ESMO 2024

The ESMO Congress 2024 opening ceremony set the stage for a landmark event in oncology

Congress Review

Review of the European Society for Medical Oncology (ESMO) Congress 2024

Location:	Barcelona, Spain
Date:	13.09.24–17.09.24
Citation:	EMJ Oncol. 2024;12[1]:10-17. https://doi.org/10.33590/emjoncol/CQJB8024.

KNOWN for its research excellence in the fields of oncology, bionanomedicine, and cardiovascular disease, Barcelona, Spain, provided the ideal setting for the European Society for Medical Oncology (ESMO) Congress 2024. The event was attended by 34,000 participants from across the globe, including almost 600 speakers from 149 different countries, and saw the presentation of 2,186 research abstracts, featured 1,828 posters, and offered 208 programme sessions.

2,186
research abstracts

1,828
posters

208
programme sessions

The Congress formally opened with the welcome address, delivered by the current (2023–2024) President of ESMO, Andrés Cervantes, University of Valencia, Spain. During this speech, he highlighted several new initiatives to aid in the research and practice of clinical oncologists. The establishment of an ESMO fellowship on digital and computational pathology, and a webinar series on genomics-guided care, were among some of the initiatives mentioned.

The scientific address was delivered by Rebecca Dent, National Cancer Center, Singapore. She highlighted that over 2,000 abstracts, including 151 proffered papers and 207 mini oral sessions, covering a wide range of topics from precision oncology to AI-driven cancer care, were embedded into the 2024 programme. The programme also included exciting keynote lectures on leveraging DNA repair pathways, the transformative potential of AI in oncology, and the global epidemic of young-onset cancers.

Several prestigious awards were presented during the opening ceremony. The first of which was bestowed to Ann H. Partridge, Dana-Farber Cancer Institute, Boston, Massachusetts, USA. Partridge discussed the long-term impact of cancer care, particularly focusing on survivorship issues. Her presentation highlighted how the majority of cancer survivors face unintended consequences, such as quality of life deterioration, particularly in young adults diagnosed with breast cancer. Partridge emphasised the need for targeted support systems for survivors to address issues such as fertility, mental health, and adherence to post-treatment therapies. She showcased the success of programmes like 'Young and Strong', which provides a comprehensive support system for young patients with breast cancer.

Serena Nik-Zainal, University of Cambridge, UK, presented a thought-provoking lecture on how mutational signatures derived from cancer genomes can be leveraged for clinical applications. Her work has made

substantial contributions to understanding cancer genomics and how whole-genome analysis can inform treatment strategies. In recognition of this, she was awarded the ESMO Award for Translational Research. Nik-Zainal emphasised the use of mutational signatures to decode environmental and genetic influences on cancer, pushing the boundaries of precision medicine. The evolution of this field was traced from early studies to current AI-driven platforms that allow clinicians to analyse mutational signatures and apply this knowledge to personalise treatment.

The ESMO Women for Oncology Award for bridging gaps in lung cancer research and gender equity was awarded to Myung-Ju Ahn, Samsung Medical Center, Seoul, Republic of Korea. Ahn delivered an insightful talk touching on her career path as well as research advancements in the field of non-small cell lung cancer. Finally, John Haanen, Netherlands Cancer Institute, Amsterdam, the Netherlands, was awarded the ESMO Lifetime Achievement Award for his work in cancer immunotherapy. Haanen's presentation shared insights into T cell therapies for cancer, particularly in the context of adoptive T cell transfer. Haanen highlighted the success of these treatments in metastatic melanoma, showcasing how adoptive T cell transfer can provide durable responses and effective tumour targeting.

The ESMO Congress 2024 opening ceremony set the stage for a landmark event in oncology, highlighting groundbreaking advances in personalised medicine, immunotherapy, and the transformative role of AI in cancer care. With over 2,000 abstracts presented and key sessions spanning global collaborative efforts, the congress emphasised the importance of multidisciplinary approaches in tackling cancer's most pressing challenges.

Read on for more coverage from the 2024 ESMO Congress, and stay tuned for the ESMO Congress 2025, which will take place in Berlin, Germany, from 17th–21st October 2025!

Long-Term Outcomes of Early Switch from Targeted Therapy to Immunotherapy in Advanced *BRAF*^{V600}-Positive Melanoma: Results from the ImmunoCobiVem Trial

RESULTS of the ImmunoCobiVem trial were presented at the ESMO Congress 2024. The trial explored the optimal sequencing of targeted therapies (TT) and immune checkpoint inhibitors (ICI) in patients with advanced *BRAF*^{V600}-positive melanoma, aiming to determine whether starting with TT and then switching early to ICI would improve patient outcomes compared to continuing TT until disease progression.

In this randomised Phase II study, one group (Arm A) received continuous treatment with the targeted drugs vemurafenib (960 mg twice daily) and cobimetinib (60 mg, daily d 21–28, then every 4 weeks) until disease progression, at which point they switched to the immunotherapy drug atezolizumab (1200 mg every 3 weeks). The other group (Arm B) switched early to atezolizumab after a 3-month period of TT, with the option to switch back to the targeted therapies if progression occurred. The primary endpoint was progression-free survival (PFS) during the initial phase of treatment, while secondary outcomes included overall survival (OS), further progression-free survival (PFS2 and PFS3), overall response rates, and safety.

The final analysis, after a median follow-up of 57 months (interquartile range [IQR]: 22.7–63.0), showed that continuous TT (Arm A [69 patients]; hazard ratio [HR]: 0.61; 95% CI: 0.41–0.91; p=0.006) provided better initial tumour control, as seen in higher PFS during the initial phase. However, patients who switched early to immunotherapy (Arm B) had better long-term OS at the 4- and 5-year marks (3-, 4- and 5-year landmark OS were 55% [95% CI: 41–66], 42% [95% CI: 29–55], and 40% [95% CI: 27–53] for Arm A; 55% [95% CI: 41–67], 53% [95% CI: 38–65], and 45% [95% CI: 31–58] for Arm B; and descriptive HR [A versus B] was 1.17; 95% CI: 0.71–1.91). In terms of response rates, both groups performed well, but Arm B had a slightly higher overall response rate than Arm A (89% versus 81%), with more patients achieving complete responses (29% versus 22%, respectively).

Importantly, when patients in Arm B who had switched to ICI experienced disease progression and were retreated with TT, and had better outcomes than those in Arm A who switched to ICI after failing on TT.

In conclusion, the early switch to immunotherapy after an initial period of targeted therapy showed a trend toward better long-term survival. However, the overall benefit remained modest, and there was no clear evidence that any specific subgroup gained a distinct clinical advantage from this approach.

> **The early switch to immunotherapy after an initial period of targeted therapy showed a trend toward better long-term survival**

10-Year Study Confirms Long-Term Survival Benefit of Nivolumab in Advanced Melanoma

THE FINAL results of the landmark CheckMate 067 trial were presented at the ESMO Congress 2024. The presentation showed the results of a minimum 10-year follow-up and revealed the long-term survival benefits of nivolumab (NIVO), alone or in combination with ipilimumab (IPI), for patients with advanced melanoma.

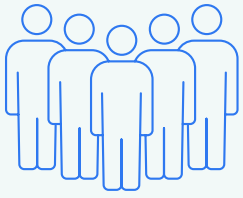
The study was the longest Phase III trial of a PD-1-based therapy to date and aimed to investigate the transformative impact of these immune checkpoint inhibitors on melanoma prognosis.

The study involved 945 patients with untreated advanced melanoma, and the trial compared three treatment arms: NIVO combined with IPI, NIVO alone, and IPI alone. The results showed a difference in overall survival (OS) across these groups. Median OS reached 71.9 months for the NIVO + IPI group, compared to 36.9 months for the NIVO-only group, and 19.9 months for the IPI group. The combination therapy reduced the risk of death by 47% compared to IPI alone, demonstrating consistent benefits across all subgroups, including patients with varying PD-L1 expression levels and *BRAF* mutation statuses.

Furthermore, melanoma-specific survival (MSS) rates were notably high. For patients receiving the NIVO + IPI combination, the median MSS was not reached, indicating survival beyond 120 months. Patients treated with NIVO alone had a median MSS of 49.4 months, while those on IPI alone had a median MSS of 21.9 months. In patients who achieved progression-free survival for at least 3 years, the 10-year MSS rates were 96% for the NIVO + IPI group, 97% for the NIVO group, and 88% for the IPI group.

The study also showed the durability of response in patients who discontinued treatment due to adverse events during the induction phase. These patients demonstrated similar 10-year OS and MSS rates as the broader intention to treat population, showing that early discontinuation due to side effects did not compromise long-term survival benefits.

These final results from CheckMate 067 confirm the sustained efficacy of NIVO-based therapies, offering hope for a potential cure in responsive patients and marking a significant milestone in the treatment of advanced melanoma.



In patients who achieved progression-free survival for at least 3 years, the 10-year MSS rates were 96% for the NIVO + IPI group, 97% for the NIVO group, and 88% for the IPI group.

Neoadjuvant and Adjuvant Pembrolizumab Improves Survival for High-Risk Early-Stage Triple-Negative Breast Cancer

RESULTS of the Phase III KEYNOTE-522 study have shown that compared to neoadjuvant chemotherapy alone, neoadjuvant and adjuvant pembrolizumab with chemotherapy significantly improves overall survival in patients with high-risk early-stage triple-negative breast cancer (TNBC) (Stage T1c N1-2 or T2-4 N0-2 per the American Joint Committee on Cancer staging).

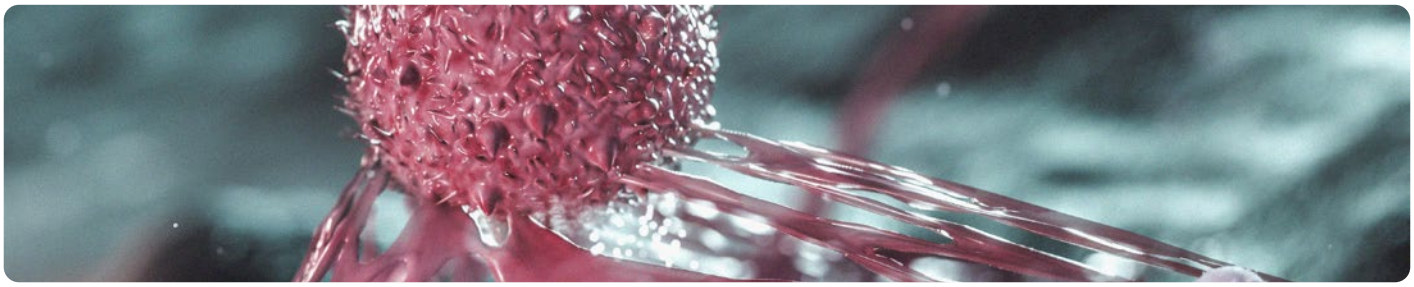
In the study, 1,174 patients with untreated, non-metastatic, centrally confirmed TNBC either received neoadjuvant pembrolizumab 200 mg every 3 weeks (n=784), or placebo (n=390), before four cycles of paclitaxel and carboplatin, followed by four cycles of doxorubicin or epirubicin, and cyclophosphamide. After definitive surgery, patients received adjuvant pembrolizumab or placebo for nine cycles, or until recurrence or unacceptable toxicity occurred.

At the prespecified data cutoff of 22 March 2024, the median follow-up was 75.1 months. At this point, 115 patients (14.7%) in the pembrolizumab group and 85 patients (21.8%) in the placebo group had died. The analysis revealed that the hazard ratio for mortality was 0.66 (95% CI: 0.50–0.87; p=0.0015), meaning that the treatment group had a 34% lower mortality risk than the placebo group. The data also showed that the 5-year overall survival rate was 86.6% (95 CI: 84.0–88.8) for pembrolizumab and 81.7% (95% CI: 77.5–85.2) for placebo. Improvements in overall survival were across different subgroups of patients, such as PD-L1 expression level and nodal status.

The 5-year event-free survival rate for patients in the pembrolizumab group was 81.2% (95% CI: 78.3–83.8), compared to 72.2% (95% CI: 67.4–76.4) in the placebo group, with a hazard ratio of 0.65 (95% CI: 0.51–0.83). Meanwhile, the rate of Grade 3 or higher adverse events was 77.1% in the pembrolizumab group and 73.3% in the placebo group, and immune-related adverse events occurred in 35.0% of patients who received pembrolizumab, compared to 13.1% in the placebo group.

Overall, the results presented at the ESMO Congress 2024 revealed that patients treated with neoadjuvant and adjuvant pembrolizumab had a lower mortality risk, higher overall survival rate, and higher 5-year event-free survival rate. However, pembrolizumab was associated with a higher risk of Grade 3 or higher adverse events and immune-related adverse events. Nevertheless, the study demonstrates pembrolizumab's efficacy in improving overall and event-free survival, highlighting a beneficial treatment strategy for patients with high-risk early-stage TNBC.

> **The treatment group had a 34% lower mortality risk than the placebo group**



Targeted Enzyme Inhibitor Shows Promise in Treating Deleted Gene Tumours

A NEW clinical trial presented at the ESMO Congress 2024 has detailed the safety, tolerability, and preliminary antitumour efficacy of AMG 193, an investigational oral inhibitor designed to selectively target protein arginine methyltransferase 5 (PRMT5) in tumours with methylthioadenosine phosphorylase (*MTAP*) deletions.

MTAP deletions are present in approximately 10–15% of solid tumours, including non-small cell lung cancer (NSCLC), pancreatic ductal adenocarcinoma (PDAC), and biliary tract cancer (BTC). By exploiting synthetic lethality, AMG 193 aims to destroy cancer cells while sparing healthy tissues.

In the trial, patients with NSCLC, PDAC, BTC, and other *MTAP*-deleted tumours received AMG 193 orally, either once daily (QD) or twice daily. All 143 patients included in the study had a history of a median of two prior therapies before starting AMG 193, 80 of whom were placed in a dose escalation (dES) phase treatment group, receiving doses ranging from 40–1,600 mg. The remaining 63 patients were in the dose expansion (dEX) phase, all at a dose of 1200 mg. The trial evaluated safety, anti-tumour activity, pharmacokinetics, and pharmacodynamics.

The most common treatment-related adverse events were nausea (50%), fatigue (30%), vomiting (29%), and decreased appetite (19%). Dose-limiting toxicities, specifically Grade 3 vomiting and Grade 3 hypokalaemia, were observed in two patients in the 1200 mg QD cohort, which was determined to be the maximum tolerated dose. Notably, no dose-limiting cytopaenias were reported, distinguishing AMG 193 from earlier PRMT5 inhibitors.

Efficacy results showed that patients receiving active doses (800 mg and 1200 mg) demonstrated promising responses. Two out of 11 patients with NSCLC, two out of 16 patients with PDAC, and two out of 11 patients with BTC achieved objective responses, with the median duration of response lasting 8.3 months. Tumour biopsies revealed that AMG 193 disrupts key pathways including RNA splicing, cell cycle regulation, and DNA damage response.

The most common treatment-related adverse events were...

Nausea **50%**	Fatigue **30%**
Vomiting **29%**	Decreased Appetite **19%**

Non-operative Management Shows Promise for Patients with Rectal Cancer in NO-CUT Trial

EARLY results of the NO-CUT trial presented at the ESMO Congress 2024 suggest that non-operative management (NOM) following total neoadjuvant treatment (TNT) could be a viable alternative to surgery for patients with proficient mismatch repair locally advanced rectal cancer (pMMR LARC).

Patients in the NOM group demonstrated a DRFS rate of 96.9% at 30 months, compared to 74% for those who underwent surgery

The Phase II trial involved 180 patients across four cancer centres over 6 years, and aimed to examine the effectiveness of TNT followed by either surgery or NOM for patients who achieved a clinical complete response (cCR).

In the trial, patients received a combination of chemotherapy (4 cycles of CAPOX) followed by long-course chemoradiotherapy. Of the patients who completed treatment, 46 (25.5%) were assigned to the NOM cohort based on achieving a cCR after TNT. These patients were closely monitored with intensive follow-up instead of undergoing rectal surgery.

The primary goal of the trial was to assess whether NOM compromises distant relapse-free survival (DRFS). The results were promising, with patients in the NOM group demonstrating a DRFS rate of 96.9% at 30 months, compared to 74% for those who underwent surgery. Local regrowth was slightly higher in the NOM group (15%) than in the surgical group (9%), but overall survival outcomes remained strong, with 12 deaths reported among the entire cohort.

Additionally, early multiomic analyses, including circulating tumour DNA from liquid biopsies, showed correlations with cCR and DRFS, highlighting potential biomarkers for future treatment decisions.

The findings from the NO-CUT trial indicate that NOM, with rigorous follow-up, could be a safe and effective option for a subset of patients with rectal cancer, reducing the need for invasive surgery while maintaining high survival rates. Further analysis of biomarkers may help refine patient selection for this non-operative approach.