

Update Breast Cancer 2023 Part 3 – Expert Opinions of Early Stage Breast Cancer Therapies

Update Mammakarzinom 2023 Teil 3 – Expertenmeinungen zu Brustkrebs in frühen Krankheitsstadien



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ABSTRACT

The St. Gallen (SG) International Breast Cancer Conference is held every two years, previously in St. Gallen and now in Vienna. This year (2023) marks the eighteenth edition of this conference, which focuses on the treatment of patients with early-stage breast carcinoma. A panel discussion will be held at the end of this four-day event, during which a panel of experts will give their opinions on current controversial issues relating to the treatment of early-stage breast cancer patients. To this end, questions are generally formulated in such a way that clinically realistic cases are presented – often including poignant hypothetical modifications. This review reports on the outcome of these discussions and summarises the data associated with individual questions raised.

ZUSAMMENFASSUNG

In einem 2-jährigen Rhythmus fand in St. Gallen in früheren Jahren und nun in Wien die „St. Gallen (SG) International Breast Cancer Conference“ statt. Dieses Jahr (2023) wurde diese Konferenz, die sich mit der Behandlung von Patientinnen in Frühstadien des Mammakarzinoms beschäftigt, zum 18. Mal durchgeführt. Am Ende dieser 4-tägigen Veranstaltung wird eine Panel-Abstimmung abgehalten, bei der ein Expertengremium über aktuelle kontroverse Themen bei der Behandlung von Brustkrebspatientinnen in Frühstadien abstimmt. Hierbei werden die Fragen meistens so formuliert, dass klinisch realistische Fälle – oft in verschiedenen Modifikationen – vorgestellt werden. Diese Übersichtsarbeit berichtet von den Abstimmungsergebnissen und fasst die mit den jeweiligen Fragen verbundene Datenlage zusammen.

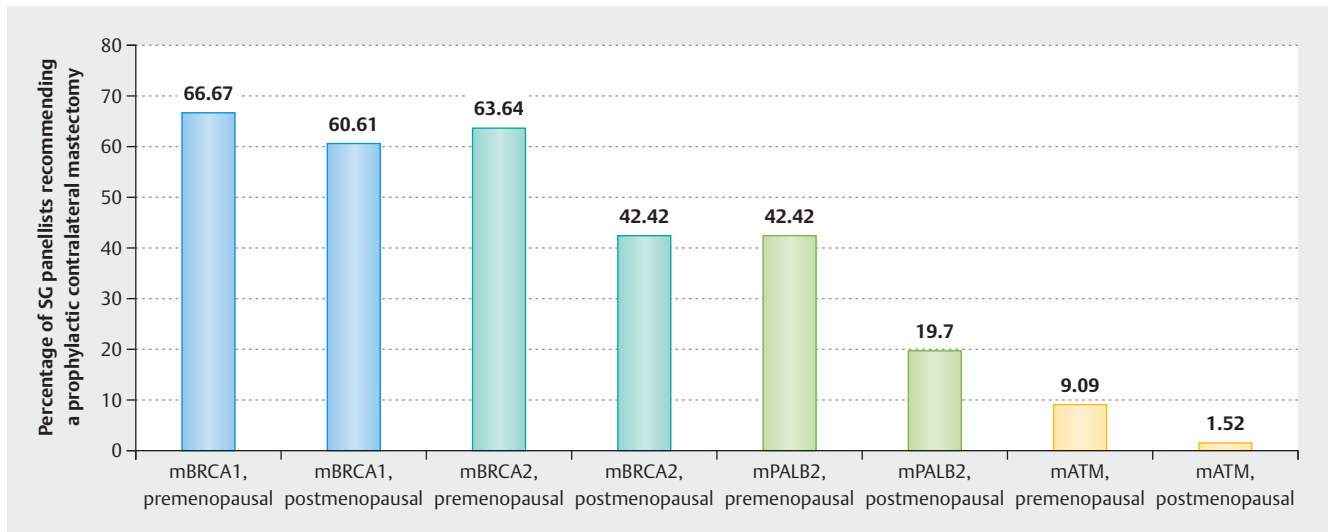
Background

The St. Gallen International Breast Cancer Conference in Vienna focuses on the treatment of patients with early stages of breast carcinoma. After three days of predominantly review lectures on key topics, on day four, a panel discusses key topics on the treatment of patients with early-stage breast carcinoma. The questions and their responses are recorded in this paper (Supplementary Table S1), which were assessed by the St. Gallen panellists (SG panellists; Supplementary Table S2). Furthermore, a number of selected topics are presented in a research context, which provides more detailed background information for the assessment of the questions.

Quality of Life and Survivorship

One study that has been discussed since the Breast Cancer Conference in San Antonio in 2022 because of its clinical relevance to patients is the POSITIVE study. This study included young female patients on antihormone therapy who wanted to have children. The

relapse rate was determined if endocrine therapy was interrupted for a maximum of two years. Out of the 516 patients included in the study, approximately 75% became pregnant and 44 had a relapse at a median follow-up of 41 months [1]. In Vienna/St. Gallen, two cases were presented, one of a premenopausal patient with more than three positive lymph nodes (high risk of relapse) and one of a still relatively young woman intending to preserve fertility after endocrine therapy (age 28). In both cases, the majority of SG panellists (approx. 78%) would not have opted to follow the POSITIVE study approach (Supplementary Table S1; Questions 4 and 5). Apparently, the high risk of relapse in the cases presented and the prospect of pregnancy after the end of regular endocrine therapy discouraged experts to opt to discontinue endocrine therapy. It remains to be determined how the data from the POSITIVE study will be assessed clinically based on a longer follow-up period.



► **Fig. 1** Presentation of results across multiple questions on how many SG panellists would recommend contralateral mastectomy in breast cancer patients in different situations and with different identified germline mutations (mBRCA1: BRCA1 germline mutation; mBRCA2: BRCA2 germline mutation; mPALB2: PALB2 germline mutation; mATM: ATM germline mutation).

Genetics

Although a number of breast cancer risk genes have been previously established [2–8] and approximately 40% of the family breast cancer risk can be explained [9], the mutation frequencies for most established breast cancer risk genes are low. After *BRCA1/2* mutations, *PALB2* mutations are among the most common germline mutations. However, the frequency among breast cancer patients is still very low at 0.5–2%, and in individuals without breast cancer, the mutation rate is approximately 0.1% [3]. Therefore, for most genes genotyped in panel testing [10], individual evidence for preventive and therapeutic interventions will be difficult to collect, simply because of low case numbers. Against this backdrop, the SG panel decisions were of particular interest. Here, the SG panel asked for opinions on contralateral prophylactic mastectomy for patients who received a new breast carcinoma diagnosis and a diagnosis of a mutation in different breast cancer risk genes. The panel decisions are shown in ► **Fig. 1**. It can be concluded that SG panellists are less likely to recommend contralateral mastectomy for lower lifetime risk and postmenopausal patients than for higher risk and younger patients. Particularly in the case of intermediate-risk constellations, opinions still differ considerably (e.g. in the case of *PALB2* mutations or in postmenopausal patients with *BRCA2* mutations). These results are consistent with the lifetime risk estimates published by the Breast Cancer Association Consortium (BCAC) (► **Fig. 2**) [3].

Adjuvant Endocrine Therapy and Chemotherapy Decisions in HRpos/HER2neg Patients

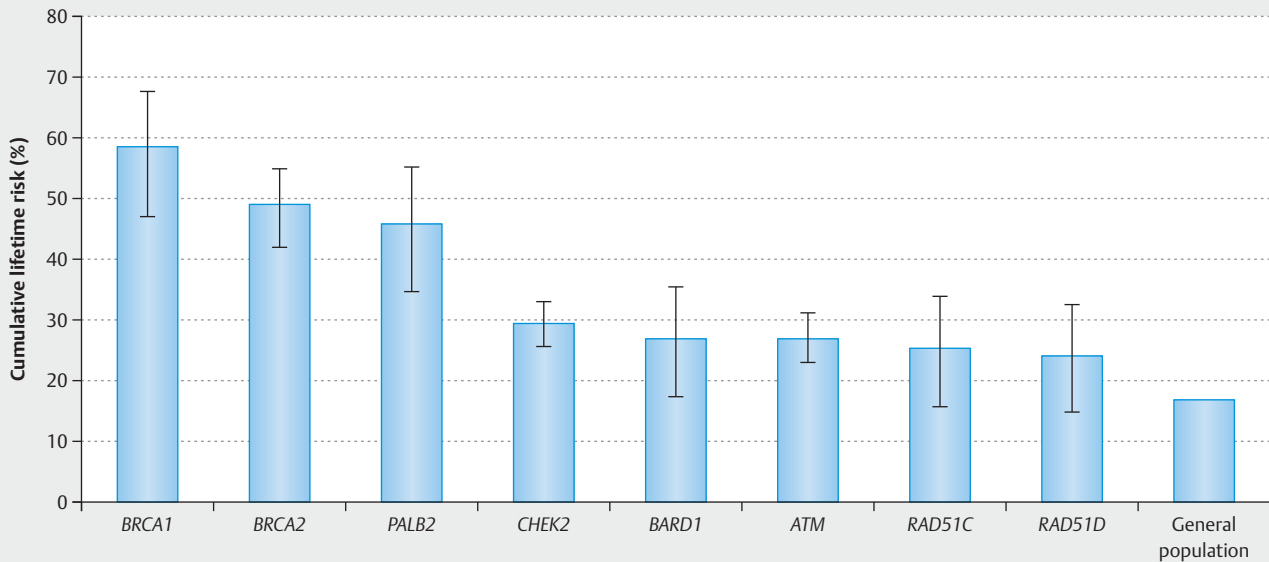
Endocrine therapies and abemaciclib

The main issues discussed in adjuvant endocrine therapy are:

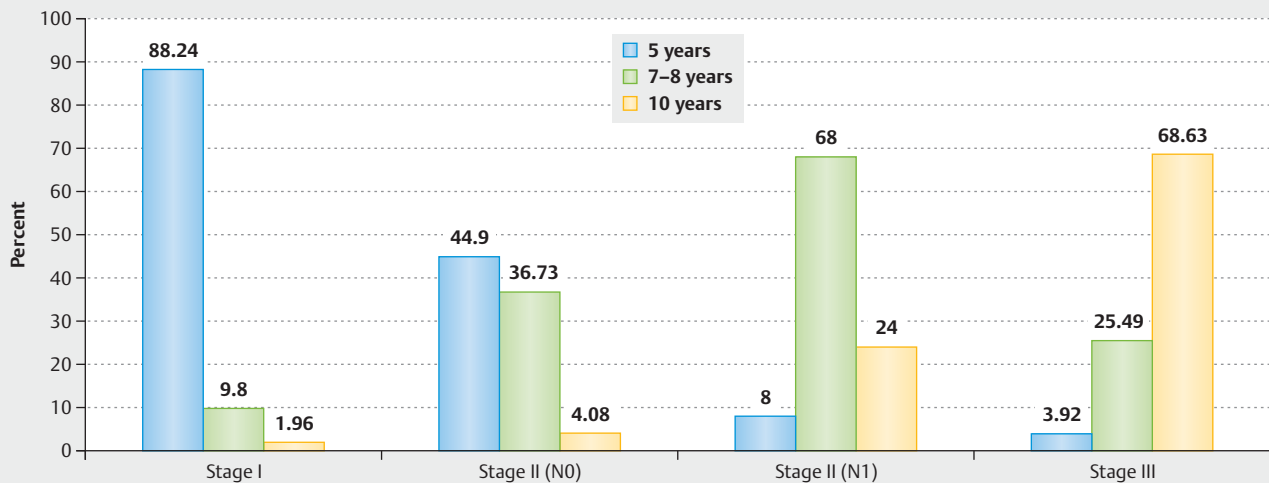
- the length of the adjuvant endocrine therapy,
- the use of CDK4/6 inhibitors (only abemaciclib has been approved to date),
- the use of aromatase inhibitors + ovarian function suppression (OFS) in premenopausal patients,
- the addition of OFS to tamoxifen therapy in premenopausal patients.

With regard to the indication for chemotherapy, different biomarkers have been established that can reliably identify patients with an excellent prognosis [11–14]. In premenopausal patients, the situation is more complex because, in principle, three different endocrine therapies (tamoxifen, tamoxifen + GnRH analogue and aromatase inhibitor + GnRH analogue) are available. Ovarian Function Suppression (OFS) with GnRH analogues is an effective medication to suppress ovary function. However, after chemotherapy, a large proportion of premenopausal patients have persistent chemotherapy-induced amenorrhea [15–17]. In the premenopausal setting, risk, indication for chemotherapy and implementation of endocrine therapy therefore influence each other.

With regard to the length of endocrine therapy, there is a clear trend among SG panellists to consider that the length of therapy is dependent on stage (► **Fig. 3, Questions 74 to 77**). Interestingly, a length of 7–8 years encompasses a pertinently large group of patients of all stages. The assessment of the benefit/risk ratio based on the large number of studies conducted appears to favour the duration of 7–8 years of general therapy [18–26]. A ge-



► **Fig. 2** Lifetime risk until the age of 80. The age of onset for the eight validated breast cancer risk genes [3] (Illustration from [65]).

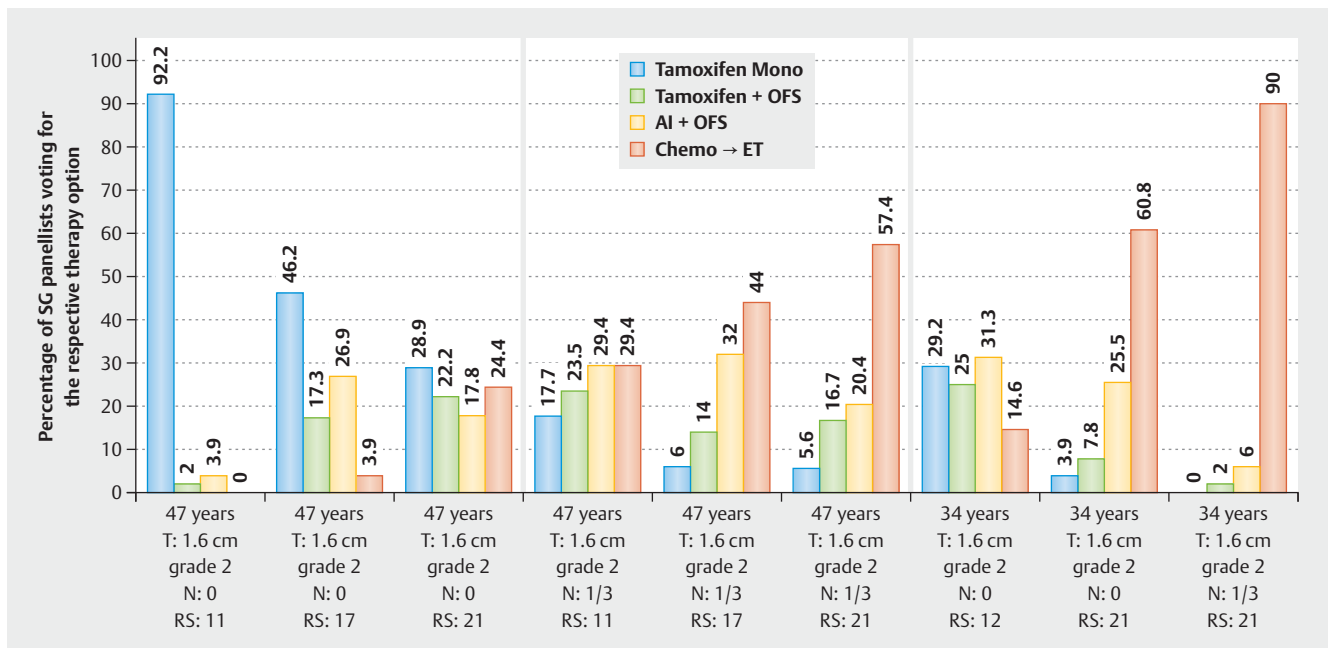


► **Fig. 3** The panel decision for different stages of HRpos/HER2neg breast carcinoma in relation to the length of endocrine therapy.

nomic test does not appear to be necessary (**Questions 78 and 79**) to determine the duration of endocrine therapy.

To date, there are positive studies for two CDK4/6 inhibitors, the monarchE study [27–29] and the NATALEE/TRIO-033 study [30]. Abemaciclib is already approved for patients at high risk. In Europe, the approval is based on patients corresponding to cohort I. These were patients with at least 4 positive lymph nodes or 1–3 positive lymph nodes and additionally a tumour of at least 5 cm in size or a tumour grading of 3. In the USA, the use of abemaciclib was additionally dependent on the biomarker Ki-67. This has been repeatedly criticised by the research and clinical community [31, 32]. This was also the view of the majority of SG pan-

ellists (77.27%, **Question 80**). In fact, the US Food and Drug Administration (FDA) recently adjusted the indication so that the criteria in the US are now the same as in Europe [33]. In relation to the indication for abemaciclib, the exact prognosis of patients is expected to play an important role in the future. For example, determining the lymph node status in the context of the current clinical procedure is also important for axillary staging. It is not always feasible to remove four lymph nodes. For example, the SG panel dealt with the situation where only one lymph node was assessed as part of an axillary sentinel node biopsy and this lymph node contained tumour cells. With a grading of 2 and a tumour size of 2.3 cm, this hypothetical patient would have received adju-



► **Fig. 4** SG panellists therapy choices for different scenarios involving treatment of premenopausal patients with HRpos/HER2neg breast carcinoma (T: Tumour size; N: Nodal status; RS: Oncotype Recurrence Score).

vant chemotherapy. A considerable proportion of SG panellists (33.6%) would have extended the axillary resection to obtain all of the necessary information to support an indication amenable to abemaciclib (Supplementary Table S1, Question 81). Most colleagues would not have carried out any further therapy (44.4%). Some models are described in the literature that calculate the risk for further lymph nodes [34]. In the case presented in Question 81, the risk of additional positive lymph nodes is 15% [35] with the MSKCC calculator and 26% [36] with the MD Anderson calculator, assuming otherwise average patient and tumour characteristics. It is unclear whether SG panellists also assessed the risk in this way and the distribution of the answers given was based on this assumed risk, or whether a different risk was intuitively assumed.

Chemotherapy in HRpos/HER2neg patients

One of the most important clinical questions of our time is to identify which HRpos/HER2neg patients can be spared chemotherapy. Accordingly, a large block of the SG panellist discussions were devoted to this issue. Decisions were formulated for different scenarios. It became clear that the Recurrence Score played a major role in the treatment decision for or against chemotherapy, particularly in young patients (in this case a 34-year-old woman). In the case study of the 34-year-old patient, 90% of panellists opted for chemotherapy if at least one lymph node was involved and the Recurrence Score was 21. The same situation in a 47-year-old female patient, resulted in only 57% of panellists opting for chemotherapy (Supplementary Table S1, Questions 86 and 92). If necessary, SG panellists were guided by the recently presented subgroup analysis of the TailorX trial, which investigated the effect of chemotherapy in node-negative patients [37]. The

analysis showed a benefit of chemotherapy especially in premenopausal patients who had a Recurrence Score of at least 21 and also a high clinical risk. In this group, the absolute difference for distant metastasis-free survival was 11.7% after 12 years, if chemotherapy had also been given before endocrine therapy [37].

On the other hand, SG panellists were only convinced of tamoxifen monotherapy without prior chemotherapy in 92.2% of cases if the patient was 47 years old, had no involved lymph nodes and the recurrence score was 11 or less. All panel decisions for the case variants are shown in ► Fig. 4 and further questions on the topic can be found in the Supplementary Table S1, Questions 83 to 103.

Triple Negative Therapy and BRCA-associated Tumours

For patients with triple-negative breast carcinoma and increased risk of relapse, the two therapy options olaparib [38,39] and pembrolizumab [40,41] have been included in therapy management in recent years.

Pembrolizumab in the adjuvant situation

The design of the Keynote 522 study has raised specific questions that have been discussed more or less prominently in several countries [42]. The SG panellists also faced some of these controversies.

Obviously, the question is whether pembrolizumab therapy should be continued after pCR following neoadjuvant therapy. At just under 60%, the majority of SG panellists were in favour of continuing therapy in any case (Supplementary Table S1, Ques-

tion 107). In the Keynote 522 trial, no dose-dense chemotherapy was given in combination with pembrolizumab. This naturally leads to the question of whether dose-dense chemotherapy should be given in combination with pembrolizumab, as should be the standard of care for patients at increased risk of relapse [43]. This is countered by considerations that dose-dense therapy in combination with pembrolizumab has not been tested and the toxicity of this regimen is also unknown. Almost 30% of SG panellists indicated that they would opt for a dose-dense chemotherapy in this background, also in combination with pembrolizumab (Question 106). The remaining SG panellists would not support this or were unsure about this issue.

Even though the criteria for pembrolizumab therapy are set by the Keynote 522 study (tumour of at least 2 cm or at least one positive lymph node), the question was discussed whether patients with smaller tumours without positive lymph nodes should also receive neoadjuvant therapy with chemotherapy and pembrolizumab. This question was answered “yes” by only 4.6% of SG panellists (Question 109). Accordingly, most colleagues fall within the scope of the approval in this regard. There are data from small single-arm trials in which stage I patients were also treated with chemotherapy and pembrolizumab [44]. The pCR rates appeared to be comparable to those in the Keynote 522 study.

BRCA-associated tumours

In the case of a germline mutation in *BRCA1* or *BRCA2*, the additional question arises as to whether treatment with olaparib should be administered in addition to pembrolizumab after neoadjuvant therapy. Given the overall survival benefit of olaparib, the PARP inhibitor is a therapy recommended in most national and international treatment guidelines. SG panellists addressed this question in the context of a patient who had not achieved pCR after neoadjuvant therapy with chemotherapy and pembrolizumab (Question 114). The vast majority of SG panellists recommended the administration of olaparib (86% overall). A total of 62% of SG panellists would combine the therapies and 24% would prescribe them sequentially. SG panellists did not consider capecitabine if this hypothetical patient presented with a *BRCA1* mutation.

In the case of a patient with HRpos/HER2neg breast carcinoma, a germline mutation in *BRCA1* or *BRCA2* raises the question of combination or sequential abemaciclib treatment. A hypothetical patient with a *BRCA2* mutation and a high risk of relapse was considered to address this issue (Question 115). Just under half of SG panellists favoured a sequential treatment. Combination therapy is generally not supported for these types of cases and did not figure among the possible responses that could be selected by panellists. It is important to note that in the OlympiA trial, standard adjuvant endocrine therapy was given together with olaparib [39].

While in patients without a *BRCA1/2* mutation with stage II or III TNBC tumours, most of the SG panellists (78%) had opted for platinum-containing chemotherapy (Question 104), the question is slightly different in patients with a *BRCA1/2* mutation. In this case, only 37% of SG panellists clearly opted in favour of platinum-containing chemotherapy. This is for instance in line with the GeparSixto data. In this study, which randomised for or

against platinum-containing chemotherapy, it turned out that patients with a *BRCA1/2* mutation also responded extremely well to platinum-free chemotherapy and it was rather the patients without a *BRCA1/2* mutation who benefited most from platinum therapy [45].

HER2-positive Disease

For patients with HER2-positive disease, three standard therapies are established with trastuzumab, pertuzumab [46–48] and T-DM1 [49]. Neratinib is also approved for the later therapy setting [50–52]. Innovations can be expected, for example, from the Destiny-Breast05 trial, which compares T-DM1 post-neoadjuvant with trastuzumab-deruxtecan [53]. This study is still recruiting.

Accordingly, no major controversies have to date arisen in this setting. The majority of SG panellists agreed that chemotherapy with paclitaxel monotherapy is an option for small tumours (Question 111) and that after neoadjuvant therapy with trastuzumab, pertuzumab, taxane and platinum which achieves pCR, pertuzumab does not need to be continued after surgery as an adjuvant (Question 112).

Oligometastatic Disease

The boundaries between palliative and curative therapy intentions are shifting

A number of retrospective studies have shown that patients with favourable advanced breast cancer prognoses achieve better overall survival (hazard ratios between 0.6 and 0.7) when they are treated locally like an early-stage patient (including surgery and radiotherapy) [54–58]. Against this background, this therapy strategy is accepted, but it can be argued that most patients will nevertheless die from their advanced tumour disease and that considerations regarding the side effects and adverse effects of the therapy should be paramount [58]. Data based on high-quality evidence on the topic are currently not available.

Three questions have been asked in this context (Questions 118 to 120). Three different cases of oligometastatic disease were presented, one triple negative patient and two HER2 positive patients (one hormone receptor positive and the other hormone receptor negative). For all cases, SG panellists voted for extensive therapy of the primary disease (57–68%) analogous to the situation of patients with early-stage disease. With the new therapy options with which an overall survival advantage could already be demonstrated in the metastatic situation (CDK4/6 inhibitors, trastuzumab-deruxtecan, sacituzumab-govitecan), this question will certainly gain further relevance.

Molecular Diagnostics

Analysis of ctDNA not yet clinical routine in patients with early-stage breast carcinoma

Several studies have shown the added prognostic value of determining circulating tumour DNA (ctDNA) for patients with early

stages of disease [59–61]. It is quite conceivable that circulating tumour DNA will make a significant contribution to prognosis and therapy planning for patients with early-stage breast cancer. It can also be assumed in further follow-up that an indication for active disease can be beneficial. With tumour markers and circulating tumour cells, it has already been shown that even 2 years after the primary diagnosis, a further classification into prognostic groups is possible [62, 63].

It should be noted, however, that despite advances in ctDNA determinations in the early treatment setting, no studies have yet been conducted that have included ctDNA in a treatment or therapy management decision either at the time of primary diagnosis or in the further course of disease. The SG panellists' responses to these questions are therefore also relatively clear (Questions 122 to 126). Almost all SG panellists believed that ctDNA testing should not be performed as a routine test at this point in time (86%) and that prospective studies on the topic should be conducted first (89%). Also, results from clinical trials should not currently be used to support routine treatment decisions. The SURVIVE study (<https://www.survive-studie.de>) [64], which is currently recruiting in Germany, is looking at precisely this issue. The study design of the SURVIVE study is shown in ► Fig. 5. Patients who have a high risk of recurrence are included in this study. Primary therapy must not have been completed for more than two years. Patients will be randomised into an arm where intensified follow-up will take place based on regular examinations of individualised (informative) ctDNA determinations. For this purpose, the primary tumour is examined for mutations. This individual mutation profile is then examined in the blood sample in addition to established tumour markers and circulating tumour cells.

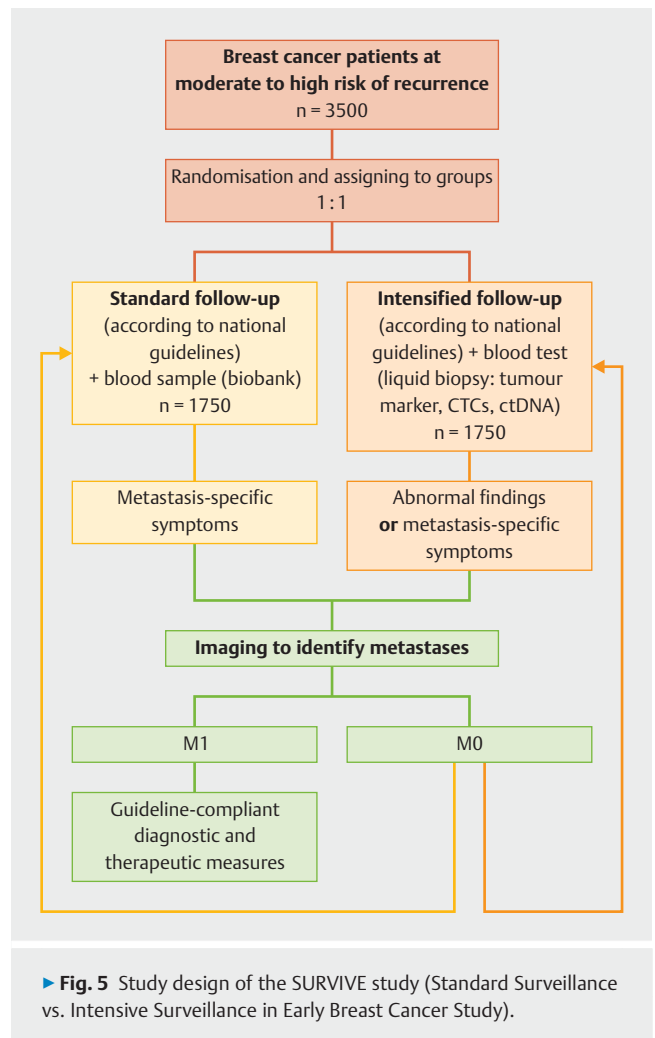
Available data on the interesting ctDNA biomarker is likely to increase significantly over the next few years. In addition to measuring tumour activity, ctDNA assays also provide insights on the genomic profile of tumour activity and could therefore influence treatment decisions in the case of a corresponding positive test.

Prospects

Further aspects on histopathological factors, ductal carcinoma in situ, male breast cancer, radiotherapy, surgical therapies and bone therapies are also included in Supplementary Table S1.

The decisions of the SG panel in Vienna represent a sentiment of many international colleagues (Supplementary Table S2) and therefore also take into account the preferences of different countries and health systems. It cannot be ruled out that this was also taken into account in the decisions and that SG panellists voted along these lines.

Since the implementation of oncology therapies is always an individual decision between the patient and the caregivers, the case variations are of particular value, because they shed light on the trends that cause slight changes in the disease constellation like no other conference. This should help the patients and the practitioners to better understand their situation and gain perspective.



Supplementary Data

- Supplementary Table S1: Polling questions among the St. Gallen panellists.
- Supplementary Table S2: Panellists of the St. Gallen Conference 2023 (after [66]).

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Conflict of Interest

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T. N. F. has participated on advisory boards for Amgen, Daiichi-Sankyo, Novartis, Pfizer, and Roche and has received honoraria for lectures from Amgen, Celgene, Daiichi-Sankyo, Roche, Novartis and Pfizer.

A. D. H. received speaker and consultancy honoraria from AstraZeneca, Genomic Health, Roche, Novartis, Celgene, Lilly, MSD, Eisai, Teva, Tesaro, Daiichi-Sankyo, Hexal and Pfizer.

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References

- Partridge AH, Niman SM, Ruggeri M et al. Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsive breast cancer. San Antonio Breast Cancer Symposium 2022; 2022: GS4-09
- Hu C, Hart SN, Gnanaolivu R et al. A Population-Based Study of Genes Previously Implicated in Breast Cancer. *N Engl J Med* 2021; 384: 440–451. doi:10.1056/NEJMoa2005936
- Breast Cancer Association Consortium; Dorling L, Carvalho S, Allen J et al. Breast Cancer Risk Genes – Association Analysis in More than 113,000 Women. *N Engl J Med* 2021; 384: 428–439. doi:10.1056/NEJMoa1913948
- Couch FJ, Hart SN, Sharma P et al. Inherited mutations in 17 breast cancer susceptibility genes among a large triple-negative breast cancer cohort unselected for family history of breast cancer. *J Clin Oncol* 2015; 33: 304–311. doi:10.1200/JCO.2014.57.1414
- Fasching PA, Yadav S, Hu C et al. Mutations in BRCA1/2 and Other Panel Genes in Patients With Metastatic Breast Cancer—Association With Patient and Disease Characteristics and Effect on Prognosis. *J Clin Oncol* 2021; 39: 1619–1630. doi:10.1200/JCO.20.01200
- Rhiem K, Auber B, Briest S et al. Consensus Recommendations of the German Consortium for Hereditary Breast and Ovarian Cancer. *Breast Care (Basel)* 2022; 17: 199–207. doi:10.1159/000516376
- Rhiem K, Bucker-Nott HJ, Hellmich M et al. Benchmarking of a checklist for the identification of familial risk for breast and ovarian cancers in a prospective cohort. *Breast J* 2019; 25: 455–460. doi:10.1111/tbj.13257

- [8] Hauke J, Horvath J, Gross E et al. Gene panel testing of 5589 BRCA1/2-negative index patients with breast cancer in a routine diagnostic setting: results of the German Consortium for Hereditary Breast and Ovarian Cancer. *Cancer Med* 2018; 7: 1349–1358. doi:10.1002/cam4.1376
- [9] Wunderle M, Gass P, Haberle L et al. BRCA mutations and their influence on pathological complete response and prognosis in a clinical cohort of neoadjuvantly treated breast cancer patients. *Breast Cancer Res Treat* 2018; 171: 85–94. doi:10.1007/s10549-018-4797-8
- [10] Foulkes WD. The ten genes for breast (and ovarian) cancer susceptibility. *Nat Rev Clin Oncol* 2021; 18: 259–260. doi:10.1038/s41571-021-00491-3
- [11] Cardoso F, van't Veer LJ, Bogaerts J et al. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer. *N Engl J Med* 2016; 375: 717–729. doi:10.1056/NEJMoa1602253
- [12] Paik S, Shak S, Tang G et al. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. *N Engl J Med* 2004; 351: 2817–2826. doi:10.1056/NEJMoa041588
- [13] Sparano JA, Gray RJ, Makower DF et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. *N Engl J Med* 2018; 379: 111–121. doi:10.1056/NEJMoa1804710
- [14] Sparano JA, Gray RJ, Makower DF et al. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer. *N Engl J Med* 2015; 373: 2005–2014. doi:10.1056/NEJMoa1510764
- [15] Wang Y, Li Y, Liang J et al. Chemotherapy-Induced Amenorrhea and Its Prognostic Significance in Premenopausal Women With Breast Cancer: An Updated Meta-Analysis. *Front Oncol* 2022; 12: 859974. doi:10.3389/fonc.2022.859974
- [16] Guerrero A, Gavila J, Folkler E et al. Incidence and predictors of ovarian function recovery (OFR) in breast cancer (BC) patients with chemotherapy-induced amenorrhea (CIA) who switched from tamoxifen to exemestane. *Ann Oncol* 2013; 24: 674–679. doi:10.1093/annonc/mds464
- [17] Ruddy KJ, Schaid DJ, Partridge AH et al. Genetic predictors of chemotherapy-related amenorrhea in women with breast cancer. *Fertil Steril* 2019; 112: 731–739.e1. doi:10.1016/j.fertnstert.2019.05.018
- [18] Davies C, Pan H, Godwin J et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet* 2013; 381: 805–816. doi:10.1016/S0140-6736(12)61963-1
- [19] Gray RG, Rea D, Handley K et al., and on behalf of the aTTom Collaborative Group. aTTom: Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6,953 women with early breast cancer. *J Clin Oncol* 2013; 31: 18_suppl, 5-5
- [20] Petrelli F, Coinu A, Cabiddu M et al. Five or more years of adjuvant endocrine therapy in breast cancer: a meta-analysis of published randomised trials. *Breast Cancer Res Treat* 2013; 140: 233–240. doi:10.1007/s10549-013-2629-4
- [21] Goss PE, Ingle JN, Martino S et al. Randomized trial of letrozole following tamoxifen as extended adjuvant therapy in receptor-positive breast cancer: updated findings from NCIC CTG MA.17. *J Natl Cancer Inst* 2005; 97: 1262–1271. doi:10.1093/jnci/dji250
- [22] Goss PE, Ingle JN, Pritchard KI et al. Extending Aromatase-Inhibitor Adjuvant Therapy to 10 Years. *N Engl J Med* 2016; 375: 209–219. doi:10.1056/NEJMoa1604700
- [23] Jakesz R, Greil R, Gnant M et al. Extended adjuvant therapy with anastrozole among postmenopausal breast cancer patients: results from the randomized Austrian Breast and Colorectal Cancer Study Group Trial 6a. *J Natl Cancer Inst* 2007; 99: 1845–1853. doi:10.1093/jnci/djm246
- [24] Mamounas EP, Bandos H, Lembersky BC et al. Ten-year results from NRG Oncology/NSABP B-42: A randomized, double-blinded, placebo-controlled clinical trial of extended adjuvant endocrine therapy with letrozole (L) in postmenopausal women with hormone-receptor+ breast cancer (BC) who have completed previous adjuvant therapy with an aromatase inhibitor (AI). *San Antonio Breast Cancer Symposium 2019; 2019: GS4-01*
- [25] Del Mastro L, Mansutti M, Bisagni G et al. Extended therapy with letrozole as adjuvant treatment of postmenopausal patients with early-stage breast cancer: a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol* 2021; 22: 1458–1467. doi:10.1016/S1470-2045(21)00352-1
- [26] Gnant M, Fitzal F, Rinnerthaler G et al. Duration of Adjuvant Aromatase-Inhibitor Therapy in Postmenopausal Breast Cancer. *N Engl J Med* 2021; 385: 395–405. doi:10.1056/NEJMoa2104162
- [27] Johnston SRD, Toi M, O'Shaughnessy J et al. Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial. *Lancet Oncol* 2023; 24: 77–90. doi:10.1016/S1470-2045(22)00694-5
- [28] Harbeck N, Rastogi P, Martin M et al. Adjuvant abemaciclib combined with endocrine therapy for high-risk early breast cancer: updated efficacy and Ki-67 analysis from the monarchE study. *Ann Oncol* 2021; 32: 1571–1581. doi:10.1016/j.annonc.2021.09.015
- [29] Johnston SRD, Harbeck N, Hegg R et al.; monarchE Committee Members and Investigators. Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2-, Node-Positive, High-Risk, Early Breast Cancer (monarchE). *J Clin Oncol* 2020; 38: 3987–3998. doi:10.1200/JCO.20.02514
- [30] Slamon D, Stroyakovskiy D, Yardley D et al. Phase III NATALEE trial of ribociclib + endocrine therapy as adjuvant treatment in patients with HR+/HER2- early breast cancer. *ASCO Annual Meeting 2023; 2023: LBA500*
- [31] Tarantino P, Burstein HJ, Lin NU et al. Should Ki-67 be adopted to select breast cancer patients for treatment with adjuvant abemaciclib? *Ann Oncol* 2022; 33: 234–238. doi:10.1016/j.annonc.2021.12.004
- [32] Royce M, Mulkey F, Osgood C et al. US Food and Drug Administration Expanded Adjuvant Indication of Abemaciclib in High-Risk Early Breast Cancer. *J Clin Oncol* 2023; 41: 3456–3457. doi:10.1200/JCO.23.00615
- [33] United States Food and Drug Administration (FDA). FDA expands early breast cancer indication for abemaciclib with endocrine therapy. Accessed April 03, 2023 at: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-expands-early-breast-cancer-indication-abemaciclib-endocrine-therapy>
- [34] Coutant C, Olivier C, Lambaudie E et al. Comparison of Models to Predict Nonsentinel Lymph Node Status in Breast Cancer Patients With Metastatic Sentinel Lymph Nodes: A Prospective Multicenter Study. *J Clin Oncol* 2009; 27: 2800–2808. doi:10.1200/jco.2008.19.7418
- [35] Memorial Sloan Kettering Cancer Center. Breast Cancer Nomogram: Breast Additional Non SLN Metastases. 2023. Accessed April 02, 2023 at: <https://nomograms.mskcc.org/Breast/BreastAdditionalNonSLNMetastasesPage.aspx>
- [36] MD Anderson Cancer Center. Breast Cancer Nomogram to Predict Additional Positive Non-SLN, without Neoadjuvant Chemotherapy. 2023. Accessed April 03, 2023 at: http://www3.mdanderson.org/app/medcalc/bc_nomogram2
- [37] Sparano J, Gray RJ, Makower D et al. Trial Assigning Individualized Options for Treatment (TAILORx): An update including 12-year event rates. *San Antonio Breast Cancer Symposium 2022; 2022: GS1-05*
- [38] Geyer CE jr., Garber JE, Gelber RD et al. Overall survival in the OlympiA phase III trial of adjuvant olaparib in patients with germline pathogenic variants in BRCA1/2 and high-risk, early breast cancer. *Ann Oncol* 2022; 33: 1250–1268. doi:10.1016/j.annonc.2022.09.159

- [39] Tutt ANJ, Garber JE, Kaufman B et al. Adjuvant Olaparib for Patients with BRCA1- or BRCA2-Mutated Breast Cancer. *N Engl J Med* 2021; 384: 2394–2405. doi:10.1056/NEJMoa2105215
- [40] Schmid P, Cortes J, Dent R et al. Event-free Survival with Pembrolizumab in Early Triple-Negative Breast Cancer. *N Engl J Med* 2022; 386: 556–567. doi:10.1056/NEJMoa2112651
- [41] Schmid P, Cortes J, Pusztai L et al. Pembrolizumab for Early Triple-Negative Breast Cancer. *N Engl J Med* 2020; 382: 810–821. doi:10.1056/NEJMoa1910549
- [42] Bonadio RC, Tarantino P, Testa L et al. Management of patients with early-stage triple-negative breast cancer following pembrolizumab-based neoadjuvant therapy: What are the evidences? *Cancer Treat Rev* 2022; 110: 102459. doi:10.1016/j.ctrv.2022.102459
- [43] Ditsch N, Kolberg-Liedtke C, Friedrich M et al. AGO Recommendations for the Diagnosis and Treatment of Patients with Early Breast Cancer: Update 2021. *Breast Care (Basel)* 2021; 16: 214–227. doi:10.1159/000516419
- [44] Fasching PA, Hein A, Kolberg HC et al. Pembrolizumab in combination with nab-paclitaxel for the treatment of patients with early-stage triple-negative breast cancer – A single-arm phase II trial (Neo-ImmunoBoost, AGO-B-041). *Eur J Cancer* 2023; 184: 1–9. doi:10.1016/j.ejca.2023.01.001
- [45] Hahnen E, Lederer B, Hauke J et al. Germline Mutation Status, Pathological Complete Response, and Disease-Free Survival in Triple-Negative Breast Cancer: Secondary Analysis of the GeparSixto Randomized Clinical Trial. *JAMA Oncol* 2017; 3: 1378–1385. doi:10.1001/jamaoncol.2017.1007
- [46] von Minckwitz G, Procter M, de Azambuja E et al. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. *N Engl J Med* 2017; 377: 122–131. doi:10.1056/NEJMoa1703643
- [47] Piccart M, Procter M, Fumagalli D et al.; APHINITY Steering Committee and Investigators. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer in the APHINITY Trial: 6 Years' Follow-Up. *J Clin Oncol* 2021; 39: 1448–1457. doi:10.1200/JCO.20.01204
- [48] Loibl S, Jassem J, Sonnenblick A et al. Updated Results of Aphinity at 8.4 years median follow up. *ESMO Virtual Plenary 2022*; July 14, 2022
- [49] von Minckwitz G, Huang CS, Mano MS et al. Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. *N Engl J Med* 2019; 380: 617–628. doi:10.1056/NEJMoa1814017
- [50] Martin M, Holmes FA, Ejlertsen B et al. Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2017; 18: 1688–1700. doi:10.1016/S1470-2045(17)30717-9
- [51] Chan A, Moy B, Mansi J et al. Final Efficacy Results of Neratinib in HER2-positive Hormone Receptor-positive Early-stage Breast Cancer From the Phase III ExteNET Trial. *Clin Breast Cancer* 2021; 21: 80–91.e7. doi:10.1016/j.clbc.2020.09.014
- [52] Chan A, Delaloge S, Holmes FA et al. Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2016; 17: 367–377. doi:10.1016/S1470-2045(15)00551-3
- [53] Clinicaltrials.gov. A Study of Trastuzumab Deruxtecan (T-DXd) Versus Trastuzumab Emtansine (T-DM1) in High-risk HER2-positive Participants With Residual Invasive Breast Cancer Following Neoadjuvant Therapy (DESTINY-Breast05). 2022. Accessed December 28, 2022 at: <https://clinicaltrials.gov/ct2/show/NCT04622319>
- [54] Ruiterkamp J, Voogd AC, Bosscha K et al. Impact of breast surgery on survival in patients with distant metastases at initial presentation: a systematic review of the literature. *Breast Cancer Res Treat* 2010; 120: 9–16. doi:10.1007/s10549-009-0670-0
- [55] Gnerlich J, Dueker JM, Jeffe DB et al. Patient and tumor characteristics associated with primary tumor resection in women with Stage IV breast cancer: analysis of 1988–2003 SEER data. *Breast J* 2008; 14: 538–542. doi:10.1111/j.1524-4741.2008.00644.x
- [56] Le Scodan R, Stevens D, Brain E et al. Breast cancer with synchronous metastases: survival impact of exclusive locoregional radiotherapy. *J Clin Oncol* 2009; 27: 1375–1381. doi:10.1200/jco.2008.19.5396
- [57] Ali D, Le Scodan R. Treatment of the primary tumor in breast cancer patients with synchronous metastases. *Ann Oncol* 2011; 22: 9–16. doi:10.1093/annonc/mdq301
- [58] Di Lascio S, Pagani O. Oligometastatic Breast Cancer: A Shift from Palliative to Potentially Curative Treatment? *Breast Care* 2014; 9: 7–14. doi:10.1159/000358750
- [59] Cullinane C, Fleming C, O'Leary DP et al. Association of Circulating Tumor DNA With Disease-Free Survival in Breast Cancer: A Systematic Review and Meta-analysis. *JAMA Network Open* 2020; 3: e2026921–e2026921. doi:10.1001/jamanetworkopen.2020.26921
- [60] Sant M, Bernat-Peguera A, Felip E et al. Role of ctDNA in Breast Cancer. *Cancers* 2022; 14: 310
- [61] Croessmann S, Park BH. Circulating tumor DNA in early-stage breast cancer: new directions and potential clinical applications. *Clin Adv Hematol Oncol* 2021; 19: 155–161
- [62] Trapp E, Janni W, Schindlbeck C et al. Presence of Circulating Tumor Cells in High-Risk Early Breast Cancer During Follow-Up and Prognosis. *J Natl Cancer Inst* 2019; 111: 380–387. doi:10.1093/jnci/djy152
- [63] Huebner H, Haberle L, Muller V et al. MUC1 (CA27.29) before and after Chemotherapy and Prognosis in High-Risk Early Breast Cancer Patients. *Cancers (Basel)* 2022. doi:10.3390/cancers14071721
- [64] clinicaltrials.gov. Standard Surveillance vs. Intensive Surveillance in Early Breast Cancer (SURVIVE). 2023. Accessed April 15, 2023 at: <https://clinicaltrials.gov/ct2/show/NCT05658172>
- [65] Stickeler E, Aktas B, Behrens A et al. Update Breast Cancer 2021 Part 1 – Prevention and Early Stages. *Geburtshilfe Frauenheilkd* 2021; 81: 526–538. doi:10.1055/a-1464-0953
- [66] Stiftung SONK St.Gallen Oncology Conferences. Faculty Members – 18th St. Gallen International Breast Cancer Conference 2023. 2023. Accessed March 10, 2023 at: <https://www.oncoconferences.ch/events/sgbcc-2023/>