Abstract Highlights

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The following highlights showcase key research presented at the European Society for Medical Oncology (ESMO) 2025 Congress. Together, these studies span major advances in breast, oesophageal, urothelial, oropharyngeal, and ovarian cancers, illuminating emerging strategies in treatment, personalisation, and long-term survivorship. From the safety of pausing endocrine therapy to pursue pregnancy, to the nuanced role of immunotherapy across tumour types, and the survival impact of intensified chemotherapy, these findings reflect the evolving intersection of biology, patient priorities, and therapeutic innovation.

POSITIVE: Temporary Endocrine Therapy Interruption for Pregnancy in Early Breast Cancer

UPDATED results from the POSITIVE trial, presented at the ESMO Congress 2025, further support the safety and feasibility of temporarily interrupting adjuvant endocrine therapy (ET) for pregnancy in women with hormone receptor-positive early breast cancer. Previous early follow-up findings (median: 41 months) demonstrated that this approach was viable. New data provide longer-term insight into breast cancer outcomes, pregnancy success, and ET resumption.[1]

The POSITIVE trial was a single-arm prospective study enrolling 518 eligible women between December 2014–December 2019. Participants paused ET after 18–30 months, for up to 2 years, to attempt pregnancy. Outcomes were compared with a matched external control group from SOFT/TEXT. At median follow-up of 71 months in POSITIVE and 80 months in SOFT/TEXT, 5-year cumulative incidence of breast cancer-free interval (BCFI) events was 12.3% in POSITIVE versus 13.2% in SOFT/TEXT (difference: -0.9%; 95% CI: -4.2–2.6%). Similarly, 5-year distant recurrence-free interval events were 6.2% in POSITIVE and 8.3% in SOFT/TEXT (difference: -2.1%; 95% CI: -4.5–0.4%), confirming no increased risk associated with treatment interruption.

Among the 497 women followed for pregnancy outcomes, 377 (75.8%) achieved at least one pregnancy, and 343 (69%) had at least one live birth, resulting in 440 newborns, including 75 women with more than one live birth. An 18-month landmark analysis showed comparable BCFI outcomes between patients who became pregnant and those who did not.

Of the 180 patients (36%) who underwent embryo/oocyte cryopreservation before enrolment, the 5-year cumulative incidence of BCFI events was 14.0% (95% CI: 9.6–20.2%), versus 11.5% (95% CI: 8.4–15.7%) in those who did not cryopreserve. Among 429 women followed for at least 2 years and remaining disease-free, 352 (82%) resumed ET per protocol.

Although long-term follow-up is still required, these findings suggest that temporary ET interruption to pursue pregnancy does not increase breast cancer recurrence risk at 5 years, with high rates of successful pregnancies and ET resumption.

SKYSCRAPER-07: New Direction for Unresectable Oesophageal Cancer?

DATA from the Phase III SKYSCRAPER-07 trial, presented at the ESMO Congress 2025, offer new insights into the potential role of immunotherapy following definitive chemoradiotherapy (dCRT) in patients with unresectable, locally advanced oesophageal squamous cell carcinoma (ESCC). Although dCRT remains the established standard of care, more than half of patients experience disease recurrence, highlighting the need for more effective post-treatment options.[2]

SKYSCRAPER-07 evaluated the efficacy and safety of tiragolumab combined with atezolizumab, as well as atezolizumab combined with placebo, in adults ≥18 years with Eastern Cooperative Oncology Group (ECOG) performance status 0–1 and Stage II–IVA, and select Stage IVB, locally advanced ESCC. All participants were deemed unsuitable for curative surgery and had completed dCRT before enrolment. A total of 760 patients were randomised in a 1:1:1 ratio to receive tiragolumab plus atezolizumab, atezolizumab plus placebo, or placebo plus placebo. Treatment was administered intravenously every 3 weeks for up to 17 cycles, or until disease progression or unacceptable toxicity. The primary endpoints were assessed using a hierarchical testing strategy, beginning with investigator-assessed progression-free survival (PFS) for tiragolumab plus atezolizumab compared with placebo, followed by overall survival (OS) comparisons.

With a median follow-up of 25.0 months, baseline characteristics were consistent across treatment arms. Median PFS was 20.8 months for patients receiving tiragolumab plus atezolizumab and 16.6 months for those receiving placebo, a difference that did not reach statistical significance. Median OS was 38.6 months in the tiragolumab plus atezolizumab arm and 36.4 months in the placebo arm, while median OS was not reached in the atezolizumab plus placebo group.

Adverse events were reported in the majority of patients across all arms, with treatment-related events more frequent in the tiragolumab combination arm. Importantly, no new safety concerns emerged.

Although the trial did not meet its primary endpoint and no survival benefit was demonstrated for the tiragolumab and atezolizumab combination, the findings indicate that atezolizumab plus placebo delivered clinically meaningful improvements in both PFS and OS compared with placebo alone. These results support further exploration of atezolizumab-based treatment strategies for patients with unresectable locally advanced ESCC.

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Adjuvant Nivolumab: 5-Year Outcomes from the CheckMate 274 Trial

THE EXTENDED 5-year follow-up results of the CheckMate 274 trial were presented at the ESMO Congress 2025, demonstrating that adjuvant nivolumab (NIVO) continues to provide meaningful clinical benefit for patients with high-risk muscle-invasive urothelial carcinoma (MIUC) following radical surgery, improving disease-free survival and extending long-term outcomes compared with placebo.[3]

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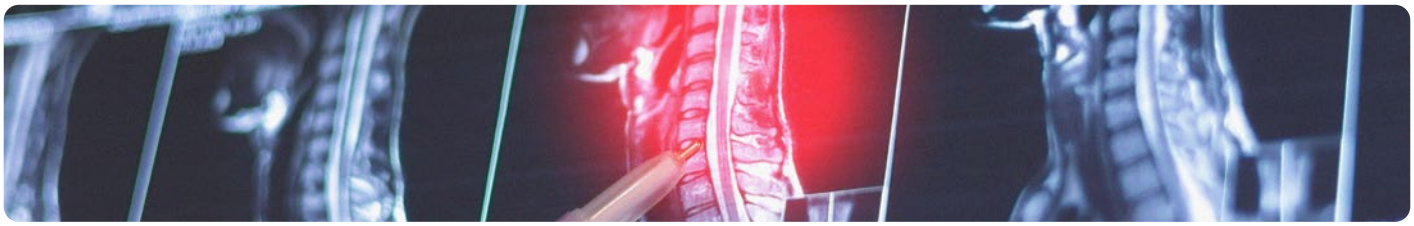
The Phase III CheckMate 274 trial has previously shown that NIVO in patients with MIUC after radical surgery significantly improves disease-free survival in intent-to-treat patients and patients with tumour programmed death ligand 1 (PD-L1) expression ≥1%. Next, the researchers analysed the 5-year follow-up data, as well as the exploratory analysis of circulating tumour DNA (ctDNA) data with the Natera Signatera (Natera, Inc., Austin, Texas, USA) assay. In this study, 709 patients who had radical surgery, neoadjuvant chemotherapy, and were at high risk of recurrence were randomised 1:1 to either NIVO 240 mg IV (n=353) or placebo (n=356) every 2 weeks for 1 year.

With a median follow-up of 43.4 months, the results revealed an improvement in disease-free survival with NIVO, and the overall survival and disease-specific survival were longer with NIVO compared to placebo. This was true for both intent-to-treat and PD-L1 ≥1% patients.

With the exploratory ctDNA analysis, the research team found that ctDNA was detected in 18.8% of patients, and 40.6% of patients were ctDNA positive. Additionally, the results demonstrated that improvement in disease-free survival was seen in patients who were ctDNA positive at Cycle 1 Day 1, but not in those who were ctDNA negative at the same time point.

In summary, the 5-year results of the Phase 3 CheckMate 274 trial show continued improvement in disease-free survival with NIVO, consistent with prior observations. These long-term results support the continued use of adjuvant NIVO as a standard of care for patients with high-risk MIUC. Furthermore, ctDNA-based risk assessment may help refine future treatment pathways, enabling more individualised decision-making and potentially guiding immunotherapy selection in clinical practice.



CompARE: Neoadjuvant and Adjuvant Durvalumab in Locally Advanced Oropharyngeal Cancer

DATA from the Phase III CompARE trial, presented at the ESMO Congress 2025, provide new insight into the role of immunotherapy (IO) combined with chemoradiotherapy (CRT) in locally advanced oropharyngeal cancer (OPC). Previous trials of IO in the radical CRT setting have failed to demonstrate its benefit. This has been attributed to concurrent administration with CRT or delayed initiation of adjuvant IO. CompARE evaluated the impact of neoadjuvant IO followed by adjuvant IO started shortly after CRT completion.[4]

CompARE is a multicentre Phase III RCT (ISRCTN41478539) using an adaptive, multi-arm, multi-stage design. Patients aged 18–70 years with an Eastern Cooperative Oncology Group (ECOG) performance status 0–1 and either intermediate-risk OPC (HPV-positive TNM7 N2b+ with more than 10 pack-year smoking history, N3 or T4) or high-risk OPC (HPV-negative) were randomised to standard therapy (70 Gy in 35 fractions with concurrent cisplatin; Arm 1) or neoadjuvant durvalumab 1,500 mg followed by standard therapy, and then durvalumab 1,500 mg every 4 weeks for 6 months, initiated 2–6 weeks after CRT (Arm 5). The primary endpoint was overall survival (OS), with interim assessment of event-free survival. Secondary outcomes included toxicity, quality of life, swallowing function, and gastrostomy dependence.

A total of 594 patients were recruited across 34 centres (306 in Arm 1 and 288 in Arm 5). In total, 85% had intermediate-risk disease and 15% had high-risk disease. In Arm 5, 98% received induction durvalumab and 81% received adjuvant treatment. At median follow-up of 37 months (95% CI: 28–37), 3-year OS was 84% (95% CI: 79–88%) in Arm 1 and 82% (95% CI: 76–86%) in Arm 5 (stratified log-rank p=0.99). Cox regression analysis showed a hazard ratio (HR) for Arm 5:Arm 1 of 0.97 (95% CI: 0.65–1.46).

In the intermediate-risk group, 3-year OS was 90% (95% CI: 84–93) in Arm 1 and 84% (95% CI: 78–89) in Arm 5, HR: 1.24 (95% CI: 0.75–2.03; p=0.40). In the high-risk group, 3-year OS was 52% (95% CI: 35–67) in Arm 1 and 65% (95% CI: 45–80) in Arm 5; HR: 0.60 (95% CI: 0.30–1.24; p=0.17). PD-L1 biomarker analysis is ongoing, and secondary outcomes and updated follow-up will be presented.

Although the addition of neoadjuvant and adjuvant durvalumab to standard care did not improve overall survival in the overall OPC population, a potential signal of benefit in high-risk HPV-negative patients was observed. These findings support further investigation of PD-1 and PD-L1 inhibition strategies in this subgroup.

> **The primary endpoint was overall survival (OS), with interim assessment of event-free survival**

Dose-Dense Regimen Extends Survival in Ovarian Cancer

ICON8B, a Phase III randomised clinical trial, presented at the ESMO Congress 2025, evaluated whether adding dose-dense weekly paclitaxel (ddwT) to standard three-weekly carboplatin (q3w C) and bevacizumab (BEV) improves outcomes for patients with high-risk Stage III–IV epithelial ovarian cancer (EOC). Earlier analysis demonstrated that ddwT increased median progression-free survival by 5.5 months compared with standard q3w paclitaxel (q3w T) when both were combined with carboplatin and BEV. The current report presents the final overall survival (OS) outcomes following long-term follow-up.[5]

Eligible patients included those with Stage III disease with >1 cm residual tumour after primary surgery or those requiring primary chemotherapy, as well as all Stage IV cases. Participants were randomised to standard therapy (Arm B1: q3w C + q3w T + BEV) or the experimental regimen (Arm B3: q3w C + ddwT + BEV). A third arm without BEV(B2) was closed early due to the lack of progression-free survival benefit. Treatment consisted of up to six cycles of chemotherapy and 18 cycles of BEV. OS was a key secondary endpoint, and follow-up continued until December 2024.

Between 2015–2020, 579 patients were randomised to Arms B1 or B3. The population reflected typical high-risk EOC: median age of 64 years, 91% with high-grade serous carcinoma, and 93% with Stage IIIC–IV disease. Most (84%) commenced treatment with primary chemotherapy.

After a median follow-up of 72 months, 411 deaths occurred. Median OS was significantly improved in the ddwT arm at 49.8 months versus 39.6 months with standard paclitaxel (hazard ratio: 0.79; p=0.010). Among patients receiving primary chemotherapy, OS remained superior in the ddwT group (47.3 versus 37.1 months).

The findings demonstrate a clinically meaningful 10-month OS improvement with ddwT when combined with carboplatin and BEV. The authors conclude that this regimen should be considered a new first-line standard of care for high-risk Stage III–IV EOC, while future research should explore the impact of homologous recombination deficiency and tumour chemosensitivity on treatment benefit.

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