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Conference Summary

ESMO 2025 Congress Highlights

Comprehensive Coverage of Groundbreaking Breast Cancer Research from ESMO 2025

The European Society for Medical Oncology (ESMO) 2025 Congress showcased breakthrough clinical trials in translational cancer science. The sessions unveiled practice-changing data for early stages of breast cancer, metastatic breast cancer, and cancer nursing. This summary offers a comprehensive overview of key clinical trials presented at the conference, emphasising their potential to redefine treatment standards for breast cancer.

Five-year outcomes from NATALEE: Adjuvant ribociclib (RIB) plus nonsteroidal aromatase inhibitor (NSAI) in patients with hormone receptor + (HR+) human epidermal growth factor receptor 2– (HER2–) early breast cancer (EBC)[1]

Background

The phase 3 NATALEE trial demonstrated that adjuvant RIB plus NSAI led to a statistically significant invasive disease-free survival (iDFS) benefit in patients with stage II and III HR+/HER2− EBC. The protocol-specified 5-year efficacy analysis was presented at ESMO 2025.

NATALEE trial

Patients with HR+/HER2− EBC were randomised 1:1 to RIB + NSAI (letrozole or anastrozole) or NSAI alone. Males and premenopausal females received goserelin. Patients were included if they had anatomical stage IIA, stage IIB, or stage III disease as per the American Joint Committee on Cancer (AJCC), 8th edition. The primary end point of iDFS and secondary efficacy end points of distant disease-free survival (DDFS), distant relapse-free survival (DRFS), and overall survival (OS) were evaluated using Kaplan–Meier methods. Statistical comparisons were made by stratified log-rank test.

Results

At data cutoff, all patients were off RIB treatment, and 36% in the RIB + NSAI arm and 34.4% in the NSAI alone arm had completed 5 years of NSAI treatment. With a median iDFS follow-up of 55.4 months, RIB + NSAI demonstrated persistent iDFS benefit over NSAI alone with a hazard ratio (HR) of 0.716 (95% confidence interval (CI): 0.618–0.829; nominal 1-sided $P < 0.0001$). Absolute iDFS rates were 90.8% vs 88.0% at 3 years, 88.3% vs 83.9% at 4 years, and 85.5% vs 81.0% at 5 years. This represented an absolute improvement of 2.7% at 3 years, 4.4% at 4 years, and 4.5% at 5 years, respectively.

iDFS benefit was observed across subgroups, including N0 (HR, 0.606; 95% CI: 0.372–0.986). RIB + NSAI also demonstrated continued DDFS (HR, 0.709; 95% CI: 0.608–0.827) and DRFS (HR, 0.699; 95% CI: 0.594–0.824) benefit when compared with NSAI alone. A positive trend for OS favouring RIB + NSAI (HR, 0.800; 95% CI: 0.637–1.003; nominal 1-sided $P = 0.026$) emerged. No new safety signals were observed with a median follow-up time of approximately 2 years after RIB completion.

Conclusion

In this 5-year landmark analysis with mature efficacy data, RIB + NSAI reduced the risk of invasive and distant disease recurrence compared with NSAI alone, including in patients with high-risk N0 disease. The clinical findings point to a continued positive trend for OS in favour of RIB + NSAI.

The growing survival advantage, the sustained benefits, and the meaningful reduction in recurrence risk establishes the benefits of treatment with adjuvant RIB plus NSAI in patients with HR+/HER2− EBC.

Primary OS results of adjuvant abemaciclib plus endocrine therapy (ET) for HR+ HER2−, high-risk EBC from the MonarchE[2]

Background

In patients with HR+ HER2−, node-positive, high-risk EBC, adjuvant therapy for 2 years with abemaciclib + ET demonstrated statistically significant and clinically meaningful improvement over ET alone in iDFS and DRFS. However, approximately 650 deaths in the intent-to-treat (ITT) population triggered a primary OS analysis.

MonarchE trial

MonarchE is an open-label, randomised, phase 3 trial in patients with HR+ HER2−, high-risk EBC. Patients were randomised (1:1) to receive ET for at least 5 years ± abemaciclib for the first 2 years. High-risk EBC was defined as either ≥4 positive axillary lymph nodes (ALN), or 1–3 ALN + either grade 3 disease and/or tumour ≥5 cm (Cohort 1). Patients with 1–3+ ALN and central Ki67 ≥20% were enrolled to Cohort 2. The ITT population consisted of Cohorts 1 (n = 5,120) and 2 (n = 517).

Results

One of the highlights of ESMO 2025 was the updated data from MonarchE trial showing primary OS (secondary endpoint) results and updated IDFS and DRFS from the MonarchE trial. In the ITT population, with a median follow-up of 6.3 years, 301 patients in the abemaciclib + ET and 360 patients in the ET arm had died. Compared with ET alone, the addition of abemaciclib to ET reduced the risk of death by 15.8% with an HR of 0.84 (95% CI 0.72–0.98; *P* = 0.027). IDFS and DRFS benefit persisted up to 7 years with an HR of 0.73 (95% CI 0.66–0.82) and 0.75 (95% CI 0.66–0.84), respectively. At 7 years, IDFS was 77.4% with abemaciclib + ET versus 70.9% with ET, and DRFS was 80.0% versus 74.9%.

Key findings

The addition of 2 years of adjuvant abemaciclib to ET resulted in statistically significant improvement in OS over ET in patients with HR+ HER2− EBC. At 7 years, abemaciclib + ET demonstrated a sustained IDFS and DRFS benefit, and the long-term safety data raised no concerns of delayed toxicities.

Conclusion

Adjuvant abemaciclib significantly improves OS in high-risk HR+ EBC, especially in premenopausal patients and those with >10 positive nodes. IDFS benefits were persistent.

First data from the DESTINY-Breast11 trial investigating neoadjuvant trastuzumab deruxtecan alone (T-DXd) or T-DXd followed by paclitaxel,

trastuzumab, and pertuzumab (T-DXd-THP) versus chemotherapy for high-risk HER2+ EBC[3]

Background

For patients with HER2+ EBC, the current standard of care (SOC) neoadjuvant is trastuzumab (H) plus pertuzumab (P), concurrently or in sequence with polychemotherapy. T-DXd, an antibody–drug conjugate made of trastuzumab linked to a topoisomerase I inhibitor payload, is approved for the treatment of adults with unresectable or metastatic HR+ HER2-low or HER2-ultralow BC. The DESTINY-Breast11 trial compares neoadjuvant T-DXd or T-DXd-THP over dose-dense doxorubicin + cyclophosphamide (ddAC)-THP in a phase III, multicentre, open-label, randomised study.

DESTINY-Breast11 trial

Adults with untreated high-risk HER2+ EBC were randomised to T-DXd, T-DXd-THP, or ddAC-THP. Primary endpoint investigated was pathologic complete response (pCR) and secondary endpoints included were event-free survival (EFS) and safety.

Results

As of March 2025, 321 and 320 patients were randomised to T-DXd-THP and ddAC-THP, respectively. pCR rates observed were 67.3% for T-DXd-THP and 56.3% for ddAC-THP groups. At data cutoff, an early favourable EFS trend was observed in T-DXd-THP versus ddAC-THP.

Grade ≥3 adverse event (AE) rates were 37.5% for T-DXd-THP versus 55.8% for ddAC-THP. Increased incidence of left ventricular dysfunction was noted, with 1.9% in T-DXd-THP versus 9.0% in ddAC-THP groups. However, no AE prevented surgery in any arm.

Conclusion

Neoadjuvant T-DXd-THP demonstrated a statistically significant improvement in pCR, an early favourable EFS trend, and improved safety profile versus ddAC-THP. Improved clinical efficacy and less toxicity of neoadjuvant T-DXd-THP over ddAC-THP indicates potential as a new anthracycline-free regimen for patients with high-risk HER2+ EBC.

Five-year follow-up results from the POSITIVE (Pregnancy Outcome and Safety of Interrupting Therapy for Women with Endocrine Responsive Breast Cancer) trial[4]

Background

The majority of young women with EBC have HR+ disease and long-term ET after surgery prevents conception. The POSITIVE trial is a study evaluating the pregnancy outcomes and safety of interrupting adjuvant ET for young women with HR+ BC who desire pregnancy.
Now, updated results on breast cancer free interval (BCFI), distant recurrence-free interval (DRFI), pregnancy and *in vitro* fertilisation outcomes, and ET resumption are available.

POSITIVE trial

A single-arm prospective trial evaluating temporary interruption of adjuvant ET, after 18–30 months for up to 2 years, for pregnancy in young BC survivors. The study enrolled 518 eligible women from 2014 to 2019, with comparison to a matched external control group of SOFT/TEXT trial patients, for estimation of 5-year BCFI and DRFI event rates.

Results

At median follow-up of 71 months and 80 months in the POSITIVE and SOFT/TEXT control cohorts, respectively, 5-year cumulative incidence of BCFI events was 12.3% in POSITIVE and 13.2% in SOFT/TEXT. Five-year cumulative incidence of DRFI events was 6.2% in POSITIVE and 8.3% in SOFT/TEXT. Among the 497 women followed for pregnancy outcomes, 75.8% had at least one pregnancy on trial, 69% had at least one live birth with 440 newborns, and 75 patients had more than one live birth on trial.

An 18-month landmark analysis confirmed that patients who had a pregnancy had similar BCFI events compared to those who did not. The 5-year cumulative incidences of BCFI events were 14.0% (95% CI 9.6% to 20.2%) in the 180 patients who had embryo/oocyte cryopreservation done prior to enrolment compared to 11.5% (95% CI 8.4% to 15.7%) in those who did not. Of the 429 patients followed for at least 2 years and remained disease-free, 352 (82%) have resumed ET. Ongoing follow-up will help assess long-term outcomes.

Conclusion

In young patients with BC, temporary interruption of ET for pregnancy does not increase risk of BC events at 5-year follow-up. More than two-thirds of women had a live birth and most resumed ET as per protocol.

Temporarily halting of ET enables young BC survivors to conceive and have a successful pregnancy, and this break in therapy does not alter disease-free intervals or recurrence-free intervals in these patients.

Primary results from ASCENT-03: A randomised phase III study of sacituzumab govitecan (SG) versus chemotherapy in patients with previously untreated advanced triple-negative BC (TNBC) who are unable to receive PD-(L)1 inhibitors (PD-[L]1i)[5]

Background

For patients with metastatic TNBC (mTNBC) who cannot receive PD-(L)1i, treatment options are limited. Results from the ASCENT trial showed significant PFS benefit with SG, a trop-2-directed antibody, linked to topoisomerase inhibitor, versus chemotherapy in pretreated mTNBC. Similarly, the ASCENT-04 trial demonstrated benefit with SG + pembrolizumab versus chemotherapy + pembrolizumab in first-line PD-L1+ mTNBC. The ASCENT-03 trial is a randomised phase III study investigating first-line SG versus chemotherapy in patients with locally advanced unresectable or mTNBC who are unable to receive a PD-(L)1i.

ASCENT-03 trial

Patients diagnosed with PD-L1-negative mTNBC or PD-L1-positive mTNBC but were unable to receive PD-(L)1i due to a comorbidity or prior use in the curative setting. Randomisation (1:1) to SG or chemotherapy (paclitaxel, nab-paclitaxel, or gemcitabine + carboplatin) was stratified by disease status and geography. The primary end point was PFS and key secondary end points included OS, objective response rate (ORR), duration of response (DOR), and safety.

Results

558 patients (279 in each group) with mTNBC were randomised with a median follow-up of 13.2 months. SG showed a significant improvement in median PFS of 9.7 months versus 6.9 months with chemotherapy, and HR of 0.62 (95% CI 0.50–0.78; *P* < .0001).

Median DOR was 12.2 months versus 7.2 months, while the OS data were immature. The most frequent grade ≥3 treatment-emergent AE (TEAE) was neutropenia observed at 43% with SG and 41% with chemotherapy. Diarrhoea was observed at 9% with SG and anaemia at 16% with chemotherapy.

Conclusion

SG led to a statistically significant improvement in PFS and more durable responses compared with chemotherapy in first- line mTNBC. The safety profile of SG was manageable and treatment discontinuation rate due to TEAEs was lower with SG.

The data supports SG as a potential new SOC for patients with previously untreated mTNBC who are unable to receive a PD-(L)1i.

Patient-reported outcomes (PROs) from the SERENA-6 trial of camizestrant (CAMI) + cyclin-dependent kinases 4 and 6 inhibitor (CDK4/6i) for emergent ESR1 mutations (ESR1m) during first-line endocrine-based therapy and ahead of disease progression in patients with HR+ HER2– advanced BC (ABC)[6]

Background

In patients with HR+ HER2– ABC, the emergence of ESR1m during first-line therapy with AI plus CDK4/6i is a common cause of acquired resistance to therapy. In the SERENA-6 trial, switching patients with ESR1m to the well-tolerated CAMI plus CDK4/6i therapy resulted in a statistically significant and clinically meaningful improvement in PFS compared with AI plus CDK4/6i. A key finding supporting the SERENA-6 treatment approach was a reduction in the risk of deterioration in global health status (GHS)/quality of life (QoL). At the ESMO 2025 congress, outcomes of additional PROs were presented.

SERENA-6 trial

PRO instruments, assessed at pre-specified timepoints, included the EORTC QoL questionnaire (QLQ-C30), BC-specific module (QLQ-BR23), and Patient Global Impression of Treatment Tolerability (PGI-TT). Time to deterioration (TTD) in breast and arm symptoms, pain, and physical functioning were predefined secondary endpoints.

Results

315 patients were randomised to switch to CAMI (n = 157) or continue AI (n = 158) while remaining on CDK4/6i. TTD analysis showed CAMI + CDK4/6i reduced the risk of clinically meaningful deterioration in overall GHS/QoL and pain; HRs for physical functioning, role functioning, breast symptoms, and arm symptoms. For PGI-TT, most patients reported they were ‘not at all’ or ‘a little bit’ bothered by the side effects of cancer therapy across timepoints. At week 2, 14% of patients receiving CAMI + CDK4/6i versus 18% receiving AI + CDK4/6i reported to be ‘somewhat,’ ‘quite a bit,’ or ‘very much’ bothered by side effects.

Conclusion

The clinical efficacy and manageable safety profile of CAMI + CDK4/6i, together with the PROs from the SERENA-6 trial support this combination as a potential new treatment strategy to improve outcomes in patients with HR+ HER2– ABC. The results show that the CAMI + CDK4/6i combination will help surmount the emergence of ESR1m, ahead of disease progression, during first-line AI + CDK4/6i.

Preliminary analysis of the SOLTI-RIBOLARIS trial: ROR after neoadjuvant ribociclib plus ET in clinically high-risk HR+ HER2– BC[7]

Background

The CDK4/6i are approved for early-stage HR+ HER2− BC. The NeoPAL and CORALLEEN trials showed that CDK4/6i in combination with ET has similar efficacy as multi-agent chemotherapy in patients with luminal B-PAM50-based-BC subtype. The RIBOLARIS trial evaluates whether patients with ROR-low disease following neoadjuvant RIB and ET can safely omit adjuvant chemotherapy.

RIBOLARIS trial

RIBOLARIS is an open-label, single-arm, multicentre trial in patients with primary operable stage II, grade 2/3, Ki67 ≥20%, HR+ HER2− BC who are candidates for adjuvant chemotherapy. The trial evaluates RIB-ET in patients with tumours showing a low ROR score after six neoadjuvant cycles of RIB-ET followed by surgery within 10 days. Patients with ROR-medium/high tumours receive chemotherapy-based treatment followed by RIB-ET.

Results

The results from the preplanned interim analysis of 686 surgeries were presented at ESMO 2025. Of these, 52.6% achieved a low ROR score with a mean of 11.3 (95% CI 10.5–12.2), while 47.4% had a medium/high ROR score with a mean of 36.9 (95% CI 34.2–39.5). The most common grade 3–4 severity TEAEs were neutropenia (grade 3: 46.3%; grade 4: 3.5%) and increase in transaminases (grade 3: 10.4%; grade 4: 1.5%). There was no new safety signal.

Conclusion

The results confirm and extend the findings from CORALLEEN and NeoPAL trials, demonstrating that a subset of patients with early-stage HR+ HER2− BC who achieve a low ROR profile following neoadjuvant therapy with RIB plus letrozol may be safely spared adjuvant chemotherapy.

References

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