Zusatzmaterial

Tabellen

Supplement Tab. S1: Panelisten der ABC7-Konferenz.

Fatima Cardoso, PT (Chair)
Eva Schumacher-Wulf, DE (Co-chair, Patient Advocate)
Eric P. Winer, US (Honorary Chair)
Larry Norton, US (Honorary Chair)
Karen Gelmon, CA (Scientific Committee)
Sandra M. Swain, US (Scientific Committee)
Sandra Franco, CO (Scientific Committee)
Birgitte V. Offersen, DK (Scientific Committee; ESTRO)
Joseph Gligorov, FR (Scientific Committee; Nice/St Paul guidelines)
Volkmar Mueller, DE (Scientific Committee; AGO)
Frederique Penault-Llorca, FR (Nice/St Paul guidelines) Alexandru Eniu, CH (ESO)
Mariana Chavez MacGregor, US (ASCO)
Ann H. Partridge, US (ASCO)
Nadia Harbeck, DE (AGO)
William J. Gradishar, US (NCCN)
Laura Biganzoli, IT (EUSOMA)
Theresa Wiseman, UK (EONS)
Silvia Neciosup, PE (ABC Latin America Guidelines)
Marion Kuper, NZ (NZ ABC Guidelines)
Ginny Mason, US (Patient Advocate)
Claire Myerson, UK (Patient Advocate)
Runde Chidebe, NG (Patient Advocate)
Ranjit Kaur, MY (Patient Advocate)
Lesley Fallowfield, UK (Psycho-Oncology)
Jenny Gilchrist, AU (Nurse)
Shani Paluch-Shimon, IL
Matti S. Aapro, CH
Hope S. Rugo, US
Carlos H. Barrios, BR
Maria Joao Cardoso, PT
Lisa Carey, US
Javier Cortes, ES
Rebecca A. Dent, SG
Nagi S. El Saghir, LB
Prudence A. Francis, AU
Xichun Hu, CN
Belinda Kiely, AU
Sung-Bae Kim, KR
Jyoti Bajpai, IN
Frederic E. Lecouvet, BE
Shinji Ohno, JP
Elzbieta Senkus, PL
Peter Vuylsteke, BW

Supplement Tab. S2: Fragen der Abstimmung unter den ABC7-Panelisten. Wegen des Live-Charakters der Abstimmungen besteht kein Anspruch auf Vollständigkeit. Die Fragen sind nummeriert zum Text dieses Artikels. Die Nummerierung war keine Vorgabe der ABC7-Konferenz.

Themenkomplexe

- Advanced breast cancer (ABC) definitions
- estrogen receptor-positive, HER2-negative (ER+/HER2−) ABC
- Triple negative ABC (TNBC)
- HERs positive ABC
- Oligo metastatic disease and surgery of the primary tumor
- Special life and healthcare system conditions and co-morbidities
- Treatment holidays and quality of life
- Brain metastases
- Contraception and pregnancy
- Inoperable locally advances breast cancer and inflammatory breast cancer
- The visceral crisis
- The elderly patient
- Leptomeningeal disease (LMD)

ABC definitions

Question 1

	ABC Definitions: Endocrine sensitivity/ resistance **ET-naive**: Unknown if there is sensitivity or resistance to endocrine therapy (ET) since has never received ET. **Primary endocrine resistance** is defined as: Relapse while on the first 2 years of adjuvant ET, or progressive disease (PD) within first 6 months of 1st line ET-based therapy for ABC (note: this definition is the same regardless of whether therapy included a CDK4/6 inhibitor [CDK4/6i] or not). **Secondary (acquired) endocrine resistance** is defined as: All other clinical situations of endocrine-resistance (examples include: 1) Relapse while receiving adjuvant ET but after at least 2 years; 2) PD after at least 6 months of 1st line ET-based therapy for ABC; 3) PD after any duration of 2nd+ line ET-based therapy for ABC; 4) Known ESR1 mutation) (note: definition unaffected by therapy with CDK4/6i, mTOR/PI3Ki, or other adjunctive drugs). **Endocrine insensitivity** is defined as: PD within 2 months of later-line ET-based therapy for ABC and no additional ET-based approaches likely to result in clinically meaningful benefit (LoE: Expert opinion/NA).	
	a) Yes	95.4%
	b) No	2.2%
	c) Abstain	2.2%

Question 2

	ABC Definitions HER2 low The pathology report must detail the HER2 score according to ASCO/CAP 2023 recommendations (0, 1+, 2+ (amplified or not amplified) or 3+). It is desirable to report the percentage of labeled cells. It is recommended to detail in the conclusion: HER2 zero, HER2 low (1+ or 2+ non-amplified), HER2+ (2+ ISH amplified or HER2 3+). (LoE/GoR: Expert opinion/A)	
	a) Yes	97.6%
	b) No	0.0%
	c) Abstain	2.3%

ER positive HER2 negative ABC

Question 3

	ER positive/ HER2 negative ABC: CDK4/6i In the RIGHT Choice trial, the combination of ribociclib + aromatase inhibitor was compared to combination chemotherapy (docetaxel + capecitabine, paclitaxel + gemcitabine or capecitabine + vinorelbine) as 1st line therapy for pre/peri-menopausal women with ER+/HER2 neg ABC with “clinically aggressive disease” defined as: symptomatic visceral metastases, rapid disease progression or impending visceral compromise, markedly symptomatic non-visceral disease, but with bilirubin <1.5 (therefore not in visceral crisis as defined by the ABC guidelines). The ET+ CDK4/6i arm yielded a 12 ms benefit in progression-free survival (PFS), with similar overall response rate (ORR) and similar time to onset of response in both arms, but substantially better toxicity profile for the ET-based arm. These results reinforce the place of ET+ CDK4/6 inhibitors as standard of care for 1st line therapy for the majority of patients with ER+/HER2 negative ABC, including those with "clinically aggressive disease". (LoE/GoR : I/ A) Although the trial was run only in pre/peri-menopausal women, the panel believes the results also apply to post-menopausal women and men with the same disease characteristics. (LoE/GoR: Expert opinion/B)	
	a) Yes	95.4%
	b) No	2.2%
	c) Abstain	2.2%

Question 4

	ER positive/ HER2 negative ABC: CDK4/6i The SONIA trial attempted to answer the question whether a CDK4/6i (90% palbociclib) combined with endocrine therapy should be given as 1st or 2nd line therapy for ER+/HER-2 neg ABC. No statistically significant differences were seen in PFS 2 (primary endpoint) nor overall survival (OS) nor quality of life (QoL), at 37 ms follow-up. It is currently unknown if the results would be the same with ribociclib or abemaciclib that have the strongest data in terms of OS. Based on these results, it is an acceptable option to use ET alone as 1st line therapy for selected patients (e.g. low volume of disease, long disease-free interval (DFI), patient preferences, accessiblity constraints), with ER+/HER-2 neg ABC. However, in view of the substantial OS benefit seen with ribociclib and abemaciclib in the 1 st line setting, the panel, still favors the use of a CDK4/6i + ET as 1st line therapy for the majority of patients with this ABC subtype. (LoE/GoR : I/ A)	
	a) Yes	93.1%
	b) No	0.0%
	c) Abstain	6.9%

Question 5

	ER positive/ HER2 negative ABC: CDK4/6i There are no data supporting the use of a combination of CDK4/6i and ET as maintenance therapy after chemotherapy. Maintenance therapy, in this situation, should be performed with ET alone. (LoE/GoR: Expert Opinion/C)	
	a) Yes	39.5%
	b) No	41.8%
	c) Abstain	18.7%

Question 6

	ER positive/ HER2 negative ABC: CDK4/6i There are no data comparing a combination of CDK4/6i and ET vs. ET alone as maintenance therapy after chemotherapy. Both options are acceptable. (LoE/GoR: Expert Opinion/B)	
	a) Yes	75.0%
	b) No	15.9%
	c) Abstain	9.0%

Question 7

	ER positive/ HER2 negative ABC: CDK4/6i The use of a CDK4/6i + ET after disease progression on a CDK4/6i (i.e. beyond progression) has been evaluated in small phase 2 trials, with conflicting results and is not recommended for routine clinical practice, outside a clinical trial. (LoE/GoR: Expert Opinion/D)	
	a) Yes	90.7%
	b) No	4.6%
	c) Abstain	4.7%

Question 8

	ER positive/ HER2 negative ABC: CDK4/6i In view of the substantial survival benefit seen with ET+ CDK4/6i in 1st line, this combination is considered the standard of care for 1st line therapy for the majority of patients with ER+/HER2 negative ABC, independently of the patient's age. (LoE/GoR: II/A) Real world-data suggest that ET +CDK4/6i can be beneficial also in unfit older patients. (LoE/GoR: III/B)	
	a) Yes	93.0%
	b) No	2.3%
	c) Abstain	4.6%

Question 9

	ER positive/ HER2 negative ABC: CDK4/6i In unfit patients, testing a reduced starting dose of the CDK4/6i, is a reasonable but not evidence-based strategy. (LoE/GoR: Expert opinion/B)	
	a) Yes	90.6%
	b) No	4.6%
	c) Abstain	4.6%

Question 10

	ER positive/ HER2 negative ABC: Oral selective estrogen receptor degraders (SERDs) Elacestrant, an oral SERD, was compared with physician's choice of fulvestrant or aromatase inhibitor, in patients with ER+/HER2 negative ABC, with 1 or 2 lines of previous ET, one of them including a CDK4/6i, and none or 1 line of chemotherapy for metastatic disease. The results showed a less than 1 ms difference in median PFS in the overall population and about 2 months difference in tumors harboring ESR1 mutation. The benefit was somewhat higher in patients who had their disease controlled with CDK4/6i for more than 12 months and in the tail of the KM curves. OS data is still immature. GI toxicity, especially nausea, and fatigue were the most common side effects. In view of the limited benefit in PFS and the absence of OS benefit so far, the existence of other treatment options and the lack of data after an ADC, elacestrant can not yet be recommended for routine clinical practice use. (LoE/GoR: I/C)	
	a) Yes	51.1%
	b) No	44.1%
	c) Abstain	4.6%

Question 11

	ER positive/ HER2 negative ABC: Oral SERDs Elacestrant, an oral SERD, has been approved by the US FDA as 2nd/3rd line therapy for patients with ER+/HER2- ABC with an ESR1 mutation based on a randomized phase III trial demonstrating a PFS advantage. This advantage was most notable in patients who were previously on a CDK4/6i for >6 months. Where available, Elacestrant is an option for patients in 2nd/3rd line setting with an ESR1 mutation. (LoE/GoR: I/C)	
	a) Yes	81.3%
	b) No	6.9%
	c) Abstain	11.6%

Question 12

	ER positive/ HER2 negative ABC:antibody-drug conjuguates (ADCs) Sacituzumab govitecan was compared with chemotherapy of physician's choice, in patients with ER+/HER2 negative ABC, previously treated with at least 1 line of ET, taxane, and CDK4/6i in any setting and at least 2, but no more than 4, lines of chemotherapy (CT) for metastatic disease (60% of pts has received 3 or more lines of CT). Results showed an 1.5 months improvement in median PFS and 3.2 months median OS, both in HER2 low and HER2 zero. No new safety signals were seen. Education, prophylaxis and early management of side effects, in particular diarrhea and nausea/vomiting, remain important. The OS benefit seen in this heavily pretreated population makes sacituzumab govitecan a treatment option for this patient population. (LoE/GoR: I/B)	
	a) Yes	95.3%
	b) No	2.3%
	c) Abstain	2.4%

Question 13

	ER positive/ HER2 low ABC: ADCs Trastuzumab deruxtecan (T-DXd) was compared to chemotherapy of physician's choice, in patients with HER2 low ABC, treated with 1-2 lines of chemotherapy in the metastatic setting and ER+ disease considered endocrine refractory, and yielded a 6.3 months benefit in median OS and 5.8 months in median PFS, making it a preferred treatment option in this setting. Treatment with T-DXd was associated with ILD/pneumonitis (including 4 toxic deaths), increased GI toxicity and fatigue. ILD/Pneumonitis can be fatal and requires active surveillance (including non-contrast CT scans every 6-8 weeks) and proper management. Nausea and vomiting require adequate prophylaxis. (LoE/GoR: I/ A)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 14

	ER positive/ HER2 low ABC: ADCs There are very few data regarding the best sequence of administration of ADCs for ER+/HER2 negative or HER2 low ABC. In view of the populations treated and results of the trials of T-DXd and sacituzumab govitecan (SG), the panel believes that T-DXd should be used earlier than SG. (LoE/GoR; Expert opinion/B)	
	a) Yes	95.3%
	b) No	0.0%
	c) Abstain	4.6%

Triple negative ABC

Question 15

	Triple negative/ HER2 low ABC: ADCs There are very few data regarding the best sequence of administration of ADCs for ER negative/HER2 low ABC. In view of the results of the trials of T-DXd and sacituzumab govitecan in this patient population, the panel believes that sacituzumab govitecan should be used in earlier than T-DXd. (LoE/GoR: II/A)	
	a) Yes	90.4%
	b) No	4.7%
	c) Abstain	4.7%

HER2 positive ABC

Question 16

	HER2 positive ABC If no absolute cardiac contra-indications exist, older patients with HER2- positive ABC should have access to anti-Her2 agents (LoE/ GoR: I/A) Certain, anti-HER2 agents such as tyrosine kinase inhibitor (TKI) (e.g. tucatinib) and ADCs (e.g. T-DXd), which are usually associated with more side effects, may need a lower starting dose, careful monitoring and dose adjustments according to toxicity in older frail patients. (LoE/GoR: Expert opinion/ A)	
	a) Yes	83.7%
	b) No	6.9%
	c) Abstain	9.3%

Oligo metastatic disease and surgery of the primary tumor

Question 17

	Oligo-metastatic disease management A randomized phase 2 trial (NRG-BR002) in patients (n=125) with oligometastatic breast cancer (< 4 extra-cranial sites) evaluated use of SBRT and/or Surgical Resection to all oligometastatic sites, in context of ≤ 12 months of first-line systemic therapy without progression. Most enrolled pts had oligometastatic recurrence (78%) and ER+/HER2-negative breast cancer (80%). The results showed no difference in median PFS and 3-yr OS, no difference in rate of metastases outside index area, and the trial did not proceed to phase 3. A small randomized phase 2 trial (SABR-COMET) in patients with different types of advanced cancers including breast (18 patients only), evaluated the use of SABR or SBIRT to all sites of oligometastatic disease, in the context of a controlled primary tumor, and showed a significant OS benefit. Based on available data, routine ablation of extra-cranial asymptomatic oligometastatic sites is not recommended, outside a clinical trial, until further data is available. (LoE/GoR: II/0) It may however be discussed on a case-by-case basis.	
	a) Yes	97.6%
	b) No	2.3%
	c) Abstain	0.0%

Question 18

	Surgery of the primary tumor To date, the removal of the primary tumor in patients with de novo stage IV breast cancer has not been associated with prolongation of survival. However, it can be considered in selected patients, particularly to improve quality of life, always taking into account the patient's preferences. (LoE/GoR: I/C) (70%) Examples of situations where surgery of the primary may be considered include: • Symptomatic primary site (for palliation) • Progression of the primary tumor when distant disease is controlled • Oligometastatic disease (to try to induce a complete remission) • No evidence of disease except the primary tumor (to try to induce a complete remission) Of note, some studies suggest that surgery is only valuable if performed with the same attention to detail (e.g. complete removal of the disease), as in patients with early stage disease. (LoE/GoR: II/B) (70%)	
	a) Yes	97.6%
	b) No	0.0%
	c) Abstain	2.3%

Special life and healthcare system conditions and co-morbidities

Question 19

	Caring for patients with ABC during war and conflict War and conflict can cause major disruption to delivery of care for patients with cancer. It access to medical care is disrupted or erratic, when possible, consider treatment with oral regimens and treatment regimens requiring minimal routine monitoring and blood work. Telemedicine should be utilized to ensure continuity of care and contact with patients. All efforts should be made to ensure access to pain medications. Providing online support for colleagues in regions of conflict, who may themselves be at risk but who are essential workers trying to ensure best delivery of oncology care under difficult circumstances, is meaningful and important.	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 20

	Access of patients with advanced breast cancer to intensive care units Patients with ABC should receive patient-centered communications regarding their prognosis and treatment options and have the right to forgo treatment as well as to pursue treatments to the degree they desire where available and appropriate for the disease setting. They should not be denied access to ICU (intensive care units) based solely on their ABC diagnosis, in particular in cases of potentially reversible serious adverse events or complications of comorbidities other than ABC. (LoE/GoR: Expert Opinion/B)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 21

	Caring for patients with ABC and pre-existing serious mental health illness Individuals diagnosed with serious mental illness (SMI) (including but not limited to major depression, bipolar disorder and schizophrenia) are more likely to be diagnosed with advanced stage cancer and to have poorer outcomes than individuals without SMI. Attention needs to be given to the special needs of patients with ABC and SMI and there should be no discrimination against them. The oncology team should endeavor to work together with the patient's psychiatrist and mental illness care team and endeavor to engage carers in order to ensure optimization, compliance and continuity of oncology care. Special attention needs to be given to drug-drug interactions between psychiatric medication and oncological therapies. Under certain circumstances steroid and medicinal cannabis use should be minimized to avoid triggering episodes of mania and psychosis (LoE/GoR: IV/B)	
	a) Yes	95.2%
	b) No	0.0%
	c) Abstain	4.7%

Question 22

	Management of a patient with ABC and HIV Prevalence of HIV comorbidity in ABC patients depends on HIV endemicity (varies 6 - 26%). Patients living with HIV who develop breast cancer have consistently worse survival, both in early and metastatic settings. HIV+ breast cancer patients have worse toxicity, especially myelotoxicity and infections. Data on how to manage ABC in a patient living with HIV are scarce, specially concerning new anticancer agents. Breast cancer lin patients living with HIV should be co-managed by an oncologist and HIV specialist working in a multidisciplinary way. (LoE/GoR: Expert Opinion/A) HIV positivity, if under treatment and controlled (undetectable viral load), should no longer be an exclusion criteria in most clinical trials. (LoE/GoR: Expert Opinion/A) People living with HIV have a higher incidence of other diseases such as tuberculosis and hepatitis. Before starting anticancer treatment, these diseases should be looked for and if diagnosed, treatment should be initiated. (LoE/GoR: Expert Opinion/B)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 23

	Management of a patient with ABC and HIV In general, the same ABC guidelines apply to HIV+ and HIV neg patients with ABC. However, careful consideration should be given to dose reductions and/or increased intervals (G-CSF recommended for myelotoxcic CT agents). (LoE/GoR: Expert Opinion/A) Data suggest safety of immune-checkpoint inhibitors (loE/GoR: IV/B), and there are no data regarding the use of CDK4/6i (research need). (LoE/GoR: Expert Opinion/NA)	
	a) Yes	95.2%
	b) No	0.0%
	c) Abstain	4.7%

Question 24

	Management of a patient with ABC and HIV Most cytotoxic agents can be safely initiated if viral load is undetectable and CD4+ T-count is at least 200 under modern ART regimens. (LoE/GoR: Expert Opinion/B) HIV therapy should be initiated or continued during cancer therapy. (LoE/GoR: Expert Opinion/A) In anti-retroviral naive patients, it is recommended to initiate ART and wait for about 2 weeks before starting anticancer therapies, if dinicaHy possible. (LoE/GoR: Expert Opinion/B) Potential drug-drug tnteractions must always be checked. lf interactions are a concem, lt is recommended to check the viral load more often. For drugs that cause lymphopenia, CD4+ T-cell counts should be monitored more frequently. (LoE/GoR: Expert Opinion/B)	
	a) Yes	93.1%
	b) No	0.0%
	c) Abstain	6.8%

Treatment holidays and quality of life

Question 25

	Treatment Holidays Treatment holidays are an acceptable treatment option in the case of long-term responders with controlled disease. (LoE/GoR: IV/B)	
	a) Yes	97.7%
	b) No	0.0%
	c) Abstain	2.2%

Question 26

	Treatment Holidays Stopping treatment in patients with long-term complete remissions has not been adequately studied but should be considered on a case-by-case basis, after extensive discussion with the patient. It is crucial that resuming the treatment, if progression of disease occurs, is allowed in all countries. (LoE/GoR: Expert Opinion/B)	
	a) Yes	97.7%
	b) No	0.0%
	c) Abstain	2.2%

Question 27

	patient-reported outcomes (PRO)'s, e-PRO's and Quality of life assessments Strong consideration, as part of routine clinical care, should be given to the integration of patients', reports of symptoms of disease and side effects of treatment. Several remote measurement systems exist but these must be evidence-based and shown to be simple enough for use in clinical practice, in particular employ user-friendly collection platforms e.g. tablets or smartphones appropriate for different patient groups. Such regular systematic monitoring may facilitate communication between patients and their treatment teams about the toxicities of anticancer therapies. Reporting does not have to be tied to regular follow-up visits so that it may permit earlier introduction of ameliorative interventions and supportive care services. (LoE/GoR: I/B)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 28

	PRO's, e-PRO's and Quality of life assessments Trials evaluating QoL in ABC should employ standardized PROMs and not focus exclusively on reporting CTCAE symptom grades. lf generic measures are used, then appropriate symptom and treatment specific modules or subscales that exist within the EQIRTC and FACiT systems should be incorporated. Additionally, attention must be paid to collection methods, timing of assessments and handling of missing data. More sophisticated statistics should also be employed to ensure that clinicians have better, reliable data to help patients choosing between treatment options. (LoE/GoR: Expert opinion/A)	
	a) Yes	97.7%
	b) No	0.0%
	c) Abstain	2.2%

Brain metastases

Question 29

	Brain metastasis Trastuzumab deruxtecan (T-DXd) has shown activity against brain metastases, previously treated or untreated with local therapy, and can be considered a treatment option. (LoE/GoR: II/B)	
	a) Yes	97.7%
	b) No	2.2%
	c) Abstain	0.0%

Contraception and pregnancy

Question 30

	ABC, contraception and pregnancy All women of reproductive age with ABC should be counselled about use of non-hormonal contraception (independent of the tumor subtype} and the risks of conceiving while receiving treatment for ABC. (LoE: II/A)	
	a) Yes	93.0%
	b) No	6.9%
	c) Abstain	0.0%

Question 31

	ABC, contraception and pregnancy Special attention should be given to women of reproductive age with ABC being treated without OFS/OFA since several therapies used for ABC have a low gonadotoxic effect and willl not induce menopause. (LoE: II/A)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 32

	ABC, contraception and pregnancy Management of a pregnant patient with ABC is a complex and delicate situation that requires multidisciplinary discussion and experienced care. (LoE/GoR: Expert opinion/A) Advice hould be sought from experts in the field such as the International Advisory Board of ClP (Cancer In Pregnancy) (www.ab-cip.org) The patient's and her partner's preferences must always be taken into account, after appropriate and transparent sharing of information about all management options and their potentiaI impact on the patient's survival and fetaI health. (LoE/GoR: Expert opinion/A)	
	a) Yes	97.5%
	b) No	0.0%
	c) Abstain	2.4%

Question 33

	ABC, contraception and pregnancy The preferred imaging method to stage a pregnant patient with breast cancer is whole-body diffusion MRI. (LoE/GoR: Expert opinion/B)	
	a) Yes	77.2%
	b) No	9.0%
	c) Abstain	13.6%

Question 34

	ABC, contraception and pregnancy Among all available systemic therapies, only chemotherapy can be safely administered during pregnancy and only in the 2nd and 3rd trimesters. (LoE/GoR: II/A) The most complex situation relates to HER2+ disease diagnosed in the 1st and 2nd trimester, because anti-HER2 therapy is critical for optimal disease control but cannot be administered during the entire pregnancy. (LoE/GoR: Expert opinion/A)	
	a) Yes	95.2%
	b) No	0.0%
	c) Abstain	4.7%

Question 35

	ABC, contraception and pregnancy Termination of pregnancy is a major consideration in some circumstances and should be available for patients who decide in favor of it. (LoE/GoR: Expert opinion/A)	
	a) Yes	95.3%
	b) No	2.3%
	c) Abstain	2.3%

Inoperable locally advanced breast cancer and inflammatory breast cancer

Question 36

	Inoperable LABC and Inflammatory breast cancer (IBC) BEFORE starting any therapy, at least one core biopsie providing histological type, grade and biomarker expression is indispensable to guide treatment decisions. Biomarkers include: for inoperable LABC and inoperable IBC (inflammatory breast cancer, non-metastatic): ER, PR, HER2, Ki67, BRCA 1/2 for metastatic IBC: ER, HER2, PD-L1 (in TNBC), Pi3KCA (in ER/HER2 neg IBC), BRCA 1/2	
	a) Yes	88.6%
	b) No	9.0%
	c) Abstain	2.2%

Question 37

	Inoperable LABC and Inflammatory breast cancer (IBC) Inflammatory breast cancer (IBC) is a clinicopathological diagnosis that requires an interprofessional approach for diagnosis. lBC is designated as T4d or stage IV in case of metastatic disease at presentation. All of the following criteria must be met for a diagnosis of IBC: a) Rapid onset of breast erythema, edema and/ or peau d'orange, and/ or warm breast, with or without an underlying palpable mass; b) Duration of history no more than six months c) Erythema occupying at least one-third of the breast d) Pathological confirmation of invasive carcinoma e) A skin punch biopsy may help in the diagnosis, but it is not indispensable. Skin ulcerations are rare in IBC and more common in non-infllammatory LABC. (LoE/GoR: I/A)	
	a) Yes	95.5%
	b) No	0.0%
	c) Abstain	4.5%

Question 38

	Inoperable LABC and Inflammatory breast cancer (IBC) Since LABC and IBC patients have a substantial risk of metastatic disease, a full staging workup, including a complete history, physical examination, lab tests and imaging of chest and abdomen and bone, before initiation of systemic therapy is highly recommended. (LoE/GoR: I/A) (100%) For non-special type invasive breast cancers PET-CT, if available, is preferred instead of and not in addition to CT-scans and bone scan. For most invasive lobular breast cancers CT-scans and bone scans or whole-body MRI are preferred. (LoE/GoR: II/A)	
	a) Yes	95.3%
	b) No	2.3%
	c) Abstain	2.3%

Question 39

	Inoperable LABC and Inflammatory breast cancer (IBC) HRpos Options for HR+ LABC include an anthracycline- and taxane-based primary chemotherapy regimen, or endocriine-based therapy (i.e. ET + CDK4/6i). (LoE/GoR: I/A) (96%) The choice of er versus ET + CDK4/6i, as initial treatment, depends on tumor characteristics (grade, biomarker expression, burden of disease,) and patient considerations (performance status, associated symptoms, comorbidities, preferences). (LoE/GoR: Expert Opinion/ A) (89%) If chemotherapy is chosen, an anthracycline- and taxane-based primary chemotherapy regimen is recommended, followed by an endocrine-based therapy (ET + CDK4/6i) post-operatively. (LoE/GoR: I/A)	
	a) Yes	95.2%
	b) No	2.3%
	c) Abstain	2.3%

Question 40

	Inoperable LABC and Inflammatory breast cancer (IBC) TNBC Anthracycline- and taxane + platinum-based primary chemotherapy is recommended as initial treatment. (LoE/GoR: 1/A) (83%) Pembrolizumab should also be added, independently of PD-L1 status if non-metastatic disease and in PD-L1+ metastatic disease. (LoE/GoR: I/A)	
	a) Yes	93.0%
	b) No	2.3%
	c) Abstain	4.6%

Question 41

	Inoperable LABC and Inflammatory breast cancer (IBC) HER2+ Anthracyclin-based primary chemotherapy should be incorporated in the treatment regimen. (LoE/GoR: I/B) Note 1: This statement was revoted at ABC 7 after a no consensus at ABC 6 (ABC6 Vote: 54% Yes, 33% No, 13% Abstain). Note 2: This statement only referred to LABC and IBC. A previous statement already states that taxanes and anti-HER2 therapy (double blockade) should be given.	
	a) Yes	62.7%
	b) No	32.5%
	c) Abstain	4.6%

Question 42

	Inoperable LABC and Inflammatory breast cancer (IBC) gBRCAmut It is currently unknown how to optimally integrate the use of olaparib with post-operative capecitabine or pembrolizumab, in gBRCA mut triple negative initially inoperablle LABC or lBC. However, there are safety data allowing for the concomitant use of olaparib and pembrolizumab. (ILoE/GoR: III /B) lt is also currently unknown how to optimally integrate the use of olaparib with post-operative abemaciclib, in gBRCA mut ER+/HER2 neg initially inoperable LABC or IBC. lt is not possible to administer concomitantly olaparib and a CDK4/6i (safety concerns). Since there are data allowing for a later start of abemaciclib in the adjuvant setting, it can be envisioned to administer olaparib first and then abemaciclib. (LoE/GoR: III/B)	
	a) Yes	68.2%
	b) No	14.6%
	c) Abstain	17.0%

The visceral crisis

Question 43

	Management of visceral crisis Therapeutic options for patients with visceral crisis are limited and evidence is scarce since these patients are almost always excluded from clinical trials. In ER+/HER2 negative ABC with visceral crisis, ET + CDK4/6i are not contraindicated and may be a better option than chemotherapy. (LoE: II/B) In HER2+ ABC with visceral crisis, the use of anti-HER2 agents is crucial and feasible. (LoE: II/A)	
	a) Yes	92.8%
	b) No	2.3%
	c) Abstain	4.7%

Question 44

	Management of visceral crisis In situations of liver visceral crisis, options are further limited by the severe liver function impairment. Weekly regimens and lower doses are recommended. (LoE: IV/B) Platinum-based regimens are among the best options. (LoE: IV/B)	
	a) Yes	97.7%
	b) No	2.2%
	c) Abstain	0.0%

Question 45

	Management of visceral crisis For bone marrow infiltration, weekly low dose paclitaxel (LoE: IV/B) or capecitabine (LoE: IV/B) or ET + CDK4/6i (in case of ER+/HER2 neg disease) (LoE: IV/B) are among the best options.	
	a) Yes	86.0%
	b) No	6.9%
	c) Abstain	6.9%

Question 46

	Management of visceral crisis In some situations, urgent surgery and/or radiation therapy and/or other interventional techniques (i.e. laser therapy for bronchial obstruction) may be needed. (LoE: IV/B) Admission to ICU should not be denied if there is a possibility of reversing the clinical situation, after careful discussion with the patient and family, and always respecting the patient's wishes. (LoE: Expert Opinion/NA)	
	a) Yes	97.6%
	b) No	0.0%
	c) Abstain	2.3%

The elderly patient

Question 47

	Elderly ABC Patients When no specific note is made, all ABC guidelines are to be implemented independently of the age of the patient. (LoE/ GoR: Expert opinion/ A)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 48

	Elderly ABC Patients Independent of age, all patients should be involved in the treatment decision making process if they wish to do so, and their preferences should be taken into account. (LoE/GoR: Expert opinion/A). Independent of age, all eligible patients should be informed about potential clinical trials and provided with the adequate information and informed consent to be able to decide if they wish to participate. (LoE/GoR: Expert opinion/ A)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 49

	Elderly ABC Patients What determines the possibility to use a specific anticancer agent is not age by itself but the existence of co-morbidities with associated impact in liver, renal and/or neurological functions and bone marrow reserve. (LoE/GoR: I/ A)	
	a) Yes	95.4%
	b) No	2.2%
	c) Abstain	2.2%

Question 50

	Elderly ABC Patients For treatment decision making, careful evaluation of co-morbidities, performance status and geriatric assessment are crucial and more relevent than chronological age. G8 assessment should be used initially, and a full geriatric assessment is needed if low G8 scores are found. (LoE/GoR: I/A)	
	a) Yes	90.4%
	b) No	4.7%
	c) Abstain	4.7%

Question 51

	Elderly ABC Patients Special attention should be given to pocomedication/polypharmacy by older patients. (LoE/GoR: I/A)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 52

	Elderly ABC Patients The ABC Guidelines endorse the EUSOMA-SIOG guidelines for the management of older patient with breast cancer, namely the following statement: Regarding systemic treatment for metastatic disease: 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)	
	a) Yes	77.2%
	b) No	15.9%
	c) Abstain	6.8%

Leptomeningeal disease (LMD)

Question 53

	Patients with leptomeningeal disease (LMD) There is no accepted standard of care for breast cancer LMD. It is crucial that patients with LMD are included in clinical trials, namely in trials evaluating therapies for CNS disease. (LoE/GoR: Expert Opinion/A) The choice of treatment (radiotherapy, intra-CSF therapy, systemic therapy, supportive care) should consider prognostic evaluation, multidisciplinary discussion and always an in-depth discussion with the patient and the caregivers. (LoE/GoR: Expert Opinion/A) Staging of patients with lMD should indude full spine imaging with MRI with gadolinium to assess the full extension of the disease. (LoE/GoR: Expert Opinion/A)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 54

	Patients with leptomeningeal disease (LMD) Focal RT (brain or cranio-spinal) should be considered for circumscribed, notably symptomatic lesions. (LoE/GoR: III/B) WBRT can be considered for extensive nodular or symptomatic linear LMID. (LoE/GoR: III/B)	
	a) Yes	97.7%
	b) No	0.0%
	c) Abstain	2.2%

Question 55

	Patients with leptomeningeal disease (LMD) A ventriculoperitoneal shunt may be placed to palliate symptoms of increased intracranial pressure or symptomatic hydrocephalus. (LoE/GoR: Expert Opinion/B)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%

Question 56

	Patients with leptomeningeal disease (LMD) lntra-CSF chemotherapy has not been proven to improve OS nor Qol but may palliate symptoms in some cases, although significant toxicity may also occur. lt can be considered in select cases, if systemic disease is stable. (LoE/GoR: IIIC) lntra-CSF trastuzumab has been evaluated in small studies and has shown some efficacy relative to historical control data. lt may be used in some patients with HER2+ LMD. (LoE/ GoR: III/B)	
	a) Yes	95.4%
	b) No	4.5%
	c) Abstain	0.0%

Question 57

	Patients with leptomeningeal disease (LMD) The choice of systemic therapy for LMD should take into account the breast cancer subtype and previous treatments. (LoE/GoR: II/ A) Albeit in very small case series, there are some efficacy data in LMD for capecitabine monotherapy, the combination capecitabine + tucaitinib, and for T-DXd. (LoE/GoR: V/B)	
	a) Yes	100%
	b) No	0.0%
	c) Abstain	0.0%