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St. Gallen/Vienna 2023: Optimization of Treatment for Patients with Primary Breast Cancer – A Brief Summary of the Consensus Discussion

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Abstract

The St. Gallen Consensus Conference on early breast cancer treatment 2023 was again a live event and took place in Vienna, Austria. After 4 years and one virtual event due to the pandemic, more than 2,800 participants from over 100 countries came together in Vienna, and the 2023 St. Gallen/Vienna conference was a great success. Over 3 days, the global faculty reviewed the most important evidence published during the last 2 years and debated over controversial topics, and finally, the consensus votes aimed to define the impact of the new data on everyday routine practice. Focuses of this year's conference were radiotherapy and local management of the axilla, genetics, and their impact on treatment, as well as the role of the immune system and tumor-infiltrating lymphocytes in pathological reports and treatment decision-making. The traditional panel votes were moderated for the first time by Harold Burstein from Boston, and with questions previously voted on and live voting, the panel managed for the most part to clarify the critical questions. This report by editors of *BREAST CARE* summarizes the results of the 2023 international panel votes with respect to locoregional and systemic treatment as a brief news update but does not intend to replace the official St. Gallen Consensus publication that not just reports but also interprets the panel votes and will follow shortly in a major oncological journal. The next (19th) St. Gallen International Breast Cancer Conference will again take place in Vienna (save the date: March 12–15, 2025).

Introduction

It was a great pleasure to attend the 18th St. Gallen Consensus Conference on early breast cancer treatment 2023 in person in Vienna once again. Michael Gnant, Beat Thürlimann, and Walter Weber chaired the conference, also honoring the recently deceased honorary chair Hans-Joerg Senn. Harald Burstein and Giuseppe Curigliano chaired the panel discussion and the voting. The conference summarized and discussed clinical research findings of the past 2 years and focused on diagnostics, therapy recommendations, and optimization of early breast cancer patient treatment.

The discussions and recommendations were based on available evidence as well as the clinical expertise of the international faculty from 28 countries from all 5 continents – with 70 panel members (listed in Table 1),

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Table 1. Members of the 18th St. Gallen International Breast Cancer Consensus Panel

Stephan Aebi	Carsten Denkert	Frederique Penault-Llorca
Meteb Al-Foheidi	Gerd Fastner	Martine Piccart
Fabrice André	Florian Fitzal	Lori Pierce
Mikola Anikusko	Prudence Francis	Poortmans Philip
Rajendra Badwe	Heba Gamal El Din	Meredith Regan
Andrea V. Barrio	Oreste Gentilini	Jorge Reis Filho
Carlos Barrios	Michael Gnant	Isabel Rubio
Jonas Bergh	William Gradishar	Hope Rugo
Hervé Bonnéfoi	Bahadir Gulluoglu	Cristina Saura
Denisse Bretel Morales	Nadia Harbeck	Elzbieta Senkus-Konefka
Sara Brucker	Jörg Heil	Zhi-Ming Shao
Harold J. Burstein	Chiun-Sheng Huang	Christian Singer
Carlos Caldas	Jens Huober	Beat Thuerlimann
David Cameron	Ze-Fei Jiang	Masakazu Toi
Fatima Cardoso	Orit Kaidar-Person	Sara Tolaney
Maria Joao Cardoso	Marleen Kok	Nicholas Turner
Lisa Carey	Eun-Sook Lee	Andrew Tutt
Steven Chia	Sherene Loi	Marie-J Vrancken-Peeters
Javier Cortes	Sibylle Loibl	Toru Watanabe
Charlotte Coles	Miguel Martin	Walter Weber
Giuseppe Curigliano	Icro Meattini	Hans Wildiers
Jana de Boniface	Kathy D. Miller	Binghe Xu
Suzette Delaloge	Monica Morrow	
Angela DeMichele	Ann Partridge	

this was the largest consensus Panel ever, with a 44% proportion of female panelists. The panel openly disclosed any potential conflicts of interest (www.oncoconferences.ch), and it was recognized that individual panel members may have financial relationships with commercial entities engaged in research, innovation, and education; however, none were declared as substantially impacting the voting procedure. However, a number of faculty members could not contribute to the panel discussions because of declared conflicts of interests.

More than 2,800 participants from 100 different countries attended 3 days of state-of-the-art sessions with reviews of recent evidence on locoregional and systemic treatment [1] and the refinement of molecular and pathological diagnosis of breast cancer, supportive measures improving the outcome of early-stage breast cancer, and debates on the most controversial topics in treatment. A deeper insight into the biology of breast cancer and translational research potentially influencing clinical trials in the near future were discussed.

The consensus panel started Saturday at noon, and Harald Burstein elegantly moderated the discussion and led the panel through the consensus and the voting. A substantial proportion of questions had already been voted on by the panel in advance, and the results were shown during the panel discussion as more controversial and urgent topics were prioritized for discussion. As always [2], many questions were voted on in the usual manner to achieve consensus or to demonstrate which clinical questions are in need of further research and more data in order to possibly achieve consensus in the future.

As usual, for questions with clinical trials providing sufficient evidence needed for general recommendations on clinical decision-making, a clear consensus was achieved. However, it was acknowledged that evidence from randomized clinical trials does not cover all controversies. Thus, expert opinions had to be used when data were lacking. With an increasing body of evidence for important patient needs [3], some of the crucial questions had to be addressed in this manner. This remains the unique feature of the St. Gallen International Consensus.

General Practice Issues

For the first time, the panel discussed telehealth and virtual visits for the follow-up of breast cancer survivors; the majority use these tools only exceptionally (<10%: 60%), but a sizeable proportion has implemented them in their care routines (10–25%: 12%; >25%: 7%). In any case, the majority approved these methods "in addition to in-person follow-up" (69% yes). Also, the free telehealth consultation by OECD oncologists for cancer centers in "low-and-middle-income-countries (LMICs)" was endorsed.

In reflection of the global scale of the conference and the panel composition, 43% of panelists reported that they regularly have situations in which the cost of drugs

prevents some of their patients from receiving important therapies. 55% of panelists are sometimes restricted by national authorization/reimbursement decisions. In addition, burnout was – for the first time – a subject: 12% of panelists reported that they are burned out themselves, and additional 79% of panelists consider burnout to be a major problem for some/many of their colleagues. The majority (60%) stated that healthcare systems are not adequate to current practice needs or too labor intensive, and many suffered from excessive clinical load (12%) or inadequate clinical support (15%).

The panel did not reach perfect consensus as to whether a patient with a small (<1 cm) highly suspicious breast lesion could move to primary surgery without a diagnostic biopsy in situations for which non-neoadjuvant systemic treatment options exist; while a majority (72%) insisted on a preoperative biopsy, a sizeable minority (25%) stated that primary surgery would be appropriate in such a situation.

Breast Surgery

The 2023 Consensus Panel confirmed a number of previous decisions on breast surgery, some in more detail or with clearer majorities. For a 35-year-old patient with triple-negative breast cancer (TNBC) cT2cN0 and a pathogenic *BRCA* mutation, the majority recommended bilateral mastectomy with or without reconstruction, while some panelists voted to separate the risk-reducing aspect from the cancer surgery, thus also keeping breast conservation plus radiotherapy an option.

For the post-neoadjuvant surgery of a TNBC and complete radiological response, lumpectomy with no ink on tumor was the treatment of choice for two thirds of panelists; however, a larger margin was preferred by 25% of panelists (split 1:1 between 1 and 2 mm between ink and tumor). The panel remained uncertain on whether a preoperative mammography should be standard after the neoadjuvant treatment of a TNBC with initial baseline microcalcifications, but some endorsed the use of intraoperative specimen radiography instead.

For the first time, however, the panel endorsed breast conservation for multicentric disease; 68% of panelists preferred "double tumorectomy" in a postmenopausal patient with ER+/HER2– clinically node-negative breast cancer with two ipsilateral tumors in two neighboring quadrants (and R0 resections possible). Biology matters [4], thus in the same situation with two TNBCs, only 42% preferred a double tumorectomy, whereas 30% voted for mastectomy (27% abstention). In addition, a majority of the panel endorsed oncoplastic high-volume resections [5] or "extreme oncoplasty" as an alternative for large primary tumors as long as margins are clear [6], and post-surgical radiation can be performed (67% yes, 27% abstain).

Breast Reconstruction

The panel did not find a majority with respect to which BMI needed to be reached for an overweight patient in order to allow safe reconstruction. Also, the majority of panelists neither approved nor declined the use of fat stem cells for breast reconstruction in the absence of sufficient data.

Axillary Staging

The panel clearly endorsed the combination of clinical examination and axillary ultrasound for the staging of a postmenopausal woman with stage 1 breast cancer (85% yes).

Axillary Surgery

The panel endorsed targeted axillary dissection and sentinel node surgery to determine nodal pCR in a cN+ breast cancer who turned node negative by PST. There was no consensus on whether any axillary surgery can be omitted in patients with favorable prognostic factors (strong ER and PR, grade 1, endocrine therapy [ET] compliant), but a majority of panelists would consider such omission from the ages of 70 (47%) or 80 (12%) onward. 18% of panelists insisted on SLN surgery regardless of age.

In patients undergoing mastectomy and showing one positive SLN, a majority suggested radiation therapy (56%), but some still favored axillary dissection or observation. The panel was split over the issue of palpable nodes at time of diagnosis of postmenopausal ER+ HER2– disease; while 52% of panelists voted for primary surgery, a minority endorsed neoadjuvant chemotherapy (12%) or neoadjuvant antihormonal therapy (5%), voting results shifted toward more neoadjuvant chemotherapy for a similar situation in premenopause (28%), but the majority still favored primary surgery (42%).

The panel once more remained split over the question of whether, after neoadjuvant systemic surgery and residual disease in the axilla, axillary dissection or axillary radiotherapy should be undertaken. There was some variation of majorities with respect to the extent of residual disease and molecular tumor subtype. For TNBC and residual ITCs/micrometastasis, 34% favored ALND and 40% ART [7]. For macrometastasis after PST for TNBC, 43% preferred ALND over ART (28%). For

situations of a negative posttreatment sentinel node, a relative majority of panelists (44%) voted for no further therapy, whereas 39% would still irradiate the axilla. The panel did not recommend LYMPHA [8, 9] surgery as routine but considered lymphatic surgery in general promising (64% yes) for the treatment of clinically relevant lymphedema.

Radiotherapy

The panel re-endorsed moderate hypofractionation [10] (15–16 fractions over 3 weeks) as the standard of care (64% yes), while some even advocated for ultra-hypofractionation [11] (5 fractions in 1 week, 11%). The panel again could not agree on the age from which radiotherapy after breast conservation could be omitted; in an overall favorable clinical situation (13 mm tumor size, ER and PgR highly positive, grade 1), 41% of panelists would still offer adjuvant RT regardless of age (if life expectancy is >15 years), whereas other panelists suggest to omit RT for patients older than 65 (24%), 70 (29%), or 75 (13%) years. 27% of panelists claimed the importance of the PRIME-II trial [12] is that RT does not alter survival and therefore can be omitted, but 64% believe the trial shows that RT lowers in-breast recurrence.

A series of questions was asked on postmastectomy radiation (T2 tumor). In ER+ tumors and 1 micrometastasis, 89% of panelists do not recommend postmastectomy radiation therapy. With increasing disease burden, this percentage goes down: 72% for 1 positive node and 35% for 2 positive nodes (a situation in which a majority, 53%, of panelists would already recommend postmastectomy radiation therapy). For 3 positive nodes, 94% endorsed postmastectomy radiation therapy. For triple-negative disease, the threshold was generally lower, e.g., 23% yes for micrometastasis.

Interestingly, the panel was split on postmastectomy radiation therapy in an ER+ T3N0 tumor (49% yes, 46% no). The panel did not consider a deleterious *ATM* gene mutation as a contraindication for RT after BCS.

Local Regional Recurrence after Breast-Conserving Therapy

The first case considered was a 63-year-old woman with history of breast-conserving therapy and adjuvant systemic therapy for node-negative stage 2 breast cancer 9 years ago who is now presenting with an ER-positive and HER2-negative ipsilateral tumor recurrence (<2 cm, 3 cm distance to the nipple). No distant metastases and only very localized grade 2 side effects at the level of the skin and soft tissues are present. Clinically, it would be amenable to breast-conserving surgery with acceptable esthetic results. In this specific situation, a majority of the panelists would recommend performing breast-conserving surgery again (58% with re-irradiation and 14% without), and only 25% would primarily recommend mastectomy.

The case was then modified by assuming a rather shorter disease-free interval of 3 years, and ET stopped after the first year. Now, the majority favored the mastectomy (74%), and only a few still voted for a breast-conserving procedure (18% with re-irradiation and 6% without). In a third case, adjuvant systemic therapy recommendations were discussed for a patient who presented with an isolated local regional recurrence while on adjuvant aromatase inhibitor therapy. The recurrence was fully excised in terms of a definitive local therapy. The panelists agreed to provide a second adjuvant ET, and only 2% denied that approach.

Presumably considering potential biological reasons for endocrine resistance such as ESR1 mutation or PIK3CA mutation [13, 14], a two-thirds majority suggested switching to an alternative endocrine approach (65%) by delivering SERMs (tamoxifen, 33%) or SERDs (fulvestrant, 33%) with or without CDK4/6-inhibitors [15, 16] (29% and 36%, respectively). In total, 34% would add a CDK4/6 inhibitor to any of the endocrine treatment options. However, a substantial proportion (24%) would switch to tamoxifen alone, and one fifth (20%) would recommend fulvestrant in combination with a CDK4/6 inhibitor. A minority (16%) would switch to an alternative aromatase inhibitor (nonsteroidal to exemestane or vice versa), and only 6% would proceed with the same aromatase inhibitor plus a CDK4/6 inhibitor (abstain 11%).

As a fourth case, a patient was presented who developed isolated local regional recurrence, strongly ER-positive and HER2-negative, while on adjuvant aromatase inhibitor therapy. When originally diagnosed, she had not received adjuvant chemotherapy. The recurrence has been fully excised and is receiving definitive local therapy. The majority of the panelists (63%) would not recommend adjuvant chemotherapy in this situation in line with the results of the CALOR trial [17], and only a minority (28%) favored it anyway.

The case was slightly modified to include information about the disease-free interval of 4 years, and the panelists were asked whether they would recommend genomic signature testing to decide whether to receive chemotherapy. A vast majority (84%) do not see an indication for genomic testing, some voted for definitely not recommending chemotherapy (16%), some for recommending chemotherapy anyway (14%), and the majority voted for deciding on other factors like grade, Ki-67 or PR status, and age (53%). Only few would use genomic testing to determine suitability for chemotherapy (9%).

Table 2. Summary of recommended prevention depending on mutations detected and menopausal status

Mutated gene	Menopausal status	Surgery, %	Intensive screening, %	Abstain, %
BRCA1	Pre	67	14	20
BRCA1	Post	61	17	23
BRCA2	Pre	64	14	22
BRCA2	Post	42	32	26
PALB2	Pre	42	32	26
PALB2	Post	20	53	27
ATM	Pre	9	73	18
ATM	Post	1.5	79	20
CHEK2	Pre	8	71	21
CHEK2	Post	1.5	79	20

Impact of Genetics on Surgery and Monitoring Approach

Based on the pre-voting results, a summary of recommendations was presented for different mutations and depending on pre- or postmenopausal status. These results are summarized in Table 2 and reflect the impact of evidence and also of individual preference. It should be noted that even for premenopausal patients with *BRCA* mutations, there is a proportion of the panel that prefers intensive screening. These data should be carefully discussed with our patients.

Molecular Diagnostics and Tumor-Infiltrating Lymphocytes

Molecular staging may impact future therapy decision, but based on current knowledge, the overwhelming majority (86%) would not recommend performing ctDNA testing on patients with early-stage breast cancer after surgery in order to assess the risk for recurrence. With regard to testing for tumor-infiltrating lymphocytes (TILs), 2 cases were discussed. First, a 43-year-old woman was presented with primary surgery for stage 1 (size 16 mm), grade 3 TNBC with a TILs score of 75%. A minority (9%) would omit adjuvant chemotherapy in this case, while a vast agreement (88%) recommended adjuvant chemotherapy. In the second case, a patient was presented with primary surgery for stage T1b TNBC, measuring 0.8 cm and with a TILs score of more than 50%. The answer was less unanimous with 35% of votes favoring omission of systemic therapy, perhaps acknowledging recent data about the value of TILs as predictive markers with a favorable course of disease even without adjuvant systemic therapy [18]. Nevertheless, 58% of the panelists voted to recommend adjuvant chemotherapy, and thus essentially against the routine use of TILs since when they do not change therapy strategies, they might not need to be reported on a routine basis.

Ductal Carcinoma in situ – ET

Recently, reinforcing phase-III data with 10 years of follow-up were published with regard to the use of tamoxifen as adjuvant therapy for DCIS after surgery [19] in lower (5 mg daily) than the traditional dose of 20 mg daily, taking into account that pharmacologically the traditional dose might be overstated in many cases but with side effects provided [20]. A case of a healthy postmenopausal woman was discussed who had undergone breast-conserving surgery and radiation therapy for DCIS. The question was posed on which adjuvant therapy should be recommended considering her principal goal to prevent breast recurrence and her concerns about side effects and the presumed modest benefit of ET. Nearly 40% voted to prescribe tamoxifen 5 mg daily according to the convincing Italian data (39.3%), while 26.8% of the panelists would recommend a traditional type of ET (either tamoxifen 20 mg or aromatase inhibitors). A substantial proportion (28.6%) refused to recommend any of these ET options.

Systemic Therapy: Luminal Breast Cancer

The duration of ET depends on the risk of recurrence. In stage I disease, 88% supported 5-year duration of ET. In stage II node-negative disease, 45% favored 5 years and 37% favored 7–8 years, whereas in stage II node-positive disease, 68% would recommend 7–8 years, and in stage III disease, 69% favored 10-year duration. Almost all panelists (97%) agreed that the duration of ET should be based on risk factors, tolerability, and patient preferences [21]. 61% stated that they would not use a genomic assay to determine ET duration. In a premenopausal patient with stage 3 breast cancer after 5 years of GnRH agonist plus nonsteroidal AI, only 8% of the experts would discontinue therapy, and the majority (35%) would recommend continuing with tamoxifen.

Table 3. Adjuvant systemic therapy decisions in a 1.6 cm grade 2 tumor according to nodal involvement and RS (majority vote shaded in gray)

Age	Nodal status	RS	Tamoxifen	OFS + TAM	OFS + AI	Chemo, then ET
47 years	N0	21	29%	22%	18%	24%
47 years	1/3 SLN	21	6%	17%	20%	57%
47 years	N0	17	46%	17%	27%	4%
47 years	1/3 SLN	17	6%	14%	32%	44%
47 years	N0	11	92%	2%	4%	0%
47 years	1/3 SLN	11	18%	23%	29%	29%
34 years	N0	21	4%	8%	26%	61%
34 years	1/3 SLN	21	0%	2.00%	6.00%	90.00%
34 years	N0	12	29%	25%	31%	15%

RS, recurrence score.

Several questions dealt with the indication for chemotherapy in a patient with 0–3 lymph nodes depending on age, the number of involved lymph nodes, and the recurrence score value. In general, the higher the risk and the younger the patient, the more experts opted for a chemotherapy – ET sequence (Table 3). 76% of the panelists (and 79% of the audience) stated the assumption that premenopausal women with ER-positive stage 1–2 disease do not need a tumor genomic signature because they benefit from chemotherapy is false. Almost 70% of the panel stated that a short course of ET before surgery (2–4 weeks) and monitoring its effect on Ki-67 could provide valuable information for waiving chemotherapy. A combination of multigene assay (Oncotype DX) and endocrine response ($Ki\text{-}67_{post}$ </ = 10%) allowed omission of adjuvant chemotherapy in pre- and postmenopausal patients with recurrence score </ = 25 and endocrine response without compromising outcome in the ADAPT trial [22].

In a 57-year-old patient with a 0.7-cm screen-detected cancer (N0) and a high-risk MammaPrint result, only 27% of the panel members would recommend chemotherapy. When asked about a size threshold in such a case, the majority (29%) would recommend chemotherapy followed by ET from 1 cm onward, yet 22% stated that they would not give chemotherapy in a stage I tumor like this. In a 61-year-old patient with a T3 tumor, palpable lymph nodes strongly ER+ and PR+ HER2– and Ki-67 < 15%, 62% of the experts voted for 4 involved lymph nodes as their threshold for recommending chemotherapy.

Regarding the histological subtype, 60% voted FALSE for a statement that lobular breast cancer (grades 1–2, ER+ HER2–, stages 1–3, w/o pleomorphic features) should not receive chemotherapy. In case of a similar lobular tumor with all favorable biological characteristics (grades 1–2, strongly ER+ and PR+, Ki-67 <10%, HER2–, stages 1–3, w/o pleomorphic features) and a low genomic risk score, 63% would not give chemotherapy. In a 38-year-old patient under GnRH agonist and AI with amenorrhea and menopausal symptoms, there was no consensus on whether to monitor estradiol levels (37% no additional testing; 44% every 6 months). In a 39-year-old patient with breakthrough menstrual bleeding under 3-month GnRH agonist, 65% of the panelists would recommend monthly GnRH agonist.

Regarding the number of axillary lymph nodes, about a third of the panelists would recommend axillary dissection in a patient with 1/1 SLN if needed to inform the choice of abemaciclib [23]. In a simultaneous audience vote, 41% of the audience would also go for axillary dissection in this scenario. About 45% of the panel as well as the audience would not use further treatment. 77% of the panelists stated that the decision for adjuvant abemaciclib should only be based on tumor stage and histology but not on Ki-67. In case of a 70-year-old postmenopausal patient with a T3 N1 breast cancer, grade 2 ER+ and PR+, HER2– with low-risk genomic profile and an indicated preference for breast conservation, and thus neoadjuvant ET, 38% of the panelists would use this for 6 months and 35% until best response.

Systemic Therapy: TNBC

Based on the evidence of addition of carboplatin to neoadjuvant treatment of TNBC patients, it has been increasingly implemented as an important component of neoadjuvant regimens [24]. The panel voted on the question of whether carboplatin should be included in the chemotherapy regimen for patients receiving neoadjuvant chemotherapy for stage 2 or 3 TNBC patients also receiving taxane, anthracycline, and cyclophosphamide-based chemotherapy when pembrolizumab is not being administered. 72% of the panel voted in favor of the use of carboplatin and 16% against, whereas 12% abstained.

Including pembrolizumab according to the KEYNOTE-522 trial [25] and particularly achieving pathological complete response has caused a lively debate; however, when the panel was asked if a healthy premenopausal woman who has received a taxane and carboplatin followed by an anthracycline and cyclophosphamide with concurrent pembrolizumab as neoadjuvant

treatment for TNBC and has achieved a pCR should also receive adjuvant pembrolizumab, 59% of the panel voted for adjuvant pembrolizumab, 32% not in favor of adjuvant pembrolizumab, and 9% abstained. This vote acknowledged the lack of evidence supporting that only neoadjuvant combination of pembrolizumab with chemotherapy is beneficial, and as long as we lack this evidence, the treatment should be continued for further 9 cycles and stopped only if side effects lead to such decision.

In case of a 45-year-old woman with stage 2 TNBC who underwent primary surgery for any reason, the panel voted with great majority against the addition of pembrolizumab to adjuvant chemotherapy (62%). 32% of the panelists would consider giving the KEYNOTE-522 treatment including pembrolizumab in such individual cases. The panel of course pointed out the importance of neoadjuvant therapy for TNBC.

Based on the evidence of dose-dense adjuvant chemotherapy improving the outcome of high-risk patients, the panel voted on question whether anthracycline phase of the KN522 regimen with concurrent pembrolizumab should be given every 2 weeks and not every 3 weeks as was done in the clinical trial. Almost 30% of the panel voted in favor of the dose-dense schedule. Nevertheless, 39% of the panel was unsure, due to the lacking evidence for safety and also efficacy confirmation, while 13% voted against and 19% abstained from voting. Several individual cases were summarized, and the preference for treatment voted on by the panel. For example, a healthy 60-year-old woman with a clinical T2N0 TNBC and tumor of about 2–3 cm in size was presented. She is a candidate for BCS without needing neoadjuvant therapy. 65% of the panel still preferred the option of neoadjuvant chemotherapy and pembrolizumab, 21.4% voted only for chemotherapy, 7.7% for primary surgery, and a remaining ~6% abstained from voting. On the question of whether the neoadjuvant pembrolizumab-based chemotherapy should be used for stage 1 TNBC, 46% of the panel voted for the option no, "chemotherapy only" is appropriate neoadjuvant treatment for small TNBC tumors, and 41% voted for primary surgery for small TNBC that do not clinically have indication for neoadjuvant treatment and then to make chemotherapy recommendations. Only 5% voted in favor of pembro-chemotherapy neoadjuvant option and 8% abstained.

In a case where this patient receives neoadjuvant dose-dense AC/T chemotherapy with clinical response but, at surgery, has 0.6 cm of residual cancer in the breast, the panel pre-voted with 71% for adjuvant capecitabine. Somewhat surprising was the vote for a specific patient with TNBC and *BRCA1* mutation. After neoadjuvant KN522 treatment at surgery, this patient has residual disease; for the adjuvant setting, the panel voted with 62% that in addition to pembrolizumab, she should also receive olaparib. We hope that this will be discussed in the consensus manuscript since it may rather be the question if, in this case, only olaparib should be given according to the Olympia trial [26] and pembrolizumab discontinued until more evidence for the safety of the combination becomes available.

Systemic Therapy: HER2 Positive

There were no major clinical trials for early-stage HER2-positive breast cancer over the last 2 years, and thus, the panel did not have much to discuss at the 18th St. Gallen Consensus Conference for this specific disease. There were two pre-voted questions and one additional live vote during the panel session.

The first live question concerned patients who present with clinically node-negative breast cancer and received neoadjuvant TCHP [27]. In case of pCR, the appropriate adjuvant regimen is trastuzumab for 63% of panelists, for 33% both pertuzumab and trastuzumab, and 4% of the panel abstained from voting. For a patient with HER2-positive breast cancer who receives neoadjuvant TCHP and has residual disease at surgery that is HER2 negative by FISH and by IHC, 57% of panelists voted in favor of trastuzumab emtansine as her adjuvant therapy [28], 15% for additional anthracycline therapy, 9% for both previously mentioned, and 18% abstained from the vote.

For a healthy patient who presents with a clinical T1 N0 breast cancer that is HER2 positive in histology and who is a candidate for breast-conserving surgery, the panel was asked which procedure they would recommend. The majority of the panel with 57% voted for primary surgery including nodal assessment because the presence or absence of the nodal disease would inform the adjuvant treatment decision. 25% would prefer to treat the patient neoadjuvantly with THP because residual cancer would inform further treatment, and 9% would treat the patient neoadjuvantly with TCHP.

Impact of Genetics on Adjuvant Therapy

There was an interesting discussion and voting on the impact of genetics on adjuvant therapy. The approval of adjuvant use of olaparib is limited to patients with germline mutation of *BRCA1/2* treated for HER2-negative early breast cancer [26]. However, it was questioned whether, in analogy, adjuvant PARP inhibitor therapy should also be offered to patients with pathogenic *PALB2* mutations. Though some panelists voted in favor (38%), the majority declined its use in this setting (54%). Another question was related to the prescription of adjuvant olaparib therapy in breast cancer patients with a deleterious, somatic tumor with *BRCA1* mutation but no

hereditary germline mutation. Nearly half of the panelists (48%) would give olaparib in these cases if readily available, while 47% would not. Interestingly, nearly half of the panelists (46%) would also recommend adjuvant olaparib to a patient who was treated for ER-positive HER2-positive breast cancer by standard adjuvant therapies, with a *BRCA2* mutation, and at a stage that meets OLYMPIA eligibility criteria; 44% would not acknowledge the lack of evidence for this situation [26].

Bisphosphonates

The question came up on which women with postmenopausal breast cancer adjuvant bone modifying therapy should be recommended. In accordance with the clear trend shown by the Oxford overview [29] with regard to the impact of nodal status and the recent ASCO-OH (CCO) guideline update [30], in summary, a majority (54%) voted in favor of treating those with more advanced disease with bisphosphonates (stage 2 or 3). However, in detail, there was substantial heterogeneity, and some would give bisphosphonates to all postmenopausal patients (14%), to all with ER-positive tumors (12.0%), only to those with stage 2 or 3 if ER positive (32%) and independently from ER status, only to those with stage 2 or 3 disease (14%) or stage 3 disease (8%). A substantial proportion of panelists abstained (20%). As usual, there was no consensus on adjuvant denosumab [31, 32].

Male Breast Cancer

The panel was undecided about the preferred local regional therapy option for male breast cancer in non-*BRCA1/2* mutation carriers: some still advocate conventional mastectomy (42%), but others suggested breast-conserving therapy (lumpectomy plus radiotherapy, 36%), and nipple-sparing mastectomy (13%).

Breast Cancer Survivors

This year, in the 18th St. Gallen International Breast Cancer Consensus, special attention was paid to the well-being of breast cancer survivors. One question was whether, in patients with BMI of more than 25, there is a specific diet that can lower the risk of breast cancer recurrence, and actually nearly three quarters of the panelist (73%) voted against; however, 25% thought that there might be a diet that could help reduce recurrences. Actually, the voting corresponds to a recently published international review and meta-analysis of the evidence [33], although with regard to general health, a Mediterranean diet with ample use of olive oil seems to be beneficial [34]. The panel generally discussed that no special diet but rather keeping lower BMI seems beneficial. The panel (70%) voted in favor of a recommendation that acupuncture should be considered a standard treatment option for breast cancer survivors (and should be appropriately covered by insurance or national governments) to alleviate symptoms of arthralgia related to aromatase inhibitor-based therapy and/or neuropathy related to chemotherapy.

Pregnancy after Breast Cancer

With regard to counseling premenopausal women about the safety of being pregnant after breast cancer and the recently presented data of the IBCSG/BIG/Alliance POSITIVE trial [35], a case was constructed. It showed a 28-year-old patient receiving ovarian function suppression and tamoxifen as treatment for breast cancer with 4 or more involved axillary lymph nodes, and the question was whether one would recommend interrupting ET after 2 years of therapy. Only 14% voted in favor, but the overwhelming majority (79%) would not encourage the patient to get pregnant in that situation, acknowledging the fact that no data exist since only very few patients with more than 4 lymph nodes were included in the POSITIVE trial.

Oligometastatic Disease

A case was presented with a patient who has been diagnosed with ER-negative HER2-positive breast cancer, and staging scans disclose a 4 cm tumor in the breast, positive axillary LN, and an isolated pulmonary nodule. With primary docetaxel-trastuzumab-pertuzumab combination therapy, a complete clinical response was achieved. The majority of the panelists would proceed with local therapy (in total 86%); however, 10% would perform surgery only, 8% would perform radiotherapy only, and 68% would consequently do both surgery and radiotherapy. There were also votes for no local therapy (14%). Accompanying discussions indicated that the majority of panelists voted for "pushing the boundaries of cure" under favorable circumstances of oligometastatic disease.

Summary

The 18th St. Gallen International Breast Cancer Conference was truly a revival of the consensus meeting after the pandemic and a huge success. In this meeting, novel aspects in the treatment of early-stage breast

cancer were discussed. Telemedicine and virtual meetings were endorsed as an important addition. Also, for the first time, burnout of experts and its correlation with disparity between advances in treatment and insufficient adaptation and progress of health systems were discussed.

Both de-escalating surgical methods as well as radiotherapy continue to be important topics. While optimization of systemic treatment largely depends on correct staging at surgery, it remains a topic of debate whether better staging of the axilla in the future may allow for selection of patients in the need for more intensive treatment without further axillary surgery. There has been some improvement in selection of patients with hormone receptor-positive disease in the need for chemotherapy or more intensive endocrine treatment, including the combination of multigene assay (Oncotype DX) and endocrine response as a dynamic biomarker as suggested in the ADAPT trial.

For high-risk endocrine disease, abemaciclib has been endorsed as treatment regardless of Ki-67, and for high-risk *BRCA* mutated patients with endocrine disease even combining all options including olaparib followed by abemaciclib may be considered. Immune checkpoint inhibitor pembrolizumab has been adopted for treatment of TNBC according to the KN522 study, opening a number of questions for future consensus meetings, including the need for the adjuvant proportion of treatment.

TILs have been accepted as prognostic markers but may not need to be reported in pathological reports because their role for treatment decisions remains unclear. In the future, biomarkers such as circulating tumor DNA will increasingly be implemented in clinical trials but currently have no role in the treatment of early-stage breast cancer. Altogether, many controversial topics have been solved or at least addressed, and we are looking forward to both the full consensus manuscript as well as to the 19th SG-BCC to be held in Vienna in March 2025.

Conflict of Interest Statement

Marija Balic reports consulting fees, lecture honoraria, advisory board memberships, and travel grants from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly, Gilead, Lenis, MSD, Novartis, Pfizer, and Roche, as well as research funding from Eli Lilly, Novartis, Pierre Fabre, and Pfizer. Christoph Thomssen reports receiving honoraria for lectures for advisory boards and lectures for Amgen, AstraZeneca, Celgene, Daiichi Sankyo, Eisai, Eli Lilly, MSD, Mylan, NanoString, Novartis, Pfizer, Pierre Fabre, Roche, and Vifor as well as research support from American Diagnostica, Affymetrix, and NanoString. Michael Gnant reports personal fees/travel support from AstraZeneca, Daiichi Sankyo, Eli Lilly, Menarini-Stemline, MSD, Novartis, Pierre Fabre, and Veracyte; an immediate family member is employed by Sandoz. Nadia Harbeck reports honoraria or consultation fees from the following entities: AstraZeneca, Daiichi Sankyo, Gilead, Lilly, MSD, Novartis, Pfizer, Roche, Sandoz, Sanofi, and Seagen.

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Author Contributions

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