ABC7 Consensus: Assessment by a German Group of Experts

Nina Ditsch[a] Michael Untch[b] Peter A. Fasching[c] Steffi Busch[d] Johannes Ettl[e] Renate Haidinger[f] Christian Jackisch[g] Diana Lüftner[h] Lothar Müller[i] Volkmar Müller[j] Eugen Ruckhäberle[k] Eva Schumacher-Wulf[l] Christoph Thomssen[m] Nadia Harbeck[n] Rachel Wuerstlein[o]

[a]Department of Gynecology and Obstetrics, Breast Cancer Center, University Hospital Augsburg, Augsburg, Germany; [b]Department of Gynecology and Obstetrics, Multidisciplinary Breast Cancer and Gynecologic Oncology Center, HELIOS Klinikum Berlin Buch, Berlin, Germany; [c]Women's Hospital at the University Hospital Erlangen, Comprehensive Cancer Center Erlangen-EMN, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany; [d]Onkologische Schwerpunktpraxis, Dr. Busch MVZ GmbH, Mühlhausen, Germany; [e]Department of Gynecology and Obstetrics, Clinic for Hematology, Oncology and Palliative Care, Klinikverbund Allgäu gGmbH, Klinikum Kempten, Kempten, Germany; [f]Brustkrebs Deutschland e.V.; Patient Advocate, Board Member ABC Global Alliance, Munich, Germany; [g]Department of Gynecology and Obstetrics, Sana Klinikum Offenbach, Offenbach, Germany; [h]Immanuel Hospital Märkische Schweiz, Buckow, Germany, and Immanuel Hospital Rüdersdorf, Medical University of Brandenburg, Rüdersdorf, Germany; [i]Onkologie UnterEms, Studienzentrum UnterEms, Leer, Germany; [j]Department of Gynecology, University Hospital, Hamburg-Eppendorf, ABC7 Panel Member, Hamburg, Germany; [k]Department of Obstetrics and Gynecology of The Heinrich Heine University Düsseldorf, Düsseldorf, Germany; [l]Mamma Mia! Breast cancer magazine, Patient Advocate, Co-chair, ABC7 Panel Member, Köln, Germany; [m]Martin Luther University Halle-Wittenberg, Halle (Saale), Germany; [n]Breast Center and Comprehensive Cancer Center (CCC) Munich, University of Munich (LMU), Department of Obstetrics and Gynecology, ABC7 Panel Member, Munich, Germany; [o]Breast Center and Comprehensive Cancer Center (CCC) Munich, University of Munich (LMU), Department of Obstetrics and Gynecology, Munich, Germany

Correspondence to:
Nina Ditsch, nina.ditsch@uk-augsburg.de

Introduction

The International Consensus Conference for "Advanced Breast Cancer" on diagnosis and treatment of advanced breast cancer (ABC) was established in November 2011 and convened since then every 2 years in Lisbon/Portugal. The intention is to guide treatment decision-making in ABC worldwide and to adapt them to the specific environment of each country. As a result, the ABC consensus contributes to harmonize and standardize the treatment of patients with locally advanced or metastatic breast cancer (MBC) all over the world. This is particularly important in terms of promoting accessibility to health care services and new agents.

The Seventh Consensus Conference (ABC7) was held from November 9 to 11, 2023. Of note is that many statements focused more strongly than in previous consensus voting on the fact that not all countries have access to new therapeutic approaches. The consensus is worked out by an international and interdisciplinary group of experts in the field of breast cancer. The voting panel for ABC7 consensus consisted of 44 participants, including patient advocates, one oncology nurse, and one psycho-oncologist (shown in box). Three panel members came from Germany – the two medical experts Nadia Harbeck, Munich, and Volkmar Müller, Hamburg, and Eva Schumacher-Wulf, the patient advocate, who co-chaired the consensus session. This article does not substitute the official publication of the final consensus which will be published later this year.

Box 1.

ABC7 Panelists

1-Fatima Cardoso, PT (chair)
2-Eric P. Winer, US (honorary chair)
3-Larry Norton, US (honorary chair)
4-Alberto Costa, CH/IT (honorary chair, *not in presence*)
5-Eva Schumacher-Wulf, DE (co-chair, patient advocate)
6-Sandra Ximena Franco Millan, CO (scientific committee)
7-Karen Gelmon, CA (scientific committee)
8-JosephGligorov, FR (scientific committee)
9-Volkmar Mueller, DE (scientific committee)

(continued)

10-Birgitte V. Offersen, DK (scientific committee)
11-Sandra Swain, US (scientific committee)
12-Matti S. Aapro, CH
13-Jyoti Bajpai, IN
14-Carlos H. Barrios, BR
15-Laura Biganzoli, IT
16-Maria João Cardoso, PT
17-Lisa A Carey, US
18-Mariana Chavez MacGregor, US
19-Runcie CW Chidebe, NG (patient advocate)
20-Javier Cortés, ES
21-Rebecca Dent, SG
22-Nagi S. El Saghir, LB
23-Alexandru Eniu, CH
24-Lesley Fallowfield, UK (psycho-oncologist)
25-Prudence A. Francis, AU
26-Jenny Gilchrist, AU
27-William Gradishar, US
28-Nadia Harbeck, DE
29-Xichun Hu, CN
30-Ranjit Kaur, MY (patient advocate)
31-Belinda Kiely, AU
32-Sung-Bae Kim, KR
33-Marion Kuper-Hommel, NZ
34-Frédéric E. Lecouvet, BE
35-Ginny Mason, US (patient advocate)
36-Claire Myerson, UK (patient advocate)
37-Silvia Neciosup, PE
38-Shinji Ohno, JP
39-Shani Paluch-Shimon, IL
40-Ann Partridge, US
41-Frédérique Penault-Llorca, FR
42-Hope S. Rugo, US
43-Elzbieta Senkus, PL
44-Peter Vuylsteke, BW
45-Theresa Wiseman, UK (nurse)

ABC7 Consensus Discussed from a German Perspective

This "post-ABC7" publication is discussing the ABC7 consensus voting with regard to the German treatment guidelines, specifically the annually updated treatment recommendations of the "Breast" Committee of the Gynecological Oncology Working Group (AGO Mamma) [1]. Of note is that the ABC7 panelists only voted on updated or new statements. Not modified statements from earlier ABC consensus conferences continue to be valid. The grading system of the ABC7 consensus is shown in Table 1.

General Statements on Hormone Receptor-Positive and HER2-Negative ABC

The ABC7 panel confirmed the definition for primary and secondary (acquired) endocrine resistance but pointed out that they do not apply solely to endocrine

Table 1. Level of evidence grading system used by ABC7 panelists [2]

Levels of evidence	
I	Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without control group, case reports, experts' opinions
Grades of recommendation	
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

therapy (ET), but also to endocrine-based therapy with CDK4/6 inhibitors. This corresponds to the recommendations of AGO Mamma [1]. Endocrine resistance is a continuum. The definitions therefore are primarily relevant as inclusion criteria for clinical studies and do not necessarily dictate clinical practice (ABC majority vote: 95.4%). From the German perspective, the clinical course of the disease is key for treatment decisions [1].

CDK4/6 Inhibition: First-Line Standard Even for Aggressive Disease

With regard to the overall evidence and the RIGHT Choice trial [3], the ABC panel confirmed endocrine-based therapy with a CDK4/6 inhibitor as first-line standard for the majority of pre- or postmenopausal patients with hormone receptor (HR)+/HER2– ABC and clinically aggressive disease (LoE/GoR: I/A) as well as for men with breast cancer – this in case that the inclusion criteria of RIGHT Choice trial are met (LoE/GoR: expert opinion/B; ABC majority vote: 95.4%). Within this randomized phase II trial, ET-based first-line therapy with ribociclib/aromatase inhibitor (AI) was compared to combination chemotherapy (docetaxel/capecitabine, capecitabine/vinorelbine, or paclitaxel/gemcitabine). Patients had a median 12-month advantage in progression-free survival (PFS) with ET-based first-line therapy compared with combination chemotherapy (HR 0.42) [3].

In patients with visceral crisis, ET-based therapy was as effective as chemotherapy. The toxicity profile was better for the ET-based arm [3]. That is why, according to ABC panel, ET-based therapy with CDK4/6 inhibitor may be the preferred option also for patients with visceral crisis although the definition is not completely uniform (LoE: II/B; ABC majority vote: 95.4%).

The German expert group agrees with both voting results, but points out that in the RIGHT Choice trial about 60% were de novo metastatic [4]. Actually, it is not known whether the results can be transferred to tumors with lower ER expression, especially to those with ER expression ≤20% [1].

HR+/HER2 Low ABC

With regard to the approval of trastuzumab deruxtecan (T-DXd) in patients with HR+ ABC and low HER2 expression (HER2 low), the ABC panel voted on the HER2 scoring. The scoring should be based on the updated ASCO/CAP recommendations (2023) [5] which differentiates immunohistochemically between IHC0, IHC1+, IHC2+ (amplified or not), and IHC3+. For clinical practice, it is recommended that the pathologist should be informed about the clinical relevance and that the details in the conclusion between HER2zero (IHC0), HER2 low (IHC1+ or IHC2+ non-amplified), and HER2-positive (ISH 2+ amplified or HER2 3+) (LoE/GoR: expert opinion/A; ABC majority vote: 97.6%). This corresponds to the AGO recommendations [1].

Oligometastatic Disease

Looking at the results of the randomized phase II study NRG-BR002 [6], which contradict those of the smaller randomized phase II study SBR-COMET [7], the ABC panel voted on stereotactic body radiotherapy and stereotactic ablative body radiotherapy (SABR) as a treatment option for oligometastatic ABC. While there were no efficacy benefits in the NRG-BR002 study [6], stereotactic body radiotherapy/SABR achieved an overall survival (OS) advantage in the SABR-COMET study [7] in patients with a controlled primary tumor (HR 0.47; $p = 0.006$).

The ABC panel does not recommend routine ablation of asymptomatic extracranial oligometastases in these patients outside clinical trials. In clinical practice, this

may only be an option for individual cases. Further evidence is needed (LoE/GoR: II/D; ABC majority vote: 97.6%). In Germany, ablation for extracranial asymptomatic oligometastases is an option only on a case-by-case basis. There is also agreement that such an approach should be decided by a multidisciplinary team.

Is Surgery of the Primary Tumor an Option for MBC?

In patients with "de novo" MBC (stage IV), surgery of the primary tumor is generally not recommended because this is not associated with an OS benefit. However, there may be exceptions regarding patients' quality of life or patients' preference which must be considered (LoE/GoR: I/C [70%]). These considerations are widely accepted in Germany [1]. A clinical scenario where surgery of the primary tumor may be an option is symptoms of the primary tumor (palliation), progression of the primary tumor with controlled distant disease, or no evidence of disease except the primary tumor (ABC majority vote: 97.6%). This corresponds to clinical practice in Germany [1].

ABC Patients during War and Conflicts

In view of military conflicts worldwide, the ABC panel adopted various statements to support medical care. The German experts agree this includes, when possible, to consider oral medications and treatment regimens requiring minimal routine monitoring and blood work. Telemedicine should be used to ensure continuity of care and contact with the patients. A challenge of maximum priority is to ensure access to pain medications. All those who provide support in regions of conflict and who may themselves be at risk must be supported via online tools (LoE/GoR: expert opinion/B).

ABC Patients with Pre-Existing Serious Mental Illness

Patients with pre-existing serious mental illness are more likely to be diagnosed with advanced ABC at initial diagnosis than those patients without serious mental illness. The German expert group agrees with the ABC panel voting: attention must be given to the special needs of these patients. Care should be taken to avoid discrimination. For optimal treatment and good compliance, the oncology team should endeavor to work together with the patient's psychiatrist and the mental illness care team. Special attention needs to be given to potential drug interactions that may require dose adjustments. Under certain circumstances, steroids and medical cannabis, for example, can potentially trigger manic and psychotic episodes (LoE/GoR: IV/B; ABC majority vote: 95.2%).

Access to Intensive Care Units

During the COVID pandemic, the question was how to deal with non-oncologic diseases requiring intensive care in ABC patients. In various countries, tumor patients were denied access to intensive care units (ICUs) during the pandemic. The ABC panel demanded (ABC majority vote: 100%) that ABC patients must be informed about their prognosis and treatment options ("patient-centered communication"). After appropriate information, patients' preference – to forgo or to pursue treatments – must be considered. The ABC diagnosis is not a reason to deny access to ICUs. This applies to potentially reversible serious adverse events as well as to complications due to comorbidities that are not associated with the breast cancer (LoE/GoR: expert opinion/B).

In Germany, ABC patients were not denied access to ICUs during COVID pandemic. From a German perspective, it should be discussed with the patient what should be done in case of a life-threatening situation requiring intensive care. The issue should be addressed proactively and clarified in the spirit of "advance care planning". The German expert group refers to the extended "S3 guideline for palliative care for patients with incurable cancer" [8].

"Treatment Holidays" for Long-Term Responder?

According to the ABC panel, "treatment holidays" is an acceptable option for ABC patients with long-term response and controlled disease (LoE/GoR: IV/B; ABC majority vote: 97 0.7%). In individual cases, this may also apply to patients with long-term complete remission. However, "treatment holidays" must always be discussed in detail with the patient. In case of progression, treatment must be resumed (LoE/GoR: expert opinion/B; ABC majority vote: 97.7%).

For both votes, there are no evidence-based data supporting "treatment holiday." Especially for new agents, data are very limited due to the short real-world experience. From the German perspective, "treatment holidays" may be justified regarding patient's quality of life and her preferences. However, standard in Germany is to treat patients with distant disease as long as possible with an effective treatment in order to maintain quality of life [1]. "Treatment holidays" should not be suggested proactively. An alternative may be a treatment de-escalation to reduce treatment intensity and side effects, for example, by pausing the CDK4/6 inhibitor and continuing the et alone. Regarding chemotherapy, a short delay of treatment (some weeks depending on the activity of the disease) may be suitable if desired for individual activities (for example, vacations).

Health-Related Quality of Life in Focus

Disease-related symptoms and treatment-related toxicity reported by patients (patient-reported outcome) must be considered in clinical practice. The ABC panel demands assessing patient-reported outcomes by using evidence-based remote assessment tools that are easy to use in clinical practice as well as for patients. The panel recommends, for example, user-friendly collection platforms, for example, tablets or smartphones. Such regular and systematic monitoring may support communication. Side effects may be detected and treated more promptly (LoE/GoR: I/B).

The German expert group welcomes this important statement. In Germany, this was taken up with the legislation on digital health applications (digitale Gesundheitsanwendung), which enables prescription of quality-assured apps in routine medical care [further information: https://diga.bfarm.de/de/verzeichnis]. Still, the interaction between treating physician and patient cannot be replaced by remote tools but professionally supported.

Standardized Assessment Necessary

Standardized tools must also be used to assess patients' health-related quality of life. The German expert group agrees with the ABC panel who rejects an assessment focusing exclusively on reporting Common Terminology Criteria for Adverse Events (CTCAE) symptom grades (further information: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm). In case of generic measures, specific modules or subscales should be used that exist, for example, within the European Organization on Research and Treatment of Cancer (EORTC) questionnaires. Furthermore, collection methods, timing of data assessments, and handling of missing data are important for evidence-based results (LoE/GoR: expert opinion/A; ABC majority vote: 97.7%).

Treatment of ER+/HER2– ABC

Use of CDK4/6 Inhibitors

Regarding the results of the SONIA trial [9], the ABC panel confirmed ET-based therapy with CDK4/6 inhibitor as first-line standard for ER+/HER2– ABC, but still regards endocrine monotherapy as an acceptable alternative for selected patients, for example, those with low tumor burden, long disease-free interval, or according to patients' preference (ABC majority vote: 93.1%). The SONIA trial addressed the question whether in ER+/HER2– ABC ET-based therapy with CDK4/6 inhibitor (90% received palbociclib) should be used as first- or second-line therapy. Although PFS in first line was much longer with the CDK4/6 inhibitor, after a median follow-up period of 37.3 months, there were no statistically significant differences in survival. According to the ABC panel, it remains unknown whether ribociclib and abemaciclib would have identical results. Also, the rate of patients that moved to second-line therapy from monotherapy (loss of patients) is not completely clear.

In Germany, endocrine monotherapy is a first-line option only for selected patients with ER+/HER2– ABC. However, first-line standard is ET-based therapy with CDK4/6 inhibitor. Of note, unlike the ABC panel, the AGO recommends individual CDK4/6 inhibitors according to their evidence based on PFS and OS data [1].

Maintenance Therapy after First-Line Chemotherapy

There are currently little data to support ET-based maintenance therapy with a CDK4/6 inhibitor in ER+/HER2– ABC after first-line chemotherapy [10]. Nevertheless, 75.0% of the ABC panelists see both ET-based therapy and endocrine monotherapy as maintenance therapy following first-line chemotherapy. Within a separate vote, 39.5% decided in favor of maintenance therapy with endocrine monotherapy and 41.8% against it. For subsequent maintenance therapy, AGO recommends endocrine monotherapy [1].

A topic of discussion is whether patients with progression on ET-based first-line therapy with CDK4/6 inhibitor may benefit from subsequent second-line use of endocrine-based therapy with CDK4/6 inhibitor ("treatment beyond progression" [TbP]). Small phase II studies showed contradictory results. The ABC panel rejects "TbP" outside clinical studies by a clear majority vote (LOE/GoR: expert opinion/D; ABC majority vote: 90.6%).

From the German perspective, "TbP" might be an option due to side effects. In the MAINTAIN trial [11], CDK4/6 inhibitor plus switching endocrine monotherapy was superior to endocrine monotherapy and showed a benefit in median PFS (HR 0.57; $p = 0.006$). The German experts also point to the numerous treatment alternatives after ET-based first-line therapy such as elacestrant in case of *ESR1* mutation, alpelisib/fulvestrant for patients with PIK3CA mutation, as well as everolimus plus ET or fulvestrant as monotherapy [1].

Oral Selective Estrogen Receptor Degraders: Elacestrant: A New Option

Elacestrant is the first oral selective estrogen receptor degrader approved in the USA and Europe for ER+/HER2– ABC with activating *ESR1* mutation. This makes elacestrant monotherapy a new option for second- and/or third-line therapy in the metastatic setting for these patients (ABC majority vote: 81.3%) and corresponds to the AGO recommendation [1]. The approval is based on

the randomized phase III trial EMERALD [12, 13] in patients with 1–2 previous ETs, including ET-based therapy with CDK4/6 inhibitor. Patients with an activating *ESR1* mutation who are pretreated with CDK4/6 inhibitor for more than 12 months benefited more than those with shorter prior CDK4/6 inhibitor therapy [14]. Several test systems are currently available. The implementation of standardized *ESR1* testing is ongoing in Germany.

Integrate Capivasertib in Clinical Practice

Since November 2023, the combination capivasertib/fulvestrant has been FDA approved in the USA for patients with endocrine-resistant ER+/HER2- ABC and *PIK3CA/AKT1/PTEN* alterations. According to the ABC panel, this is a new treatment option for these patients independent of menopausal status (+GnRH in premenopausal women) and also for men (LoE/GoR: I/B). Since approval was not available at the time of the ABC7 consensus meeting, there was no panel voting onsite. This will follow online depending on the approval.

The approval is based on the randomized phase III trial CAPItello-291 [15] in patients with ER+/HER2- ABC pretreated with several lines of systemic treatment (including 1–2 previous ETs; 70% had a CDK4/6 inhibitor). The combination capivasertib/fulvestrant showed a median PFS advantage over fulvestrant monotherapy (+placebo) for the overall population and the subgroup of patients with altered *AKT* signaling pathway (~41%) ($p < 0.001$ in each case). The OS data were not yet mature. All patients of the study had recurrence or progression within 12 months after adjuvant therapy with an AI or under AI therapy in the metastatic setting.

For use in Germany, European approval from the European Medicine Agency (EMA) must be awaited. It is unknown whether the approval will be linked to the biomarker (altered *AKT* signaling pathway). AGO did not discuss this treatment in 2023 as it had not been approved at the time.

Sacituzumab Govitecan in ER+/HER2− ABC

The ABC panel confirmed the anti-Trop2-targeted ADC sacituzumab govitecan (SG) as a new treatment option for heavily pretreated patients with ER+/HER2− ABC (LoE/GoR: I/B; ABC majority vote: 95.3%). This corresponds to the AGO recommendations [1]. In the randomized phase III trial TROPiCS02 [16, 17], SG showed a statistically significant PFS benefit (HR 0.66; $p = 0.0003$) and a substantial OS advantage of 3.2 months in heavily pretreated patients with ER+/HER2− ABC (60% had at least three chemotherapy regimens in the metastatic setting) [16, 17]. Both the HER2-zero and the HER2-low tumors benefited. Due to an increased risk of gastrointestinal side effects, especially diarrhea and nausea/vomiting, a proactive management, including detailed information for patients, is necessary. From the German perspective, side effects of SG can be managed proactively.

T-DXd in ER+/HER2-Low ABC

According to the ABC panel, T-DXd is the preferred treatment option for patients with endocrine-resistant ER+/HER2-low ABC who have been previously treated with 1–2 chemotherapies for metastatic disease. Reference is made to the median PFS (HR 0.51; $p < 0.001$) and OS advantage (HR 0.64; $p = 0.003$) compared to chemotherapy (treatment physician's choice) in the Destiny-Breast (DB) 04 study [18].

The ABC panel recommends monitoring with proactive management for side effects. Given the risk of interstitial lung disease and/or pneumonitis as well as gastrointestinal toxicities, computed tomography (CT) should be performed every 6–8 weeks. Prophylactic intervention against nausea/vomiting is recommended (LoE/GoR: I/A; ABC vote: 100%). The German expert group basically agrees but does not agree with CT examinations every 6–8 weeks. A CT imaging should be done according to the summary of product characteristics, "Fachinformation".

ADC Sequencing under Discussion

T-DXD and SG are two ADCs, both indicated for advanced therapy line in ER+/HER2-low ABC. There are currently little data on ADC sequencing in these patients. Regarding study data and inclusion criteria of the pivotal trials [17, 18], the ABC panel recommends using T-DXd before SG (LoE/GoR: expert opinion/B; ABC majority vote: 95.3%).

The panel voting corresponds to the recommendation of AGO [1]. The study population of the TROPiCS02 study [17] was more intensively pretreated than that in the DB04 study [18]. This is reflected in the approval of each ADC.

Triple-Negative/HER2-Low ABC

The approval of T-DXd for HER2-low ABC is independent of HR expression and therefore also includes triple-negative HER2-low ABC. In the pivotal trial, DB04 [18], only 11.3% had a negative HR status. This subgroup benefited from T-DXd to a similar extent as the overall population (PFS: HR 0.46; OS: HR 0.48). According to the ABC panel, T-DXd is also an effective therapy option for these patients after the first-line chemotherapy in the metastatic setting. Regarding side effect management, the same recommendations apply as for ER+/HER2-low ABC tumors (LoE/GoR: I/B; ABC majority vote: 88.6%). The German expert group refers to the statements on ER+/HER2− ABC.

The question of the ADC sequence also arises in triple-negative/HER2-low ABC. Unlike in ER+/HER2– ABC, the ABC panel recommends using SG *before* T-DXd in triple-negative/HER2-low ABC. The evidence for T-DXd is lower in triple-negative/HER2-low ABC than for SG due to the small triple-negative subgroup in the DB04 study [18]. SG however achieved significant efficacy benefits in the randomized phase III trial ASCENT [19] in patients with advanced or metastatic triple-negative breast cancer (TNBC) (PFS: HR 0.41; $p < 0.001$; OS: HR 0.48; $p < 0.001$) versus chemotherapy (treatment physician's choice). The ABC vote corresponds to the AGO recommendations [1]. The German expert group points out that the reverse ADC sequence may only be justifiable in view of potential side effects.

T-DXd for Brain Metastases

Systemic treatment options for patients with ABC and brain metastases (BM) have expanded with new agents, for example, T-DXd. According to the ABC panel, T-DXd is a treatment option for patients with HER2+ ABC with both locally pretreated and locally untreated BM (LoE/GoR: II/B; ABC majority vote: 97.7%). This is based on the three DB01, DB02, and DB03 studies [20–22] as well as an exploratory pooled analysis of the three trials, which focused on efficacy in patients with active BM [23].

The German expert group agrees with the caveat that the pooled analysis of DB01/DB02/DB03 studies is exploratory. The evidence is less robust than in a prospective randomized trial, such as the HER2CLIMB with tucatinib/capecitabine/trastuzumab [24] – this should be considered when deciding on the therapy for active BM. The phase III trial DB12 will provide data on the efficacy of T-DXd in BM (https://www.destinyclinicaltrials.com/de-de#DESTINY-breast).

Contraception and Pregnancy in ABC Patients

The ABC panel recommends that all female ABC patients of reproductive age – regardless of breast cancer subtype – should be counselled about use of non-hormonal contraception. It is important to make patients aware of the risk of conceiving during breast cancer treatment (LoE/GoR: II/A; ABC majority vote: 93.0%). Particular attention should be given to ABC patients who are treated without ovarian function suppression or ablation since some therapies have a low gonadotoxic effect and do not induce menopause (LoE/GoR: II/A; ABC majority vote: 100%). The German expert group adds that patients must be informed that hormonal contraception is not indicated during oncological treatment for breast cancer and that ovarian function suppression does not offer safe contraception.

Comprehensive Information for Pregnant Patients

With a clear majority vote (97.5%), the ABC panel emphasizes that treatment and care of a pregnant patient with ABC require a multidisciplinary approach and an appropriately experienced team (LoE/GoR: expert opinion/A). The preference of the patients and – may be – her partner must be considered for all decisions. Patient (and partner) must be fully informed about the complex situation and the therapeutic options. They should be aware of potential consequences for the life of the patient (mother) as well as the health of the fetus (LoE/GoR: expert opinion/A). In Germany, this is clinical practice.

Imaging during Pregnancy

The ABC panel favors whole-body diffusion magnetic resonance imaging (MRI) as preferred imaging method to stage a pregnant patient (LoE/GoR: expert opinion/B; ABC majority vote: 77.2%). From the German perspective, it should be discussed whether staging is necessary at all. Alternative options during early pregnancy include chest CT or X-ray and upper abdominal sonography. MRI may be increasingly relevant in clinical practice for patients in long-term remission. No contrast agent should be used during pregnancy.

Chemotherapy during Pregnancy

The ABC panel confirmed that chemotherapy is currently the only systemic therapy that can be administered safely in the 2nd/3rd trimesters (LoE/GoR: II/A). The situation is particularly difficult in HER2+ ABC, as anti-HER2-targeted therapies are contraindicated throughout pregnancy (LoE/GoR: expert opinion/A; ABC majority vote: 95.2%). The German expert group adds that in general no targeted therapies at all, including immunotherapy and ET, may be used during pregnancy.

Abortion of Pregnancy in Focus

There was a lot of discussion whether abortion may be considered an option under certain circumstances and should be available for patients who decide in favor of it (LoE/GoR: expert opinion/A). A clear majority (95.3%) of the ABC panel agreed.

The German expert group puts the ABC statement into perspective: the patient (mother) must be comprehensively informed in a multidisciplinary discussion about her situation. The possibility of maintaining the pregnancy should be discussed. If there is no danger to the life of the mother and/or the child during pregnancy, there is no medical need for abortion. Pregnancy may be prolonged until the child can be delivered. During this time,

chemotherapy can be safely administered. If the patient's preference is abortion, this is a legal option in Germany if there is a medical indication.

Locally Advanced/Inflammatory Breast Cancer

According to ABC consensus, locally ABC (LABC) is defined as inoperable, non-metastatic, locally advanced disease. Inflammatory breast cancer (IBC) is a clinicopathological diagnosis that requires an interdisciplinary approach for diagnosis (T4d or stage IV if there are metastases). The following criteria must be met to diagnose IBC: (1) rapid onset of breast erythema, edema, and/or peau orange and/or warm breast with/without palpable tumor, (2) short duration of clinical history (≤6 months), (3) erythema covers at least one-third of the breast, (4) pathological confirmation of invasive carcinoma. Skin ulcerations are rare in IBC. A skin punch biopsy may support the diagnosis (LoE/GoR: I/A; ABC majority vote: 95.4%).

Diagnostics and Staging

At least one core biopsy is standard and important for treatment decision providing histological type, grade, and biomarker expression. The panel voted that biomarkers for inoperable locally advanced/inflammatory breast cancer (LABC/IBC) (M0 each) include HR status (ER/PR), HER2 status, *Ki67* and *germline(g)BRCA1/2* status. In case of metastatic IBC, the PD-L1 status should additionally be assessed for TNBC and the *PIK3CA* status in case of ER+/HER2– IBC. Assessment of *Ki67* may be omitted (LoE/GoR: I/A; ABC majority vote: 88.6%).

The German group pointed out that biomarkers for inoperable LABC/IBC (M0 each) include HR status (ER/PR), HER2 status, and *Ki67*. In case of metastatic IBC, the following markers should additionally be assessed: *gBRCA* for HER2– ABC, PD-L1 status for TNBC and ESR1-mutation, and PIK3CA status in case of ER+/HER2– IBC.

Due to the high risk for metastases in LABC and IBC, a full staging workup with complete histology, physical examination, and laboratory tests plus imaging (chest, abdomen, bone) is necessary before starting systemic therapy (LoE/GoR: I/A, 100%). For non-lobular invasive breast cancer, the ABC panel favors PET-CT instead of CT scans and bone scan. For most lobular breast cancers, CT scans and bone scan or a whole-body MRI is preferred (LoE/GoR: II/A; ABC majority vote: 95.2%).

There are no guideline recommendations and no reimbursement for PET-CT in Germany regarding patients with breast cancer. But, from the medical perspective, the German expert group supports the use of PET-CT in these high-risk patients, as around 20% more metastases can be detected [25–27]. It is currently unknown whether this is associated with a better prognosis. What is crucial is the differentiation between stage III and stage IV which is important for treatment decision and duration. In stage III with a potentially curative chance, the duration of therapy is limited for a certain time – unlike in stage IV.

Therapy of HR+ LABC/IBC

Primary systemic therapy for HR+ LABC (M0) is an anthracycline- and taxane-based chemotherapy or an ET-based therapy, for example, with a CDK4/6 inhibitor (LoE/GoR: I/A). The treatment decision is based on tumor characteristics and patient considerations like performance status, symptoms, comorbidities, and her preference (LoE/GoR: expert opinion/A). In case of patients with inoperable HR+ IBC and no distant metastases (M0) who are treated with primary anthracycline/taxane-based chemotherapy, the ABC panel recommends postoperative treatment with ET-based therapy plus CDK4/6 inhibitor (LoE/GoR: I/A; ABC majority vote: 95.2%). The German expert group agrees [1].

Therapy for Triple-Negative LABC/IBC

Patients with unresectable triple-negative LABC/IBC are primarily treated with an anthracycline/taxane-based chemotherapy (LoE/GoR: I/A) plus additional pembrolizumab which is given regardless of PD-L1 status in non-metastatic patients [28]. In the metastatic situation, additional immunotherapy is only indicated in case of PD-L1 positivity (CPS ≥10 for pembrolizumab; IC ≥1% for atezolizumab) [29] (LoE/GoR: I/A; ABC majority vote: 93.0%). This corresponds to the AGO recommendation [1].

Therapy for HER2-Positive Tumors

For primary systemic therapy in patients with inoperable HER2+ LABC/IBC, the ABC panel recommends integrating an anthracycline in addition to anti-HER2-directed therapy (double blockade) plus taxane-based chemotherapy (LoE/GoR: I/B; ABC majority vote: 62.7% with 32.5% rejection). There had not yet been a majority for this in the ABC6 consensus. From the German perspective, anthracyclines are an option for these patients. Anthracycline/taxane-based chemotherapy plus anti-HER2 therapy is an equivalent alternative to the TCHP regimen (taxane/platinum plus trastuzumab/pertuzumab [dual blockade]) for a total of six cycles [1].

Therapy for gBRCA1/2-Mutated LABC/IBC

It is currently an ongoing debate how best to combine the PARP inhibitor olaparib into the postoperative treatment with capecitabine or pembrolizumab for *gBRCA1/2*-mutant triple-negative LABC and IBC. The ABC panel confirmed this with a majority vote (79.5%) for these patients. The German experts agree for M0 patients with LABC/IBC and *gBRCA1/2* mutation who

achieved no pathologic complete remission with systemic therapy of pembrolizumab plus olaparib given in combination or sequentially. Safety data are currently available from the metastatic situation (LoE/GoR: III/B). These data suggest that the combination olaparib/pembrolizumab may be an option [30, 31].

There is an analogous situation for patients with *gBRCA1/2*-mutated and primarily inoperable ER+/HER2− LABC/IBC: the question is whether olaparib can be administered in the postoperative setting in addition to abemaciclib. For safety reasons, the combined use of both agents is not possible. However, the ABC panel and the German expert group see an option in the postoperative sequence with olaparib followed by abemaciclib (LoE/GoR: III/B; ABC majority vote: 68.2%; rejection: 14.6%).

Treatment for Visceral Crisis

Definition of "visceral crisis" often differs from the ABC definition. Nevertheless, patients with visceral crisis are mostly excluded from clinical trials, which is why data are limited and therapeutic evidence is low. According to the ABC panel, visceral crisis in ER+/HER2− ABC is not a contraindication to ET-based therapy with a CDK4/6 inhibitor. On the contrary, ET-based therapy may even be preferable to primary chemotherapy. Patients with HER2+ ABC and visceral crisis should receive anti-HER2-directed therapy (LoE: II/A; ABC majority vote: 95.4%) [1].

Visceral Crisis in the Liver

For patients with visceral crisis in the liver, treatment options are particularly limited because of the substantial deterioration in liver function. The ABC panel recommends weekly regimens with reduced dose (LoE/GoR: IV/B; ABC majority vote: 92.8%). The German expert group adds that a visceral crisis in the liver is defined as bilirubin value >1.5 mg/dL [32]. Special caution is required if the bilirubin value is >2 mg/dL. Patients should not be treated with agents metabolized in the liver. Therapeutic options include capecitabine and platinum, which both can usually be given without dose reduction.

Visceral Crisis and Bone Marrow Infiltration

For patients with bone marrow infiltration, the ABC panel recommends treatment with weekly administration of paclitaxel (LoE: IV/B) or the use of capecitabine (LoE: IV/B) and for ER+/HER2− ABC an endocrine-based therapy with a CDK4/6 inhibitor (LoE: IV/B; (ABC majority vote: 86.0%). The German expert group agrees [1].

Access to ICUs

In case of urgent surgery and/or radiation therapy due to visceral crisis or in case of other interventions, for example, laser therapy for bronchial obstruction, access to an ICU should not be denied if there is a chance to reverse the clinical situation. It must be discussed carefully in advance with the patient and her family whether intensive care treatment is an option. The patient's preference must be respected, according to the ABC panel (LoE: expert opinion/NA; ABC majority vote: 97.6%). This is common practice in Germany.

ABC Patients and HIV

Regardless of tumor stage, ABC patients with HIV not only have a worse prognosis than those without HIV, but also have a higher risk of side effects during treatment. Myelotoxicities and infections, for example, occur more frequently. The challenge is that there are little data on the treatment of ABC patients with HIV. This is particularly concerning new anticancer agents. Against this background, the ABC panel made recommendations for the treatment of these patients. The German experts agree with all statements:

- When treating breast cancer patients with HIV disease, oncologists and HIV specialists must work together in an interdisciplinary way (LoE/GoR: expert opinion/A).
- A well-controlled HIV disease (no detectable viral load) should no longer be an exclusion criterion in clinical trials (LoE/GoR: expert opinion/A).
- Before starting anticancer treatment for ABC patients with HIV, it is recommended to look for diseases with an increased incidence due to HIV, for example, tuberculosis or hepatitis (LoE/GoR: expert opinion/B) and, if diagnosed, to initiate treatment.
- The ABC consensus applies to ABC patients with HIV as well as to those without HIV. Nevertheless, careful consideration should be given to dose reduction and/or increased treatment intervals. For myelotoxic chemotherapy, primary G-CSF prophylaxis is recommended (LoE/GoR: expert opinion/A).
- There are currently no data for CDK4/6 inhibitors in ABC patients with HIV (LoE/GoR: expert opinion/NA), safety data suggesting that immune checkpoint inhibitors are a potential treatment option (LoE/GoR: IV/B).
- Most cytotoxic agents are safe if there is no detectable viral load and CD4+T-cell count is ≥200/μL under modern anti-retroviral therapy (ART) (LoE/GoR: expert opinion/B).
- HIV treatment must be done during breast cancer treatment, i.e., ART must be continued and, if necessary, initiated (LoE/GoR: expert opinion/A). In ART-naive patients, breast cancer treatment should start delayed – 2 weeks after initiation of ART – if this is clinically justifiable (LoE/GoR: expert opinion/B).
- Potential drug-drug interactions must always be checked. In case of clinically relevant interactions, the viral load must be checked more closely. For

medications with an increased risk of lymphocytopenia, this also applies to the CD4+T-cell count (LoE/GoR: expert opinion/B).

Treatment of Older ABC Patients

The statements of the ABC panel on treatment of older ABC patients correspond to the recommendations of AGO Mamma and the clinical practice in Germany [1]:

- All patients – regardless of age – must be part of the treatment decision-making process if they wish. Their preferences must be considered (LoE/GoR: expert opinion/A). In addition, they should be informed about clinical trials and get all information necessary for the decision whether they want to take part in the study (LoE/GoR: expert opinion/A; ABC majority vote: 100%).
- For treatment decision in older ABC patients, it is primarily important to consider potential comorbidities – especially those associated with the liver, kidney, bone marrow reserve, and/or neurological illness – and not to focus on age per se (LoE/GoR: I/A; ABC majority vote: 95.4%) [1].
- Special attention must be paid to potential drug interactions, as older patients often take several medications (polypharmacy) (LoE/GoR: I/A; ABC majority vote: 100%). The German experts add that over the counter) medications must also be asked for. An electronic patient record in which all medications are documented would be helpful.
- The ABC panel recommends following the EUSOMA-SIOG guidelines for the management of older ABC patients [33]. The following statement on systemic treatment of metastatic disease is particularly important: "different treatment schedules, dose reductions, or stepwise dose escalation before reaching standard recommended dose might be required in older patients and reduce the risk of adverse outcomes" (LoE/GoR: expert opinion/A; ABC majority vote: 77.2%).

Geriatric Assessment Desirable

The German expert group supports the ABC majority vote (90.4%) to implement a geriatric assessment for treatment decision in older patients. The ABC panel recommends for initial use the G8 questionnaire as geriatric screening tool [www.mdcalc.com]. In case of low scores, a more detailed geriatric assessment should be done additionally (LoE/GoR: I/A). This approach is still unusual in Germany. The G8 screening tool consists of eight questions and can be integrated into clinical practice provided that appropriate resources are available [34, 35].

Elderly Patients with ER+/HER2− ABC

ET-based therapy with CDK4/6 inhibitor is first-line standard for most older patients with ER+/HER2− ABC (LoE/GoR: II/A). Real-world data suggest that this also applies to older patients with poor ("unfit") performance status [36–40] (LoE/GoR: III/B; ABC majority vote: 93.0%).

According to the ABC panel, the CDK4/6 inhibitor may initially be used in a reduced dose for unfit ABC patients – even if there is a lack of evidence-based data for this approach (LOE/GoR: expert opinion/B; ABC majority vote: 90.6%). The German expert group is more restrictive. If well tolerated, the evidence-based standard dose should be given. Dose reduction should be an exception. If necessary, it may be switched to endocrine monotherapy [1].

Elderly Patients with HER2+ ABC

If there are no absolute contraindications, older patients with HER2+ ABC may get anti-HER2 therapy just like younger patients (LOE/GoR: I/A; ABC majority vote: 100%). For the new anti-HER2-targeting agents, which are associated with a higher risk of side effects, the ABC panel recommends starting with a lower dose if necessary. Depending on tolerability, a careful monitoring should be done with the option of dose adjustment (LoE/GoR: expert opinion/A; ABC majority vote: 83.7%). From the German perspective, this approach is feasible. For combination regimen like tucatinib/capecitabine/trastuzumab, there is an alternative to only reduce the dose of the combination partner (capecitabine).

Leptomeningeal Disease

There is no accepted standard for the treatment of ABC patients with leptomeningeal disease (LMD).

Diagnostics for LMD

If possible, these patients should be included in clinical trials, namely, in those evaluating therapies for CNS disease (LoE/GoR: expert opinion/A). The treatment decision must be discussed by an interdisciplinary team, taking prognosis into account. It is also important to have a detailed discussion with the patient and her caregivers (LoE/GoR: expert opinion/A). To assess the full extension of the disease, the ABC panel recommends full spine MRI and brain imaging with gadolinium (LoE/GoR: expert opinion/A; ABC majority vote: 100%).

The German expert group adds that for LMD diagnosis the clinical symptoms, imaging, and cerebrospinal fluid examination are the diagnostic backbones. If two of three results are positive, the diagnosis is confirmed. Imaging alone is not sensitive enough, as false-positive results cannot be ruled out. Regardless, if LMD is suspected, imaging should always include an MRI of the neuroaxis.

Therapeutic Options for LMD

According to the ABC panel, focal irradiation (brain or cranio-spinal) is an option for circumscribed symptomatic lesions (LoE/GoR: III/B). However, in case of extensive nodular or symptomatic linear LMD, whole-brain radiation therapy (WBRT) is recommended (LoE/GoR: III/B; (ABC majority vote: 97.7%).

From a German perspective, interdisciplinary coordination is essential for treatment decisions. Radiation therapy, especially WBRT, should be carefully considered – on the one hand taking into account the poor prognosis of LMD patients and on the other hand acknowledging that other therapy options exist, such as systemic therapy. From a German perspective, systemic therapy with new agents is preferable to WBRT for extensive lesions. This is particularly true for HER2+ ABC with LMD.

Restraints to Shunt Installation

The German expert group is cautious about using a shunt system in the situations described above. However, a ventriculo-peritoneal shunt may be placed to palliate symptoms in patients with increased intracranial pressure or symptomatic hydrocephalus (LOE/GoR: expert opinion/B). This is an acute situation. The German expert group agrees with the ABC panel (ABC majority vote: 100%). Again, the therapy decision must be discussed within an interdisciplinary dialogue.

Intra-CSF Chemotherapy: An Option?

Intra-CSF chemotherapy may be an option in individual cases if the systemic disease is stable. It does not prolong OS, does not improve quality of life of patients, and can be associated with significant toxicity. In individual cases, however, it alleviates the symptoms of the disease (LoE/GoR: III/C).

Intra-CSF administration of trastuzumab showed relative efficacy in small studies compared to historical data. Therefore, the ABC panel rated it as an option for individual cases in ABC patients with HER2+LMD (LoE/GoR: III/B). From the German perspective, intra-CSF trastuzumab should be used with restriction, as there are now new systemic agents available with proven efficacy for these patients (HER2+ LMD), for example, T-DXd or tucatinib/capecitabine/trastuzumab. There are also efficacy data for capecitabine monotherapy (LoE/GoR V/B).

Patients' Concerns

The patient advocate Isabelle Aloi Timeus, who gave a lecture during the consensus session, focused on the need to improve patient-centered communication and strengthen treatment by an interdisciplinary team. She demanded that patients with MBC need an integrative medical approach. This includes first a patient-centered communication. Patients must be well informed about their disease, the therapeutic options, as well as possible drug interactions and adverse events. To ensure this, communication training for oncologist is of major concern.

Only treatment by an interdisciplinary team may do justice to the complexity of metastatic disease. Oncology nurses are important members of the team, but in many countries these professions are not sufficiently supported. Physiotherapy, nutritional advice, psychological support or sport, and rehabilitation for cancer patients are not offered proactively and often too late in the course of illness. But well-informed patients receive better therapy and achieve better therapeutic outcome, summarized the patient advocate.

Conclusion and Outlook

The ABC7 Conference once again was a platform for intensive discussions on the most recent developments in ABC and MBC. As in previous years, the cooperation with patient advocates from Europe, Asia, the Middle East, Africa, Australia, and North, South, and Central America who expressed their concerns and requests was most important. That is also why ABC consensus makes an important contribution in terms of standardizing the treatment of ABC on an international level and optimizing treatment worldwide. The next ABC8 Consensus Conference will take place in Lisbon from November 6 to 8, 2025.

Acknowledgment

The authors would like to thank Birgit-Kristin Pohlmann, Nordkirchen, for editing the manuscript.

Conflict of Interest Statement

Nina Ditsch received honoraria from Gilead, MSD, Novartis, Pfizer, Roche, Seagen, AstraZeneca, Exact Sciences, Pierre Fabre, I-MED-Institute, Merit Medical, PFM Medical, Lilly, Aurikamed, Clinsol, and Onkowissen. Rachel Würstlein received honoraria from Agendia, Amgen, Aristo, AstraZeneca, Celgene, Clovis Oncology, Daiichi Sankyo, Eisai, Exact Sciences, Gilead, Glaxo Smith Kline, Hexal, Lilly, Medstrom Medical, MSD, Mundipharma, Mylan, NanoString, Novartis, Odonate, Paxman, Palleos, Pfizer, Pierre Fabre, PINK, Puma Biotechnology, Riemser, Roche, Sandoz/Hexal, Sanofi Genzyme, Seattle Genetics/Seagen, Stemline, TESARO Bio, Teva, Veracyte, Viatris, FOMF, Aurikamed, Clinsol, Pomme Med, MedConcept, and MCI. Michael Untch received all fees for ad boards and travel support to the employer from AstraZeneca, Daiichi Sankyo, Eisai, Lilly, MSD, Merck, Myriad Genetics, Pfizer, Roche, Pierre Fabre, Novartis, Seagen, and Gilead.

Peter A. Fasching received honoraria from BioNTech, Pfizer, Cepheid, Novartis, Daiichi Sankyo, AstraZeneca, Eisai, Merck Sharp and Dohme, Lilly, Pierre Fabre, Seagen, Roche, Agendia, Sanofi Aventis, Gilead, Mylan, and Menarini. Renate Haidinger has no conflict of interest to declare. Nadia Harbeck received honoraria for consulting and/or lectures from Amgen, AstraZeneca, Daiichi Sankyo, Gilead, Lilly, MSD, Novartis, Pierre Fabre, Pfizer, Roche, Sandoz, Sanofi, Seagen, Viatris, and Zuellig Pharma. Christian Jackisch received honoraria from AstraZeneca, Lilly, Celgene, MSD, Eisai, Novartis, Pfizer, Gilead, Daiichi Sankyo, Medupdate, STREAMED UP, EICHLER GmbH, MedConcept, and Roche and research support by Exact Sciences. Diana Lüftner received honoraria from Amgen, AstraZeneca, Celgene, Daiichi Sankyo, Eli Lilly, Gilead, GSK, high5md, Loreal, Menarini Stemline, Novartis, Onkowissen, Pfizer, Roche, and Teva. Volkmar Müller received speaker honoraria from AstraZeneca, Daiichi Sankyo, Eisai, Pfizer, MSD, Medac, Novartis, Roche, Seagen, Onkowissen, High5 Oncology, Medscape, Gilead, Pierre Fabre, and iMED Institut; consultancy honoraria from Roche, Pierre Fabre, PINK, Clinsol, Novartis, MSD, Daiichi Sankyo, Eisai, Lilly, Seagen, Gilead, and Stemline; institutional research support from Novartis, Roche, Seagen, Genentech, and AstraZeneca; and travel grants from AstraZeneca, Roche, Pfizer, Daiichi Sankyo, and Gilead. Eva Schumacher-Wulf has no conflict of interest to declare. Steffi Busch received honoraria for lectures, studies, and support for congress participation from Amgen, Roche, Novartis, Pfizer, Riemser, Lilly, Clovis, GSK, Onkovis, AstraZeneca, and MSD. She has no financial participation in any of these companies, no shares, or similar. Johannes Ettl received honoraria from AstraZeneca, Celgene, Clovis Oncology, Daiichi Sankyo, Eisai, Gilead, Glaxo Smith Kline, Lilly, Novartis, Pfizer, Pierre Fabre, Roche, Seattle Genetics, Seagen, Stemline, TESARO Bio, Teva, and Clinsol. Lothar Müller received honoraria from Roche and travel support from Pierre Fabre and Octapharm. Eugen Ruckhäberle received honoraria from AstraZeneca, Celgene, Daiichi Sankyo, Eisai, Pfizer, MSD, Novartis, and Roche, and consultancy honoraria from Genomic Health, Hexal, Roche, Pierre Fabre, Novartis, MSD, Daiichi Sankyo, Eisai, Lilly, and TESARO, and travel support by Pfizer and Pierre Fabre. Christoph Thomssen received honoraria from Amgen, AstraZeneca, Celgene, Daiichi Sankyo, Eisai, Lilly, MSD, Mundipharma, MEDA, Novartis, Roche, TESARO, and Vifor.

Funding Sources

The meeting of the German experts in Lisbon was supported and organized by onkowissen.de. onkowissen.de had no role on the content of the manuscript. The authors bear the sole responsibility for the final release of the contents of the manuscript.

Author Contributions

The ABC7 consensus meeting was discussed and prepared in writing by the Writing Committee, consisting of N.D. (first author), R.W., M.U., N.H., V.M., D.L., and P.A.F. The manuscript was revised and finalized by all authors (N.D., M.U., P.A.F., S.B., J.E., R.H., C.J., D.L., L.M., V.M., E.R., E.S.-W., C.T., N.H., and R.W.).

References

1 Thill M, Kolberg-Liedtke C, Albert U-S, Banys-Paluchowski M, Bauerfeind I, Blohmer JU, et al. AGO Recommendations for the Diagnosis and Treatment of Patients with Locally Advanced and Metastatic Breast Cancer: Update 2023. Breast Care. 2023;18:306–15.

2 Dykewicz CA, Centers for Disease Control and Prevention U.S.; Infectious Diseases Society of America; American Society of Blood and Marrow Transplantation. Summary of the guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. Clin Infect Dis. 2001;33(2):139–44.

3 Azim H, El Saghir NS, Yap Y. First-line ribociclib + endocrine therapy vs combination chemotherapy in aggressive HR+/HER2- advanced breast cancer: a sub-group analysis of patients with or without vis-ceral crisis from the phase II RIGHT Choice study. Präsentation 402P. Stand: 27.11.2023. Im Internet Available from: https://oncologypro.esmo.org/meeting-resources/esmo-congress.

4 Lu Y-S, Mahidin EIBM, Azim H, ERALP Y, Yap Y-S, Im S-A, et al. Abstract GS1-10: Primary results from the randomized Phase II RIGHT Choice trial of premenopausal patients with aggressive HR+/HER2– advanced breast cancer treated with ribociclib + endocrine therapy vs physician's choice combination chemotherapy. Cancer Res. 2023;83:GS1-10-GS1-10.

5 Wolff AC, Somerfield MR, Dowsett M, Hammond MEH, Hayes DF, McShane LM, et al. Human epidermal growth factor receptor 2 testing in breast cancer. Arch Pathol Lab Med. 2023;147(9):993–1000.

6 Chmura SJ, Winter KA, Woodward WA, Borges VF, Salama JK, Al-Hallaq HA, et al. NRG-BR002: a phase IIR/III trial of standard of care systemic therapy with or without stereotactic body radiotherapy (SBRT) and/or surgical resection (SR) for newly oligometastatic breast cancer (NCT02364557). J Clin Oncol. 2022;40(16_Suppl):1007.

7 Dunst J. Kurative Strahlentherapie von Oligometastasen: langzeitergebnisse der SABR-COMET-Studie. Strahlenther Onkol. 2021;197(4):365–7.

8 S3-Leitlinienprogramm Onkologie. Erweiterte S3-Leitlinie Palliativmedizin für Patienten mit einer nicht heilbaren Krebserkrankung. Langversion 2.2 - September 2020. AWMF-Registernummer: 128/001OL.

9 Sonke GS, van Ommen-Nijhof A, Wortelboer N, van der Noort V, Swinkels ACP, Blommestein HM, et al. Primary outcome analysis of the phase 3 SONIA trial (BOOG 2017-03) on selecting the optimal position of cyclin-dependent kinases 4 and 6 (CDK4/6) inhibitors for patients with hormone receptor-positive (HR+), HER2-negative (HER2-) advanced breast cancer (ABC). J Clin Oncol. 2023;41(17_Suppl):LBA1000.

10 Decker T, Lüdtke-Heckenkamp K, Melnichuk L, Hirmas N, Lübbe K, Zahn MO, et al. Anti-hormonal maintenance treatment with the CDK4/6 inhibitor ribociclib after 1st line chemotherapy in hormone receptor positive/HER2 negative metastatic breast cancer: a phase II trial (AMICA). Breast. 2023;72:103575.

11 Kalinsky K, Accordino MK, Chiuzan C, Mundi PS, Sakach E, Sathe C, et al. Randomized phase II trial of endocrine therapy with or without ribociclib after progression on cyclin-dependent kinase 4/6 inhibition in hormone receptor-positive, human epidermal growth factor receptor 2-negative metastatic breast cancer: MAINTAIN trial. J Clin Oncol. 2023;41(24):4004–13.

12 Bidard F-C, Kaklamani VG, Neven P, Streich G, Montero AJ, Forget F, et al. Elacestrant (oral selective estrogen receptor degrader) versus standard endocrine therapy for estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: results from the randomized phase III EMERALD trial. J Clin Oncol. 2022;40(28):3246–56.

13 [Anonymous]. Erratum: elacestrant (oral selective estrogen receptor degrader) versus standard endocrine therapy for estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: results from the randomized phase III EMERALD trial. J Clin Oncol. 2023;41:3962.

14 Kaklamani V, Bidard FC, Neven P, et al EMERALD phase 3 trial of elacestrant versus standard of care endocrine therapy in patients with ER+/HER2– metastatic breast cancer: updated re-sults by duration of prior CDK4/6 inhibi-tor in metastatic setting. 2022 San Antonio Breast Cancer Sym-posium. Abstract GS3-01. Presented December 8, 2022. 2022.
15 Turner NC, Oliveira M, Howell SJ, Dalenc F, Cortes J, Gomez Moreno HL, et al. Capivasertib in hormone receptor-positive advanced breast cancer. N Engl J Med. 2023;388(22):2058–70.
16 Rugo HS, Bardia A, Marmé F, Cortes J, Schmid P, Loirat D, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer. J Clin Oncol. 2022;40(29):3365–76.
17 Rugo HS, Bardia A, Marmé F, Cortés J, Schmid P, Loirat D, et al. Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial. Lancet. 2023;402(10411):1423–33.
18 Modi S, Jacot W, Yamashita T, Sohn J, Vidal M, Tokunaga E, et al. Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer. N Engl J Med. 2022;387(1):9–20.
19 Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. N Engl J Med. 2021;384(16):1529–41.
20 Modi S, Andre F, Krop IE, Saura C, Yamashita T, Kim SB, et al. Trastuzumab deruxtecan for HER2-positive metastatic breast cancer: DESTINY-Breast01 subgroup analysis. J Clin Oncol. 2020;38(15_Suppl):1036.
21 Hurvitz SA, Hegg R, Chung W-P, Im SA, Jacot W, Ganju V, et al. Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: updated results from DESTINY-Breast03, a randomised, open-label, phase 3 trial. Lancet. 2023;401(10371):105–17.
22 André F, Hee Park Y, Kim S-B, Takano T, Im SA, Borges G, et al. Trastuzumab deruxtecan versus treatment of physician's choice in patients with HER2-positive metastatic breast cancer (DESTINY-Breast02): a randomised, open-label, multicentre, phase 3 trial. Lancet. 2023;401(10390):1773–85.
23 Hurvitz S, Modi S, Li W. A pooled analysis of trastuzumab deruxtecan in patients with HER2-positive metastatic breast cancer with brain metastases from DESTINY-breast01, -02 and -03. Madrid: ESMO-Jahrestagung 2023. Orale presentation #377PPS 2023.
24 Murthy RK, Loi S, Okines A, Paplomata E, Hamilton E, Hurvitz SA, et al. Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. N Engl J Med. 2020;382(7):597–609.
25 Kowalski ES, Feigenberg SJ, Cohen J, Fellows Z, Vadnais P, Rice S, et al. Optimal target delineation and treatment techniques in the era of conformal photon and proton breast and regional nodal irradiation. Pract Radiat Oncol. 2020;10(3):174–82.
26 Davidson T, Ben-David M, Galper S, Haskin T, Howes M, Scaife R, et al. Use of 18F-FDG PET-CT imaging to determine internal mammary lymph node location for radiation therapy treatment planning in breast cancer patients. Pract Radiat Oncol. 2017;7(6):373–81.
27 Jacene HA, DiPiro PJ, Bellon J, Hu J, Cheng SC, Warren L, et al. Discrepancy between FDG-PET/CT and con-trast-enhanced CT in the staging of patients with inflammatory breast cancer: implications for treatment planning. Breast Cancer Res Treat. 2020;181(2):383–90.
28 Schmid P, Cortes J, Dent R, Pusztai L, McArthur H, Kümmel S, et al. Event-free survival with pembrolizumab in early triple-negative breast cancer. N Engl J Med. 2022;386(6):556–67.
29 Cortes J, Rugo HS, Cescon DW, Im SA, Yusof MM, Gallardo C, et al. Pembrolizumab plus chemotherapy in advanced triple-negative breast cancer. N Engl J Med. 2022;387(3):217–26.
30 Maio M, Shapira-Frommer R, Yap TA, Ciuleanu T, Gomez H, Hill A, et al. Abstract CT178: olaparib plus pembrolizumab in patients with previously treated advanced solid tumors with homologous recombination repair mutation (HRRm) and/or homologous recombination deficiency (HRD): initial results of the phase 2 KEYLYNK-007 study. Cancer Res. 2021;81(13_Suppl):CT178.
31 Rugo H, Robson M, Im SA. Pembrolizumab plus olaparib vs pembrolizumab plus chemotherpy after induction with pembrolizumab plus chemotherapy for locally recurrent inoperable or metastatic TNBC: randomized, open-label, phase 2 KEYLYNK-009 study. San antonio breast cancer symposium (SAVCS) 2023, san antonio, 05–9th Decembre 2023. Presentation GS01-05.
32 Cardoso F, Costa A, Senkus E, Aapro M, André F, Barrios CH, et al. 3rd ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 3). Ann Oncol. 2017;28(1):16–33.
33 Biganzoli L, Battisti NML, Wildiers H, McCartney A, Colloca G, Kunkler IH, et al. Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG). Lancet Oncol. 2021;22(7):e327–40.
34 Martinez-Tapia C, Paillaud E, Liuu E, Tournigand C, Ibrahim R, Fossey-Diaz V, et al. Prognostic value of the G8 and modified-G8 screening tools for multidimensional health problems in older patients with cancer. Eur J Cancer. 2017;83:211–9.
35 Decoster L, van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations. Ann Oncol. 2015;26(2):288–300.
36 El Badri S, Tahir B, Balachandran K, Bezecny P, Britton F, Davies M, et al. Palbociclib in combination with aromatase inhibitors in patients ≥75 years with oestrogen receptor-positive, human epidermal growth factor receptor 2 negative advanced breast cancer: a real-world multicentre UK study. Breast. 2021;60:199–205.
37 Carola E, Pulido M, Falandry C, Paillaud E, Caillet P, Tassy L, et al. First-line systemic treatment with palbociclib in women aged ≥70 years presenting with hormone receptor-positive advanced breast cancer: results from the PALOMAGE program. J Clin Oncol. 2023;41(16_Suppl):1018.
38 Blum JL, Rocque G, Ji Y. Impact of comorbidities on real-world patient-reported outcomes of patients with hormone receptor positive human epidermal growth factor 2 negative advanced breast cancer enrolled in the POLARIS trial. ESMO-Jahrestagung 2023, Madrid 24.10.2023. #461P 2023.
39 Tripathy D, Blum JL, Karuturi MS, et al. Impact of comorbidities on real-world clinical outcomes of patients with hormone receptor-positive/human epidermal growth factor 2-negative advanced breast cancer treated with palbociclib and enrolled in POLARIS. ESMO-Jahrestagung 2023, 20.-24.10.2023. #373P.
40 Roncato R, Angelini J, Pani A, Cecchin E, Sartore-Bianchi A, Siena S, et al. CDK4/6 inhibitors in breast cancer treatment: potential interactions with drug, gene, and pathophysiological conditions. Int J Mol Sci. 2020;21(17):6350.