Highlights From the 2025 ESMO Congress

Clinical Trials Connected, aims to connect you with crucial research updates and clinical trials to help you stay informed about the latest advancements in breast cancer care. In this edition, we bring you the latest news from the 2025 ESMO Congress.

Use our blog on Understanding Common Research Terms as a guide for some of the terms we reference.

Optimizing Treatment for Older Adults with Breast Cancer

At ESMO 2025, experts presented an important session on how to optimize breast cancer treatment for older adults. This is a group that is often underrepresented in clinical trials. Here are some highlights from that session:

As our population ages, more older adults will be diagnosed with breast cancer. Older adults may live with other health conditions (called comorbidities) or may take several medications. These can influence treatment options and how they are planned or managed. Aging can also affect how the body processes medicines. Breast cancer care will need to adapt to better tailor treatments for older adults.

Geriatric assessments are becoming essential when treating older adults with breast cancer. These assessments can evaluate someone's overall health, mobility, memory, mood and the medications they take. They can help your cancer team determine what treatments are best for your circumstances to reduce side effects and improve quality of life while maintaining the effectiveness of your treatment. This can give you a better chance of completing treatment safely.

Because not every older adult is the same, treatment decisions should not be based on age alone. Older adults who are fit can often receive standard treatments, while those who are frail may benefit from approaches that tailor treatment to their needs.

Some examples for how oncologists can tailor treatments include giving single-agent drug regimens instead of combinations of chemotherapy, or starting treatment with a smaller does and working up to the full dose. Oncologists should also rely on a multidisciplinary team including geriatricians, nurses, and social workers.

Experts highlighted that every oncologist would need to think like a "geriatric oncologist". The goal is not less treatment, but the right treatment for each person. We also need more real-world data and research on how to effectively guide treatment choices and dosing for aging people living with cancer.

Clinical Trial Updates

The conference also highlighted some promising new therapies for several different subtypes of breast cancer, including both early-stage and metastatic.

Giredestrant + Everolimus (evERA Trial, Phase 3)

HR positive, HER2 negative metastatic breast cancer

Background: When HR positive, HER2 negative metastatic breast cancer stops responding to hormone therapy and CDK4/6 inhibitors, treatment options become limited. Researchers are studying new ways to overcome this resistance.

Indicated for: People with HR positive, HER2 negative metastatic breast cancer whose cancer grew resistant to hormone therapy and CDK4/6 inhibitor.

What was studied: An all-oral combination of giredestrant (an estrogen-blocking drug called a SERD) and everolimus (an mTOR inhibitor)

Primary Endpoint: The main goal of this trial was to see how long patients lived without their cancer getting worse, called **progression-free survival (PFS)**. When a trial shows longer PFS, it means the treatment helped delay the cancer growth compared to standard therapy.

Results:

- In cancers with an ESR1 mutation, patients lived a median of 9.99 months without disease progression vs. 5.45 months with standard hormone therapy + everolimus
- Across all patients (ESR1-mutated and non-mutated), median PFS was 8.77 months compared to 5.49 months
- Duration of response: median of 14.9 months with giredestrant + everolimus vs. 7.3 months for standard treatment

Takeaways: This new oral treatment may delay cancer growth longer than current options for patients whose cancer has progressed after standard therapies.

Read more

Gedatolisib + fulvestrant (VIKTORIA-1 trial, Phase 3)

HR positive, HER2 negative metastatic breast cancer

Background: After hormone therapy and CDK4/6 inhibitors stop working, people with HR positive, HER2 negative metastatic breast cancer have limited treatment options. The VIKTORIA-1 trial aims to block key pathways cancer cells use to grow and resist treatment.

Indicated for: People with HR positive, HER2 negative non-mutated PIK3CA metastatic breast cancer whose cancer grew resistant to hormone therapy and CDK4/6 inhibitor.

What was studied: Two combinations that included gedatolisib, a drug that blocks the PI3K/AKT/mTOR pathway (also known as the PAM pathway).

- Triplet therapy: gedatolisib + palbociclib (a CDK4/6 inhibitor) + fulvestrant (HR therapy)
- Doublet therapy: gedatolisib + fulvestrant

Both combinations were compared to fulvestrant alone, the standard treatment after CDK4/6 inhibitors.

Primary Endpoint: The main goal of this trial was to see how long patients lived without their cancer getting worse, called **progression-free survival (PFS)**. When a trial shows longer PFS, it means the treatment helped delay the cancer growth compared to standard therapy.

Results:

- Triplet therapy: median PFS was 9.3 months vs. 2.0 months with fulvestrant alone
    - A 76% lower risk of progression or death
- Doublet therapy: median PFS was 7.4 months vs. 2.0 months with fulvestrant alone
    - A 67% lower risk of progression or death

Takeaways: Adding gedatolisib to standard hormone therapy (with or without a CDK4/6 inhibitor) helped patients live months longer before their cancer worsened. These findings suggest that gedatolisib could become a new treatment option for this population.

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Sacituzumab govitecan vs chemotherapy (ASCENT-03 trial, Phase 3)

Metastatic Triple Negative Breast Cancer

Background: About 60% of people with metastatic triple negative breast cancer (TNBC) are not eligible for PD-L1 inhibitor therapy (like pembrolizumab), making chemotherapy alone the standard of care. The ASCENT-03 trial looked for better first-line options for these patients.

Indicated for: People newly diagnosed (first-line) metastatic triple negative breast cancer who are not eligible for immunotherapy with PD-L1 inhibitor.

What was studied: Sacituzumab govitecan (SG), an anti-body drug conjugate (or ADC) that links a chemotherapy to a targeting antibody called Trop-2, which helps deliver the drug directly to cancer cells. SG was compared to standard chemotherapy.

Primary Endpoint: The main goal of this trial was to see how long patients lived without their cancer getting worse, called **progression-free survival (PFS)**. When a trial shows longer PFS, it means the treatment helped delay the cancer growth compared to standard therapy.

Results:

- Patients receiving SG had a median PFS of 9.7 months, compared to 6.9 months for standard chemotherapy
- Corresponds to approximately a 38% reduction in the risk of disease progression or death

Takeaways: For patients with previously untreated metastatic TNBC who cannot receive immunotherapy, SG may offer a meaningful improvement over standard chemotherapy.

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Datopotamab deruxtecan vs chemotherapy (TROPION-Breast02, Phase 3)

Metastatic Triple Negative Breast Cancer

Background: Up to 70% of people diagnosed with metastatic TNBC are not candidates to receive immunotherapy, and about 50% of patients do not receive treatment beyond the first-line setting. This highlights a need for new therapy options for these patients.

Indicated for: People newly diagnosed (first-line) metastatic triple negative breast cancer who are not eligible for immunotherapy.

What was studied: The trial compared Datopotamab deruxtecan (Dato-DXd), an anti-body drug conjugate that links a chemotherapy to a targeting antibody called Trop-2, which helps deliver the drug directly to cancer cells. SG was compared to standard chemotherapy to standard single-agent chemotherapy.

Primary Endpoint: The main goal of this trial was to see how long patients lived without their cancer getting worse, called **progression-free survival (PFS)**. When a trial shows longer PFS, it means the treatment helped delay the cancer growth compared to standard therapy.

Results:

- The median PFS was 10.8 months with Dato-DXd vs. 5.6 months with chemotherapy
    - A 43% reduction in risk of progression or death
- The median overall survival (OS) was 23.7 months with Dato-DXd vs. 18.7 months with chemotherapy
    - A 21% reduction in risk of death

Takeaways: For patients with metastatic TNBC who cannot receive immunotherapy, the trial of Dato-DXd shows meaningful improvement in progression free survival and overall survival. These results suggest that Dato-DXd may become a new first-line standard of care for these patients.

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Neoadjuvant trastuzumab deruxtecan (DESTINY-Breast11, Phase 3)

HER2 positive early-stage breast cancer

Background: For people with high-risk, early-stage, HER2 positive breast cancer, the standard treatment before surgery (neoadjuvant) has long been certain chemotherapy regimens plus HER2-targeted drugs.

Many still have residual disease after surgery, which raises the risk of cancer returning. This trial asks whether a new HER2-targeted therapy given before surgery could improve outcomes.

Indicated for: People HER2 positive early-stage breast cancer, who have not been treated. Both HR positive and HR negative patients were able to enroll.

What was studied: An anti-body drug conjugate (or ADC) called trastuzumab deruxtecan (T-DXd) that links a chemotherapy to trastuzumab, a targeted anti-HER2 therapy given before surgery (neoadjuvant). The 3 arms of the study included:

- T-DXd followed by paclitaxel + trastuzumab + pertuzumab (known as THP)
- Standard chemotherapy regimen (dose-dense doxorubicin, cyclophosphamide) followed by THP
- Or T-DXd alone

The goal was to see how T-DXd compares with standard chemotherapy-base regimen, before surgery.

Primary Endpoint: The main goal of this trial was **pathologic compete response (pCR)** which means that no invasive cancer was left in the breast or lymph nodes at the time of surgery.

Results:

- T-Dxd + THP: pCR rate was 67.3% compared to 56.3% in the standard chemotherapy regimen +THP arm
- HR positive subgroup: pCR rate was 61.4% vs. 52.3%
- HR negative subgroup: pCR rate was 83.1% vs 67.1%

Takeaways: This T-DXd based neoadjuvant therapy showed a significantly higher rate of pathologic complete response before surgery compared to the standard chemotherapy approach in high-risk HER2 positive early breast cancer patients.

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Adjuvant trastuzumab deruxtecan (DESTINY-Breast05 trial, Phase 3)

HER2 positive early-stage breast cancer

Background: When patients with HER2 positive breast cancer have still have cancer left after neoadjuvant therapy, the standard treatment is trastuzumab emtansine (T-DM1) given after surgery. This study looks to see if newer treatment options are available to further lower the risk of recurrence for these high-risk patients.

Indicated for: People with high-risk HER2 positive early breast cancer who, after neoadjuvant therapy and surgery, still have residual invasive cancer in the breast and/or lymph nodes.

What was studied: An anti-body drug conjugate (or ADC) called trastuzumab deruxtecan (T-DXd) that links a chemotherapy to trastuzumab, a targeted anti-HER2 therapy given after surgery (adjuvant therapy). The study compared T-DXd versus T-DM1, the standard of care for adjuvant therapy for people with residual disease at surgery.

Primary Endpoint: The main goal of this trial was **invasive disease-free survival (IDFS)**, which looks at how long patients stay free of invasive breast cancer recurrence or death.

Results:

- T-DXd reduced the risk of invasive disease recurrence or death by 53% compared with T-DM1
- At 3 years, the IDFS rate was 92.4% vs. 83.7 with T-DM1

Takeaways: For patients with HER2 positive early breast cancer who still have invasive disease after neoadjuvant therapy and surgery, T-DXd offers improvement in reducing the risk of recurrence compared with T-DM1. It lowers the risk of recurrence by about half and increases the percentage who remain cancer-free at 3 years.

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