Clarivate™

Clarivate's top takeaways from ESMO 2025

Market Event Summary

Arshiya Bhatt, Ph.D. I October 2025

Enhertu shows benefit in high-risk early-stage HER2-positive breast cancer

Context

- The antibody-drug conjugate (ADC) Enhertu is approved for metastatic breast cancer across HER2-positive, HER2-low, and HER2-ultralow populations.
- It is now being investigated in early-stage HER2-positive breast cancer in two phase 3 trials. The DESTINY-Breast11 trial evaluated neoadjuvant Enhertu followed by trastuzumab, pertuzumab, and paclitaxel (THP) vs. dose-dense doxorubicin and cyclophosphamide (AC) followed by THP in high-risk patients. The DESTINY-Breast05 trial assessed adjuvant Enhertu vs. Kadcyla in patients with residual invasive disease and at high-risk of recurrence.
- Earlier in 2025, it was announced that both the trials met their primary endpoints.

Key findings

- In the neoadjuvant setting (DESTINY-Breast11), the pCR was 67.3% with Enhertu–THP vs. 56.3% with ddAC–THP (P = 0.003), an early trend toward improved event-free survival (HR 0.56).
- In the adjuvant setting (DESTINY-Breast05), Enhertu improved 3-year iDFS to 92.4% vs. 83.7% with Kadcyla (HR 0.47; P < 0.0001).
- The safety profile of Enhertu was manageable across studies, though interstitial lung disease (ILD) occurred in 9.6% of patients in the adjuvant trial, including two fatal cases.

Clarivate's takeaways

Clinical milestone: Enhertu could become available as neoadjuvant and adjuvant treatment for certain patients with early-stage HER2-positive disease. Based on strong adjuvant data, Enhertu could become the new standard of care for high-risk patients with residual disease.

Medical practice: Neoadjuvant use of Enhertu may offer advantages over adjuvant use, such as shorter treatment duration, resulting in better safety and lower ILD monitoring costs compared with adjuvant therapy.

Constraints: Broader adoption in the neoadjuvant setting may be limited by the lack of predictive biomarkers, uncertainties around post-neoadjuvant strategies for patients who do not achieve pCR, and the absence of long-term outcome data.

Clarivate™

Perioperative Padcev plus Keytruda improves survival in cisplatin-ineligible MIBC

Context

- Neoadjuvant cisplatin-based chemotherapy plus radical cystectomy is standard for muscle-invasive bladder cancer (MIBC), but ~50% of patients are cisplatin-ineligible due to age, frailty, or comorbidities, leaving limited options and high recurrence risk.
- The Phase 3 KEYNOTE-905 / EV-303 trial evaluated perioperative Keytruda ± Padcev versus surgery alone in cisplatin-ineligible or -declined MIBC.
- In August 2025, Merck and Pfizer announced that the combination met its primary endpoint of EFS.

Key findings

- Padcev plus Keytruda reduced the risk of EFS events by 60% (HR 0.40; P < 0.0001) and the risk of death by 50% (HR 0.50; P = 0.0002) versus surgery alone.
- Median EFS and OS were not reached for the combination, vs. 15.7 months and 41.7 months with surgery alone.
- Pathologic complete response rate was 57.1% with the combination vs. 8.6% with surgery alone.
- The safety profile of Keytruda plus Padcev in this study was consistent with the known safety profiles of each agent.

Clarivate's takeaways

Unmet need: Cisplatin-ineligible MIBC patients have limited options. This landmark study demonstrates a significant perioperative survival benefit, addressing a critical unmet clinical need.

Regulatory expectations: Clarivate forecasts regulatory approval for Padcev plus Keytruda based on these data, which would make it the first perioperative regimen to be approved for cisplatin-ineligible MIBC.

Medical practice: Clarivate believes that the impressive efficacy data from this trial could position Padcev plus Keytruda as a new standard of care in this underserved population, reinforcing its role as a versatile combination across stages of bladder cancer.

Clarivate™

Pluvicto improves rPFS in PSMA-positive mHSPC

Context

- Pluvicto is the only approved radioligand therapy for prostate cancer, indicated across treatment lines of metastatic castration-resistant disease.
- The Phase 3 PSMAddition trial evaluated Pluvicto added to androgen deprivation therapy (ADT) + androgen receptor pathway inhibitor (ARPI) versus ADT + ARPI alone in patients with PSMA-positive metastatic hormone-sensitive prostate cancer (mHSPC).
- In June 2025, Novartis announced the trial met its primary endpoint of radiographic progression-free survival (rPFS) and showed a favorable overall survival trend.

Key findings

- Pluvicto plus ARPI reduced the risk of progression or death by 28% vs. ARPI alone (median PFS not reached; P = 0.002), with consistent benefit across subgroups.
- An interim analysis (16% of events) showed a favorable OS trend for Pluvicto (HR 0.84; P = 0.125).
- Pluvicto showed higher overall response (85% vs 81%) and complete response rates (57% vs 42%), as well as a longer time to PSA progression (HR 0.42), although no improvement in quality of life was observed.
- The safety profile was consistent with previous studies, but higher rates of grade ≥3 adverse events (22.7% vs 12.2%) and discontinuations (16.1% vs 9%) were observed in the Pluvicto arm.

Clarivate's takeaways

Expected filing: Clarivate expects the positive rPFS data to support Pluvicto's label expansion into PSMA-positive mHSPC.

Market outlook: The control arm's exclusion of docetaxel could be viewed as a weak comparator, and despite earlier efficacy signals, meaningful practice shifts are unlikely until stronger survival evidence is demonstrated.

Product positioning: Based on these data, we expect Pluvicto to be used selectively, mainly in high-burden, PSMA-avid disease, which may derive the greatest clinical benefit despite tolerability trade-offs.

Clarivate™

Keytruda improves PFS and OS in recurrent platinum-resistant ovarian cancer

Context

- Ovarian cancer is often considered an immunologically “cold” tumor, limiting immunotherapy effectiveness. To date, immune checkpoint inhibitors have shown limited efficacy, and none have been approved for ovarian cancer.
- The Phase 3 KEYNOTE-B96 / ENGOT-ov65 trial evaluated Keytruda plus weekly paclitaxel ± bevacizumab vs. chemotherapy ± bevacizumab in recurrent platinum-resistant ovarian cancer.
- In May 2025, Merck & Co. announced that the trial met its primary endpoint of PFS and achieved significant OS improvement in patients with PD-L1 CPS ≥ 1 expression.

Key findings

- In the overall population, median PFS was 8.3 months for Keytruda with paclitaxel, with or without bevacizumab vs. 6.4 months for control (HR 0.70; $P < 0.0001$), and in the PD-L1–positive subgroup, 8.3 months vs. 7.2 months (HR 0.72; $P = 0.0014$).
- At the second interim analysis, the Keytruda-based regimen reached a median OS of 18.2 months compared with 14.0 months in the control group (HR 0.76; $p = 0.0053$).
- The safety profile of Keytruda plus paclitaxel ± bevacizumab was consistent with the known profiles of the agents.

Clarivate’s takeaways

Clinical milestone: KEYNOTE-B96 marks a major milestone, establishing Keytruda as the first immune checkpoint inhibitor to show a statistically significant survival benefit in platinum-resistant ovarian cancer.

Expected approval: Based on these data, the U.S. FDA has accepted for priority review an sBLA, positioning Keytruda for potential approval in a previously untapped indication.

Competitive dynamics: The treatment landscape for platinum-resistant ovarian cancer is rapidly evolving. Competitive pressure from both approved (Elahere) and promising pipeline ADCs may affect uptake in clinical practice.

Clarivate™

Clarivate coverage of relevant indications

Breast cancer

- Disease Landscape & Forecast | G7
- Epidemiology | Global markets including G7
- Current Treatment: Physician Insights | US
- Treatment Sequencing | US
- Unmet Need | US and EU
- China In-Depth

Prostate cancer

- Disease Landscape & Forecast | G7
- Epidemiology | Global markets including G7
- Current Treatment: Physician Insights | US
- Treatment Sequencing | US
- Unmet Need | US and EU
- China In-Depth

Bladder cancer and Upper tract urothelial carcinoma

- Disease Landscape & Forecast | G7
- Current Treatment: Physician Insights | US
- Treatment Sequencing | US
- Unmet Need | US and EU
- Epidemiology | Global markets including G7
- China In-Depth

Ovarian cancer

- Disease Landscape & Forecast | G7
- Epidemiology | Global markets including G7
- Current Treatment: Physician Insights | US
- Treatment Sequencing | US
- Unmet Need | US and EU
- China In-Depth

About the author

Arshiya Bhatt, Ph.D.

Senior Healthcare Research & Data Analyst

DRG Commercial Solutions

Dr. Bhatt combines a decade of academic research with industry experience to deliver actionable insights in oncology. Prior to joining Clarivate, she worked as a Solution Scientist at Merck Life Science Pvt. Ltd., where she spearheaded strategic collaborations, provided tailored scientific solutions, and conducted market assessments for various biopharma clients. She holds a Ph.D. in Cellular and Molecular Immunology and an M.Sc. in Molecular Biology from the Max Planck Research School in Germany, where her research focused on studying the signaling pathways downstream of the B Cell antigen receptor.

Additional staff

Laura Ramos, Ph.D.
Senior Healthcare Research & Data Analyst

Arshiya Bhatt, Ph.D.
Senior Healthcare Research & Data Analyst

Joan Tur, Ph.D.
Senior Healthcare Research & Data Analyst

Anna Duran, Ph.D.
Healthcare Research & Data Analyst

Louis Perdios, M.Res., Ph.D.
Manager, Healthcare Research & Data Analytics

Sarvendu Kumar, B.Pharm., P.G.D.P.M.
Manager, Healthcare Research & Data Analytics

Leena Kathuria, M.Sc.
Senior Manager, Healthcare Research & Data Analytics

Khurram Nawaz, M.Sc.
Senior Manager, Healthcare Research & Data Analytics

Rachel Webster, M.Sc., M.A., D.Phil.
Director, Healthcare Research & Data Analytics

About Clarivate

Clarivate is the leading global information services provider. We connect people and organizations to intelligence they can trust to transform their perspective, their work and our world. Our subscription and technology-based solutions are coupled with deep domain expertise and cover the areas of Academia & Government, Life Sciences & Healthcare and Intellectual Property. For more information, please visit clarivate.com