Breast Cancer Highlights – 2022 ASCO Annual Meeting

Authored by Dr Zoya Marinova (United States), with contributions from Dr Vinícius Knackfuss Gonçalves (Brazil) and Prof. Bernardo L Rapoport (South Africa)

The 2022 Annual Meeting of the **American Society of Clinical Oncology (ASCO)** was held in Chicago, IL on **June 3–7, 2022** with both in-person and online attendance.

The theme of the meeting was "Advancing Equitable Cancer Care Through Innovation", and it included over 200 sessions revealing novel findings in cancer research, therapy, and care. Advances in breast cancer research and therapeutics were the conference topics attracting broadest interest.

Trastuzumab deruxtecan benefits patients with HER2-low metastatic breast cancer

The primary report of the randomized, open-label, phase 3, DESTINY-Breast04 trial (NCT03734029) was presented by Dr. Modi. The study compared the effects of HER2-directed therapy with trastuzumab deruxtecan and chemotherapy of the physician's choice in patients with previously treated, HER2-low, unresectable and/or metastatic breast cancer. The trial demonstrated for the first time the clinically meaningful and statistically significant benefit of trastuzumab deruxtecan on progression-free survival and overall survival in this group of patients. Trastuzumab deruxtecan had a generally manageable safety profile.[1]

Promising data on sacituzumab govitecan use in patients with HR+/HER2– advanced breast cancer

Findings from the randomized, phase 3, TROPiCS-02 study (NCT03901339) were delineated by Dr. Rugo. The trial investigated the effects of the anti-Trop-2 antibody-drug conjugate sacituzumab govitecan in patients with pretreated, HR+/HER2–, endocrine-resistant, unresectable locally advanced or metastatic breast cancer. The study confirmed a statistically and clinically meaningful benefit of sacituzumab govitecan over single-agent chemotherapy with regards to progression-free survival in this patient population who have limited treatment options, as well as a manageable safety profile.[2]

Efficacy of patritumab deruxtecan in patients with HER3-expressing metastatic breast cancer

Dr. Krop reported findings from a Phase 1/2, multicenter, open-label, first-in-human study (NCT02980341) that analyzed the efficacy of the HER3-directed antibody-drug conjugate patritumab deruxtecan in patients with previously treated, HER3-expressing, metastatic breast cancer. A pooled analysis demonstrated promising efficacy of patritumab deruxtecan in patients with HR+/HER2–, HER2+, and TNBC HER3-expressing metastatic breast cancer as well as adequate safety and tolerability.[3]

An update on potential of capivasertib in metastatic, estrogen receptor–positive breast cancer

An updated analysis of the Phase 2 FAKTION trial (NCT01992952) was presented by Dr. Jones. The study compared outcomes after treatment with fulvestrant plus the AKT-inhibitor capivasertib versus fulvestrant plus placebo in patients with metastatic, estrogen receptor–positive breast cancer who had experienced a relapse or progression on an aromatase inhibitor. A significant improvement in overall survival was observed with fulvestrant plus capivasertib treatment in the intention to treat population. An enhanced subgroup analysis indicated that the benefit of capivasertib with regards to both overall survival and progression-free survival might be observed predominantly in patients with PIK3CA/AKT1/PTEN pathway altered tumors.[4]

1. Trastuzumab deruxtecan (T-DXd) versus treatment of physician's choice (TPC) in patients (pts) with HER2-low unresectable and/or metastatic breast cancer (mBC): Results of DESTINY-Breast04, a randomized, phase 3 study. Shanu Modi, et al. *J Clin Oncol* 40, 2022 (suppl 17; abstr LBA3).

2. Primary results from TROPiCS-02: A randomized phase 3 study of sacituzumab govitecan (SG) versus treatment of physician's choice (TPC) in patients (Pts) with hormone receptor–positive/HER2-negative (HR+/HER2-) advanced breast cancer. Hope S. Rugo, et al. *J Clin Oncol* 40, 2022 (suppl 17; abstr LBA1001).

3. Results from the phase 1/2 study of patritumab deruxtecan, a HER3-directed antibody-drug conjugate (ADC), in patients with HER3-expressing metastatic breast cancer (MBC). Ian E. Krop, et al. *J Clin Oncol* 40, 2022 (suppl 16; abstr 1002).

4. Fulvestrant plus capivasertib versus fulvestrant plus placebo after relapse or progression on an aromatase inhibitor in metastatic, estrogen receptor–positive breast cancer (FAKTION): Overall survival and updated progression-free survival data with enhanced biomarker analysis. Robert Hugh Jones et al. *J Clin Oncol* 40, 2022 (suppl 16; abstr 1005).

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Addition of palbociclib to letrozole in patients with ER+/HER2- advanced breast cancer

Mature findings from the randomized, double-blind, Phase 3 PALOMA-2 trial (NCT01740427) were presented by Dr. Finn. The study investigated the effects of the addition of the cyclin-dependent kinase 4/6 (CDK4/6) inhibitor palbociclib to letrozole for the treatment of women with ER+/HER2- advanced breast cancer. The addition of palbociclib led to an improvement of the primary endpoint of progression-free survival. However, there was no statistically significant difference in the length of overall survival, though it was numerically longer in patients treated with palbociclib plus letrozole than in those treated with placebo plus letrozole.[5]

Data from the monarchE trial on addition of abemaciclib to endocrine therapy in patients with HR+, HER2-, high-risk early breast cancer

Novel data were shown from the Phase 3, open-label, randomized monarchE trial (NCT03155997) comparing abemaciclib combined with adjuvant endocrine therapy to endocrine therapy alone in patients with HR+, HER2-, high-risk early breast cancer. Dr. Martin emphasized that within the subgroup of patients who had received neoadjuvant chemotherapy (and were at a higher risk of recurrence), the combination abemaciclib plus endocrine therapy demonstrated a clinically meaningful treatment benefit with regards to invasive disease-free survival and distant relapse-free survival.[6] In another presentation, Dr. Tolaney reported variables significantly associated with a higher risk of abemaciclib discontinuation in the monarchE trial. The variables, which were identified in a multivariate model, included age ≥65 years, enrollment in North America or the European Union, ECOG PS=1, post-menopausal status, 1–3 positive nodes, or 4 or more pre-existing comorbidities.[7]

Novel insights on radiotherapy use in different clinical settings in patients with breast cancer

Dr. Chmura outlined the findings of a pioneering, randomized Phase IIR/III trial (NCT02364557), which assessed the efficacy of the addition of metastases-directed treatment (stereotactic body radiotherapy or a surgical resection) to standard-of-care systemic therapy in patients with oligometastatic (with up to 4 extracranial metastases) breast cancer. Notably, the addition of metastases-directed treatment did not improve the progression-free survival or overall survival in patients with oligometastatic breast cancer in comparison to standard-of-care systemic therapy alone.[8]

Dr. Whelan delineated findings from the prospective LUMINA trial (NCT01791829), which investigated whether it is useful to identify the luminal A breast cancer subtype, together with clinicopathological features, in the decision regarding radiotherapy after breast-conserving surgery. The study included women who were at least 55 years old and had grade 1-2 T1N0 luminal A breast cancer and had preceding breast-conserving surgery. In this group of patients, treatment with endocrine therapy alone resulted in very low rates of local recurrence within 5 years, identifying them as potential candidates for omission of radiotherapy after breast-conserving surgery.[9]

5. Overall survival (OS) with first-line palbociclib plus letrozole (PAL+LET) versus placebo plus letrozole (PBO+LET) in women with estrogen receptor–positive/human epidermal growth factor receptor 2-negative advanced breast cancer (ER+/HER2- ABC): Analyses from PALOMA-2. Richard S. Finn, et al. *J Clin Oncol* 40, 2022 (suppl 17; abstr LBA1003).

6. Abemaciclib combined with adjuvant endocrine therapy in patients with high risk early breast cancer who received neoadjuvant chemotherapy (NAC). Miguel Martin, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 517).

7. Adjuvant abemaciclib for high-risk early breast cancer (EBC): Factors increasing the rate of treatment discontinuations in monarchE. Sara M. Tolaney, et al. *J Clin Oncol* 40, 2022 (suppl 16; abstr 527).

8. 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). Steven J. Chmura, et al. *J Clin Oncol* 40, 2022 (suppl 16; abstr 1007).

9. LUMINA: A prospective trial omitting radiotherapy (RT) following breast conserving surgery (BCS) in T1N0 luminal A breast cancer (BC). Timothy Joseph Whelan, et al. *J Clin Oncol* 40, 2022 (suppl 17; abstr LBA501).

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