

ESMO 2023: Will ADC-IO combinations be the next big modality in cancer treatment?

The field of cancer treatment is evolving at an astonishing pace, with groundbreaking developments taking centre stage at this year's ESMO conference.

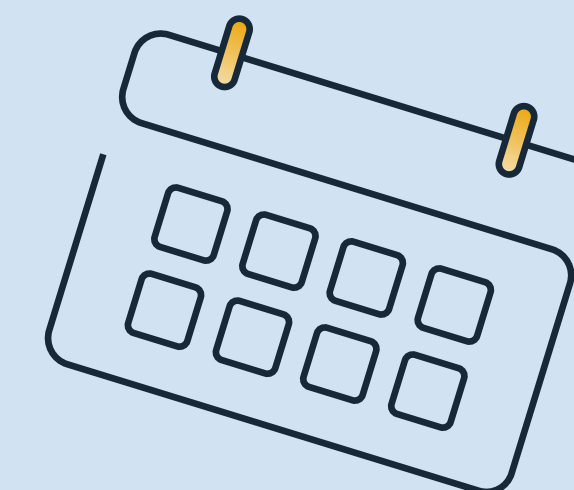
Among the most exciting and promising trends in cancer therapy are the combinations of Antibody-Drug Conjugates (ADCs) and Immuno-Oncology (IO) agents. These innovative combinations have the potential to revolutionise the way we treat various cancer types and bring renewed hope to patients. In this article, we discuss some of the key highlights from the conference and the implications of the latest advancements.



Enfortumab vedotin in combination with pembrolizumab (EV+P) sets a new standard in bladder cancer

One of the standout moments at the **ESMO conference** was the presentation of the final results of the **KEYNOTE-A39 clinical trial**. The trial showcased the remarkable efficacy of enfortumab vedotin in combination with pembrolizumab (EV+P) as a first-line therapy for advanced metastatic bladder cancer.

These results outperformed traditional chemotherapy, marking a significant breakthrough in the treatment of this challenging disease. The combination of EV+P demonstrated superior progression-free survival (PFS) and overall survival (OS) outcomes, firmly establishing it as a new standard of care for first-line advanced metastatic bladder cancer.



The success raises important questions

about the therapeutic sequence in the second-line setting and the positioning of other ADCs like sacituzumab. Whether these agents will find their place in the first line, in combination with immunotherapies, or as second-line options, is a matter of ongoing research and clinical trials.



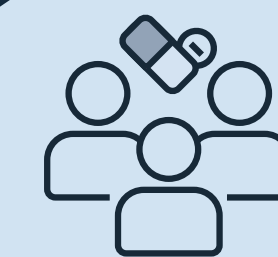
Promising data from the **BEGONIA** trial in triple-negative breast cancer

Another exciting development at the **ESMO conference** came from the **BEGONIA trial**, which showcased the combination of Daiichi and AstraZeneca's datopotamab deruxtecan (dato-DXd) with AstraZeneca's Imfinzi in first-line advanced triple-negative breast cancer (TNBC).

This notoriously aggressive cancer type saw a remarkable **79% response rate** with this regimen. While these results are from phase 1b/2 trials, they hold great promise for the future of TNBC treatment and are eagerly anticipated to be validated in phase 3 trials.

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Advancements in non-small cell lung cancer (NSCLC)

The conference witnessed several significant advancements in the treatment of **NSCLC**, which remains a focal point for cancer research. Notable developments include:

- The **PAPILLON trial**, which introduced 1L amivantamab plus chemotherapy as a new standard of care for patients with EGFR exon 20 insertions in NSCLC.

- The emergence of **potential competition for Tagrisso** with the ami-laser combination in MARIPOSA, showcasing improved progression-free survival.

- Encouraging results from the **MARIPOSA2 trial** in the second-line setting with ami-chemo and ami-laser-chemo combinations.



While these findings are **promising**, they come with considerations about the **benefit-risk ratio** for individual patients, given the **potential increase in toxicities** and the **logistics of administration**.

The long-term impact on **overall survival** is a **critical aspect** that warrants further investigation.





Precision medicine and targeted therapy in **NSCLC**

The conference highlighted the importance of **precision medicine RET fusion positive NSCLC treatment**.

Selpercatinib demonstrated superior efficacy as a first-line therapy compared to chemotherapy and pembrolizumab in patients with RET fusion-positive NSCLC. These results mark a significant shift towards targeted therapies in the treatment landscape.

Alectinib's potential role in ALK-positive early-stage NSCLC

The interim analysis of the ALINA trial revealed the potential of adjuvant alectinib versus chemotherapy in ALK-positive early-stage NSCLC. These findings could lead to changes in the standard of care for this patient population, pending further data.

Zenocutuzumab: A promising therapy for NRG1+ advanced NSCLC

The eNRGy phase 2 trial showcased the durability of zenocutuzumab in NRG1+ advanced NSCLC. This HER2 x HER3 bispecific antibody exhibited impressive efficacy, potentially becoming the first-choice therapy for this specific NSCLC subtype.

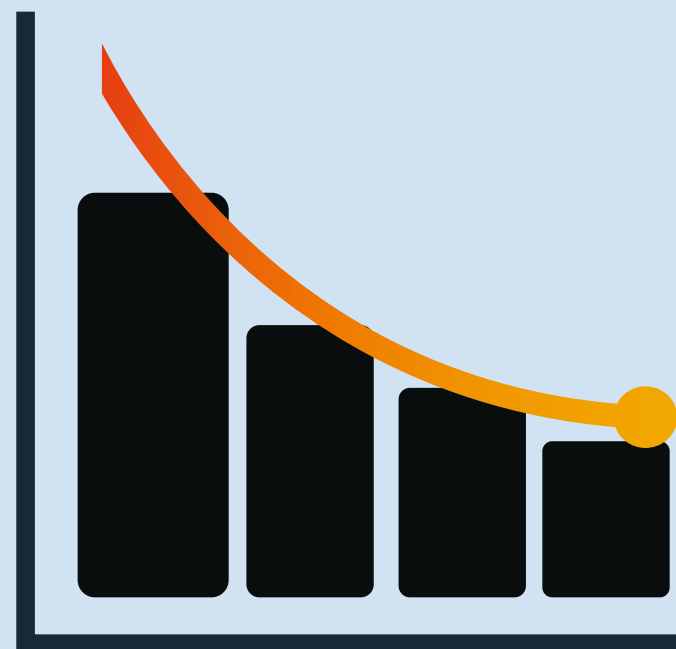
ADCs making waves in second-line NSCLC

The **TROPION-Lung01** trial, featuring AstraZeneca and Daiichi Sankyo's datopotamab deruxtecan (dato-DXd),

demonstrated a 25% reduction in disease progression or death compared to docetaxel in second-line NSCLC patients. These results suggest that dato-DXd may have a meaningful role, particularly in non-squamous disease, and offer a well-tolerated and manageable safety profile.

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The role of **hallmarks of cancer** in treatment development

The **ESMO conference** shed light on the significance of understanding the **hallmarks of cancer in guiding treatment development**. Co-targeting these hallmarks offers a rational approach to overcome drug resistance and **improve patient outcomes**.

Preclinical studies, such as the one in glioblastoma by Douglas Hanahan, suggest that targeting multiple functional capabilities of cancer cells can reprogram the tumour microenvironment and sensitise tumours to immune checkpoint blockade, offering new avenues for treatment.

The ESMO conference in 2023 showcased a multitude of groundbreaking developments in the field of cancer treatment, with ADC-IO combinations taking the spotlight. As we await further data and trials, these advancements offer hope for improved patient outcomes.

Got any questions or want to find out more?

Get in touch to chat to our expert:



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