consider no chemotherapy for favorable biology tumors especially if not pursuing OFS[d] Yes for less favorable biology tumors	No for favorable biology tumors[d] Yes for less favorable biology tumors	No
Stage II	N0 (node negative)	Consider extended therapy[e], especially after initial 5 years of tamoxifen	OFS and AI/Tam for higher risk, particularly those warranting chemotherapy, age <40 years, high grade, or intermediate genomic scores (e.g. recurrence score 16-25)	Consider chemotherapy for favorable biology tumors especially if not pursuing OFS[d] Yes for less favorable biology tumors	No for favorable biology tumors[d] Yes for less favorable biology tumors	No
	N1 (1-3+ LN)	Extended therapy[e]	OFS and AI/Tam	Consider for favorable biology tumors[d] Yes for less favorable biology tumors Abemaciclib for 2 years	No for favorable biology tumors[d] Yes for less favorable biology tumors Abemaciclib for 2 years for high-risk stage II	No[f]
Stage III		Extended therapy[e]	OFS and AI/Tam	Yes Abemaciclib for 2 years	Yes Abemaciclib for 2 years	Yes for patients with ≥4 pathologically confirmed positive lymph nodes in the adjuvant setting Yes for patients ER and/or PgR-positive/HER2-negative with residual invasive cancer in the breast and/or the resected lymph nodes (non-pCR) and a CPS and EG score ≥3.

AC, doxorubicin-cyclophosphamide; AI, aromatase inhibitor; CPS, clinical and pathological stage; EG, estrogen receptor status and histologic grade; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LN, lymph node; OFS, ovarian function suppression; pCR, pathologic complete response; PgR, progesterone receptor; Tam, tamoxifen; TC, Docetaxel and cyclophsphamide; TN, triple-negative.

[a]Historically, the St Gallen Panel has favored AI-based therapy in higher-risk tumors defined by T and N stage, grade, and Ki67 score.

[b]The panel recommended anthracycline- and taxane-based adjuvant chemotherapy regimens for stage III, ER-positive tumors; for stage I or II presentations, the panel was divided between taxane-based regimens (e.g. TC, 44%), anthracycline-only regimens (e.g. AC, 14%), and anthracycline- and taxane-based regimens (42%).

[c]Minimal risk may be managed without adjuvant treatment.

[d]Risk stratification: 'Favorable biology': lower-risk genomic signature [e.g. recurrence score <25 (node-positive) or 16-25 (node-negative), or 70-gene signature 'low']; strongly ER positive with low to intermediate grade, and/or lower baseline Ki67, or decrease in Ki67 with preoperative exposure to endocrine therapy. 'Less favorable biology': higher-risk genomic signature (e.g. recurrence score >25 or 70-gene signature 'high'); lower ER expression, intermediate to high grade, and/or higher baseline Ki67, or lack of decline in Ki67 with preoperative exposure to endocrine therapy.

[e]Extended therapy implies 10 years of treatment though some studies indicate that 10 years may not offer benefit beyond that seen with 7.5-8 years of endocrine therapy.

[f]In the original trial were eligible patients ER- and/or PgR-positive/HER2-negative with residual invasive cancer in the breast and/or the resected lymph nodes (non-pCR) and a CPS) and EG score ≥3. The CPS&EG score is a staging system for disease-specific survival in patients with breast cancer treated with neoadjuvant chemotherapy. This incorporates pretreatment clinical stage, ER status, nuclear grade, and post-neoadjuvant chemotherapy pathological stage.

recommend ET plus OFS and ChT when more lymph nodes were affected, or when the patient was very young (e.g. 34 years old). Conversely, all genomic-driven studies have shown that ChT added little benefit when genomic tests were at the very low end of the risk spectrum, conferring very favorable prognosis.

The panel also explored the use of ChT when stage and genomic tests suggest discordant risks. For patients with small, node-negative tumors, the panel was not inclined to recommend adjuvant ChT until the tumor size exceeded 1 cm even when the genomic signature was high risk (Figure 5). Conversely, the majority of the panel recommended against ChT for stage II or III lobular breast cancers when the tumor was grade 1 or 2, strongly ER/progesterone receptor positive, and had a low Ki67 score with low-risk genomic signature scores. When adjuvant ChT is recommended for patients with ER-positive tumors, anthracycline, taxane, and alkylator-based ChT regimens are standard though non-anthracycline-based regimens may be suitable for stage I and II cancers with limited nodal involvement.

Adjuvant bisphosphonate therapy is beneficial for postmenopausal patients with EBC, including premenopausal patients undergoing OFS, as it reduces the risk of tumor recurrence and helps manage the osteopenia/osteoporosis side effects associated with AIs.[54] Panelists were enthusiastic about use of adjuvant bisphosphonates; a relative majority favored the use only in patients with stage II and III, and treatment irrespective of tumor ER status.

New targeted therapies are emerging for ER-positive, HER2-negative cancers. The panelists strongly endorsed the addition of abemaciclib for a duration of 2 years in

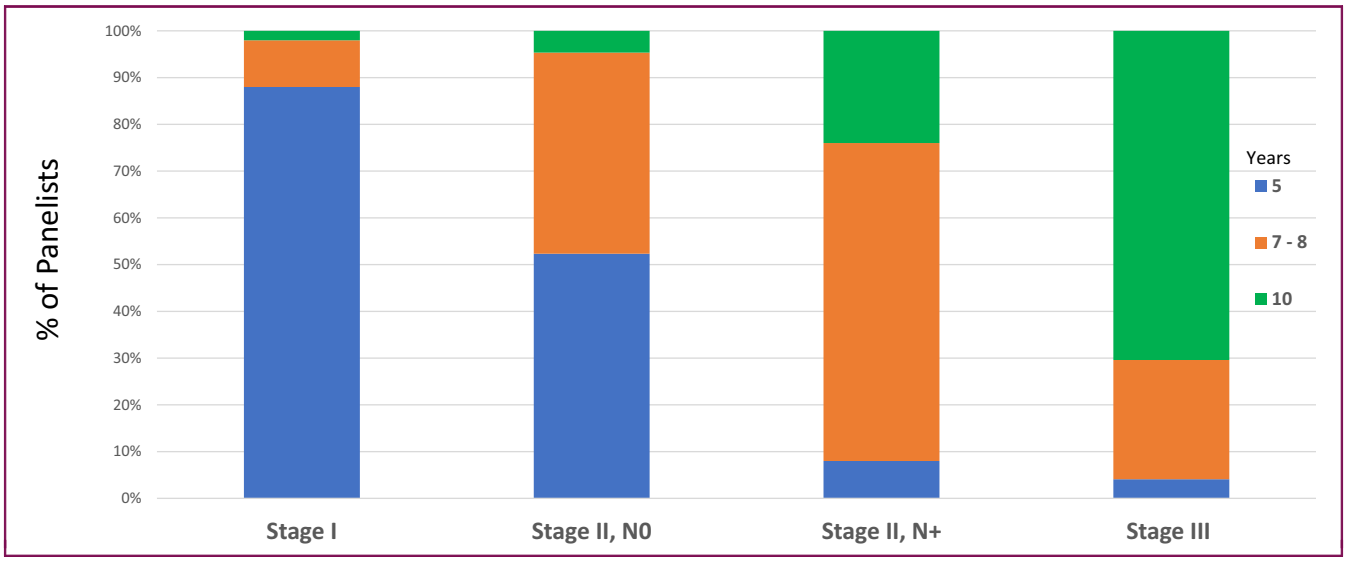

Figure 3. Recommended duration of ET by tumor stage.
ET, endocrine therapy.

patients with HR-positive/HER2-negative breast cancers who have four or more involved lymph nodes, or 1-3 positive nodes with T3 (>5 cm) tumors and/or grade 3 histology irrespective of Ki67 expression.[21] The adjuvant NATALEE trial of ribociclib suggests that a second CDK4/6 inhibitor may also be effective, and in a potentially broader population of patients.[55] For high-risk individuals with germline *BRCA1/2* PVs and HER2-negative tumors, adjuvant therapy with olaparib for a duration of 1 year was recommended.[8] Among the small cohort of patients who are potential candidates for both olaparib and abemaciclib, the panelists suggested a sequential treatment approach using the PARP inhibitor concurrent with ET for 1 year, and then introducing the CDK4/6 inhibitor, based on the observed benefit of each treatment but without data for how best to deliver both safely. The panelists acknowledged that this is not based on evidence and should be considered an expert opinion.

The panelists reiterated that while supportive interventions can help mitigate the side effects of adjuvant ChT, ET, and targeted therapies, it is important to consider that the reductions in recurrence or improvement in OS with common treatments for ER-positive breast cancer, particularly in lower-risk tumors, are modest. Thus, patients'

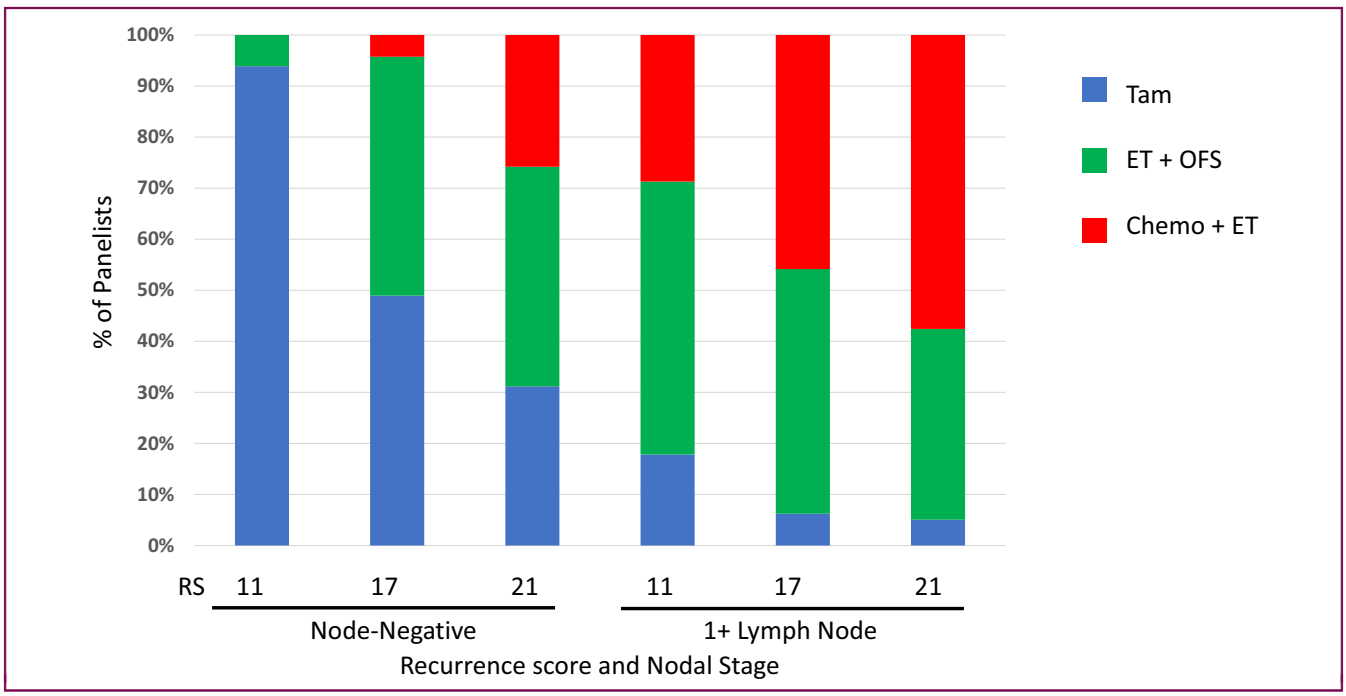

Figure 4. Adjuvant recommendations for a premenopausal 47-year-old woman with a 1.6-cm, grade 2 breast according to recurrence score and nodal status.

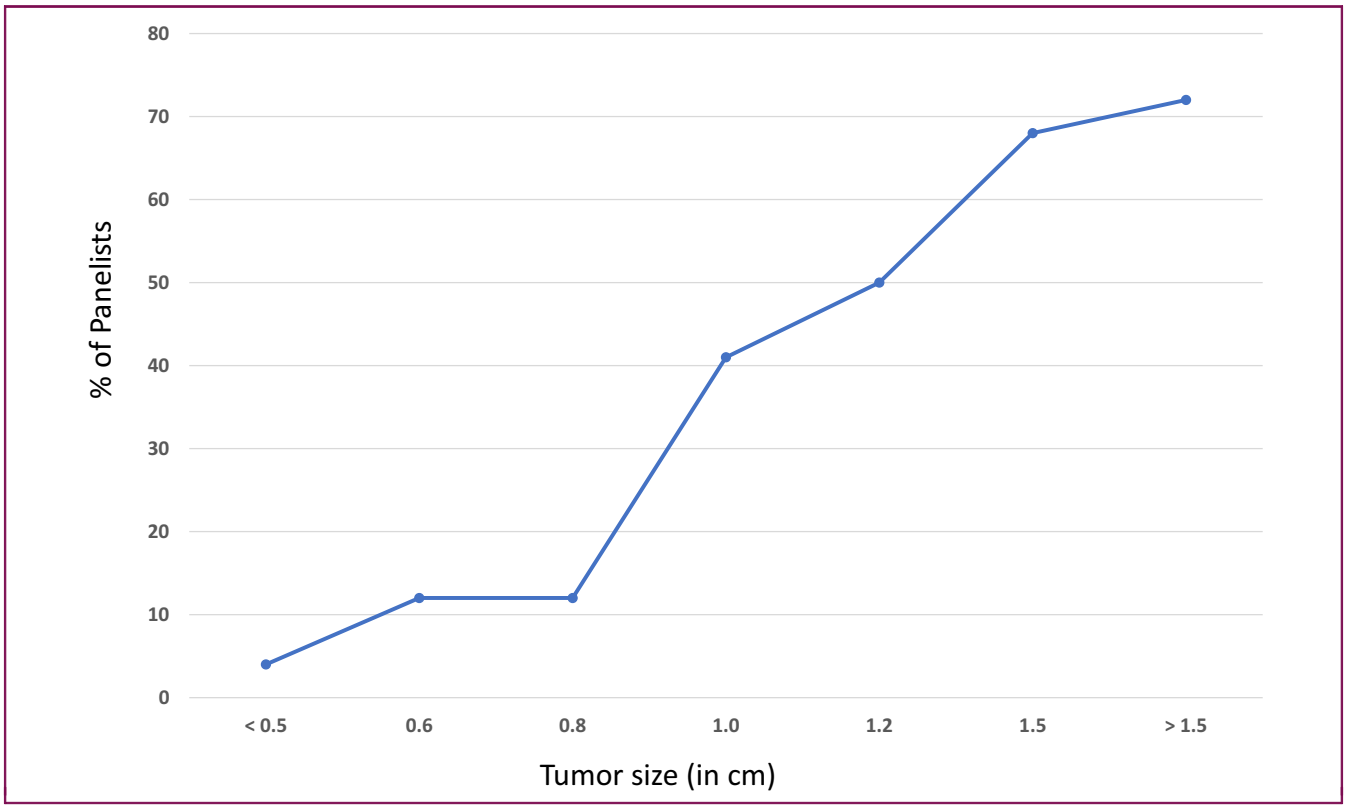

Figure 5. Percentage recommending adjuvant chemotherapy for a 57-year-old, postmenopausal patient with T1N0 ER-positive HER2-negative breast cancer and 'high-risk' tumor genomic assay result.
ER, estrogen receptor; HER2, human epidermal growth factor receptor 2.

preferences play a crucial role in determining the appropriate adjuvant treatment recommendations.

HER2-positive or triple-negative breast cancers

Adjuvant treatment recommendations for triple-negative or HER2-positive breast cancer have remained largely unchanged since 2021 (refer to Table 2 for specific details). Patients diagnosed with HER2-positive breast cancer who undergo initial surgery should receive adjuvant treatment consisting of ChT combined with HER2-targeted therapy and ET if HR-positive.

For stage I, HER2-positive breast cancer, the panelists continue to favor paclitaxel/trastuzumab as the recommended regimen.[56] For HER2-positive node-positive disease, the panelists favored the use of dual blockade with pertuzumab and trastuzumab in the adjuvant setting, with benefit independent of HR status.[35] Studies investigating the non-inferiority of a shorter duration of trastuzumab (6 months versus 12 months) support evidence of 6 months of treatment for patients with low risk of relapse and comorbidities as an option.[57] The decision regarding the duration of trastuzumab should consider the balance between the benefits of 12 months versus 6 months and the baseline risk of recurrence, particularly in resource-constrained settings with limited treatment capacity. The Extended Adjuvant Treatment of Breast Cancer with Neratinib (ExteNET) trial evaluated 1-year extended therapy with neratinib following completion of 1 year of adjuvant trastuzumab, but was conducted before common use of pertuzumab or trastuzumab emtansine as part of standard treatment regimens for higher-risk HER2-positive tumors.[58,59] Some patients, especially with ER-positive, HER2-positive tumors and extensive nodal involvement, may consider adjuvant neratinib (Table 2).

For patients with TNBC who received frontline surgery, the choice of ChT regimens does not differ between neoadjuvant and adjuvant treatments for breast cancer.[60] Standard anthracycline-based regimens such as AC or EC are typically administered for four cycles over 8 or 12 weeks, followed by a taxane for four cycles or 8-12 weeks. Dose-dense therapies are preferred.[40] Non-anthracycline, taxane-based regimens such as docetaxel-cyclophosphamide or taxanes plus carboplatin may be used as an alternative to anthracycline-taxane-based ChT, especially for patients with low-to-intermediate recurrence risk (stage I) or contraindications to anthracyclines.[61] However, a recent meta-analysis suggests that anthracyclines and taxanes, particularly when given concurrently, yield the lowest risks of recurrence particularly for node-positive cancers.[62] For high-risk individuals with a germline *BRCA1/2* PV and a HER2-negative tumor, adjuvant therapy with olaparib for a duration of 1 year was recommended. In the case of a patient who underwent primary surgery for what proved to be a stage II TNBC with nodal involvement, the panel (55%) did not recommend adjuvant

pembrolizumab, citing the lack of data for use of the checkpoint inhibitor following surgical removal of all known tumor though 34% were inclined to include pembrolizumab with adjuvant ChT.

DUCTAL CARCINOMA *IN SITU*

Following BCS, the panelists recommended RT to reduce the risk of ipsilateral recurrence of ductal carcinoma *in situ* (DCIS) or invasive breast cancer. The panel recommends considering a boost when larger areas of DCIS or other factors associated with an increased risk of recurrence such as margins <2 mm and comedonecrosis are present,[63] but not for lower-risk DCIS. The panel considered the role of radiation in a low-risk patient with DCIS spanning ≤ 2 cm, with low- or intermediate-grade features, that was ER positive, and without comedonecrosis. In this scenario, age was the primary driver of RT recommendation. For patients aged ≤ 65 years, $>75\%$ of the panel favored RT, whereas for patients ≥ 70 years, only 15% endorsed RT.

Adjuvant ET can further reduce the risk of recurrence in DCIS treated with breast conservation and RT, as well as reduce the risk of contralateral breast cancer. Both tamoxifen and AIs are options for adjuvant ET, although the panelists generally lean towards tamoxifen owing to its favorable tolerability.[64-67] The panelists considered the case of a postmenopausal patient with low-risk (small, ER positive, grade 1 or 2) DCIS treated with BCS and RT, with divided opinions. One-third recommended no adjuvant treatment. However, 41% favored low-dose tamoxifen at 5 mg for prevention of recurrence and secondary cancers.

PREGNANCY AFTER CANCER

Based on the results of the POSITIVE study,[68] the panelists supported the temporary interruption of ET in younger patients with ER-positive breast cancer in order to attempt pregnancy. In that trial, the interruption of adjuvant ET did not confer a greater short-term risk of breast cancer recurrence compared to historical controls.

However, the panel urged caution when extrapolating these results to patients with stage III cancers, as such patients still showed high risks of near-term recurrence, and noted that follow-up remains limited, and that among very young patients, who are likely to retain fertility despite several years of adjuvant ET, delaying attempts at pregnancy should be considered so as to conclude standard courses of ET.

SURVIVORSHIP

Breast cancer treatments are associated with a wide range of side effects, including physical changes, hair loss, ChT-related toxicities, and health consequences resulting from estrogen deprivation.[69] To mitigate these side effects, numerous supportive care interventions have been developed.

In this year's panel discussions, emerging data on several interventions to improve the quality of life in breast cancer survivors were addressed. The panel encouraged patients with a body mass index >30 to reduce weight for general health maintenance including prevention of diabetes, hypertension, arthritis, and to potentially reduce the risk of breast cancer recurrence. The panelists endorsed the use of acupuncture as a potential treatment option for breast cancer survivors to alleviate symptoms of arthralgia related to AI therapies and/or neuropathy related to ChT.[70,71] Mindfulness-based stress reduction was endorsed as an effective strategy to alleviate depressive symptoms in younger breast cancer survivors.[72] Aerobic exercise was also recommended as a standard approach to address various adverse effects, including fatigue and sleep disturbance. Genitourinary syndromes of menopause such as vaginal dryness and related sexual dysfunction are common in patients receiving adjuvant ET. Although topical vaginal estrogens can provide relief, concerns exist regarding potential transient increases in systemic estrogen levels.[73,74] Nevertheless, the panelists acknowledged that they would often prescribe intravaginal estrogens to alleviate symptoms in patients on AIs, particularly when symptoms are unresponsive to non-hormonal interventions including moisturizers and lubricants.

MOLECULAR DIAGNOSTICS

The Food and Drug Administration (FDA) has granted approval for the use of liquid biopsy to detect circulating tumor DNA (ctDNA) in solid tumors in the early and in the metastatic setting.

The approval of liquid biopsy in solid tumors by the FDA signifies its recognition as a potentially valuable diagnostic and monitoring tool in management of early-stage cancers. The panelists did not recommend routine ctDNA liquid biopsy testing at this time, awaiting studies showing clinical utility.[75] According to the panelists, ctDNA testing should not be used to intensify treatment in patients with favorable clinical features (pCR after neoadjuvant systemic therapy) and in the absence of radiologically or metabolically evaluable disease. The panelists were asked whether, as part of a clinical trial, they were at equipoise with the plan to switch from an AI to fulvestrant in the adjuvant setting if an *ESR1* mutation was detected by liquid biopsy.[76] Reflecting the lack of data for use in the early-stage setting, there was no consensus, with 43% of the panelists comfortable switching to fulvestrant and 38% continuing with ongoing AI.

LOCAL-REGIONAL RECURRENCE OF BREAST CANCER

Rates of recurrence in the treated breast and/or axilla have been steadily declining with improved imaging and treatment, but remain a clinical challenge when encountered.[48,77] Owing to the heterogenous presence of prior surgical, radiation, and systemic treatments, there are few guidelines for management of local-regional recurrence. Historically, mastectomy has been the recommended surgery for patients who have had in-breast tumor recurrence after prior BCS and RT. The panel considered the case of a 63-year-old with prior lumpectomy and RT for a stage II, ER-

positive breast cancer, who had an isolated, in-breast recurrence 3 years after diagnosis, and strongly (74%) recommended mastectomy. However, for the same case but 9 years after initial treatment, only 25% recommended mastectomy while 15% recommended BCS alone, and 58% recommended BCS and re-irradiation. For patients who have local recurrence while receiving adjuvant ET, the panel endorsed multidisciplinary discussion and noted multiple potential treatments but discouraged use of genomic signatures in this setting for determining whether to recommend ChT as there are no data.[78]

OLIGOMETASTATIC BREAST CANCER

Some breast cancer patients are diagnosed with *de novo*, stage IV breast cancer at the time of their initial presentation. Clinical trials have been conducted to compare optimal systemic therapy with or without breast surgery for patients with oligometastatic (typically defined as five or fewer lesions) cancer. However, early local-regional treatment for breast cancer does not improve OS in the setting of stage IV breast cancer.[79] Occasionally, patients with newly diagnosed breast cancer are found to have more limited oligometastatic cancer—typically characterized by the presence of one, or possibly two, sites of limited metastatic cancer outside the breast and regional lymph nodes—during staging evaluation.[80] Examples of oligometastatic sites may include isolated metastasis to the sternum, a solitary bone lesion, a single pulmonary nodule, or a lymph node. The panel considered specific scenarios where a patient presented after surgery for stage II breast cancer and was subsequently found to have an isolated metastasis in the sternum or other isolated bone metastasis, in case of contralateral axillary nodes, or a lung nodule that could be treated with definitive RT (in the case of bone) or excision (in the case of the lung). In each of these instances, the panel most commonly favored a multimodal, curative-intent approach, including definitive additional treatment targeting the site of metastatic disease, regardless of tumor subtype. However, for patients with multiple sites of metastatic cancer, such as three or more bone lesions, the panel recommended following standard treatments for advanced breast cancer, with a focus on palliative care for the metastatic sites based on symptom management.

GLOBAL PERSPECTIVE ON BREAST CANCER TREATMENT

The panelists recognize that barriers related to health care systems and patients were identified as common factors contributing to late-stage diagnosis of breast cancer. These barriers create clinical scenarios where patients are not diagnosed until their cancer has already progressed to locally advanced or metastatic stages.[81,82] In high-income countries, nearly 30% of new breast cancer diagnoses arise in patients aged $\geq$70 years, beyond the age of screening mammography in many societies, whose care needs have been understudied. Health care systems in lower- and middle-income countries face several shared challenges including limited national or regional data collection, deficiencies in program infrastructure and capacity (such as acquiring appropriate equipment and drugs, providing professional training and accreditation), the need for both qualitative and quantitative research to inform decision making, and the implementation of strategies to enhance patient access and compliance. Equal access to such infrastructure is a key feature of a developed health care system. Additionally, it is crucial to raise awareness among the general public, health care professionals, and policy-makers that treating breast cancer is both effective and cost-effective. Addressing these challenges will require concerted efforts to improve awareness, enhance diagnostic capabilities, streamline treatment options, and prioritize breast cancer control programs within the broader context of health care systems. By implementing these strategies, it is possible to overcome barriers and improve breast cancer outcomes in diverse socioeconomic settings.

Summary

The 2023 St Gallen Consensus Conference highlighted important strategies to optimize treatment for patients with EBC. While a significant number of treatment recommendations were provided, there was notable variability in the level of agreement among the panelists. Among the >200 questions discussed, a wide range of opinions and support levels can be observed in the voting results presented in Supplementary Appendix S1, available at https://doi.org/10.1016/j.annonc.2023.08.017, which can be found in the online version of the *Annals of Oncology*. The panel recognized that these recommendations may not apply to all patients, but rather represent the consensus for the majority of individuals in common clinical scenarios. It is important to tailor adjuvant therapies to each patient based on their tumor characteristics, coexisting medical conditions, financial considerations, and personal acceptance of the proposed treatments. This approach allows for the optimization of treatment strategies to better align with the needs and circumstances of individual patients.

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