EBR

Diving deeper into understanding patient care implications of growing oncology R&D advances: notable takeaways from ESMO and ASH 2023

Congresses and events are a cornerstone of the pharma industry and provide a way for researchers to share new developments to key people in the field. What were some of the notable announcements from two of the biggest events of 2023?

By José Luis García, Sari Heitner Enschede and Matthew Simmons at IQVIA

The global oncology drug discovery and development landscape continues to expand as researchers further explore transformative science to enhance patient care. According to a 2023 industry research report, oncology trial starts were at historically high levels in 2022 (up 22% from 2018), with global cancer medicine spending at $196bn that year as well.[1]

Whether considering novel treatments available for the first time or the expanded use of a newer therapy for varying types of cancer, there is an underlying excitement among research and development stakeholders regarding the sheer volume of innovation in cancer care.

At the European Society for Medical Oncology (ESMO) and American Society of Hematology (ASH) meetings late last year, this excitement was experienced as more than 66,000 global experts collectively came together at these events to present and discuss a wide range of oncology research abstracts and practice-shifting advances.[2,3]

Oncology drug innovation is a priority for everyone in the industry, especially as it relates to improving equitable treatment access and making sure patients' quality of life is considered alongside drug efficacy. With the numerous breakthroughs happening, including the noteworthy cancer care advances shared below, regulators, researchers and clinical trial sponsors are keeping these factors in mind during drug development.

Evolving from the chemotherapy treatment paradigm

In traditional cancer treatment paradigms, higher doses of chemotherapy may mean better efficacy but also higher toxicity, which can significantly impact patients' physical, emotional and social functioning. This is where the breadth of novel therapies is showing potential to shift care plans that can make a tangible impact on patient health outcomes.

Antibody-drug conjugates

Antibody-drug conjugates (ADCs), for example, are a class of targeted cancer therapies for which the industry has anxiously awaited outcomes results, as they are intended to give

patients and clinicians a chance to better align with disease requirements. Clinical development for ADCs is complex and time intensive, which is why several major ADC-related research highlights at ESMO 2023 were well-received.

For example, phase 3 trial results showed that Padcev (enfortumab vedotin) jointly owned by Agensys and Seagen in combination with Keytruda (pembrolizumab) by Merck reduced risk of death by 53% compared to chemotherapy in patients with untreated bladder cancer. In December 2023, the US Food and Drug Administration fully approved this Padcev-Keytruda combination for this indication, and the European Medicines Agency is currently reviewing the application.[4,5]

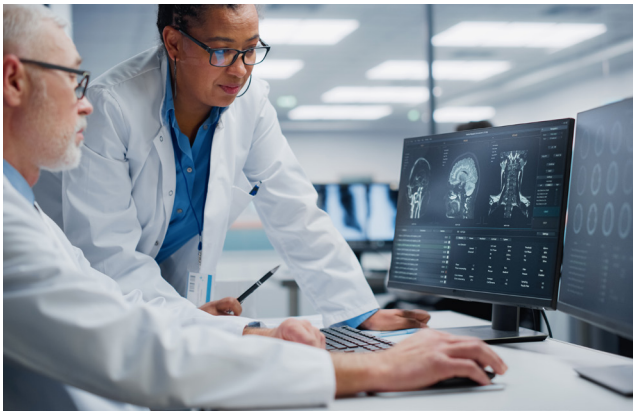
ADCs are also changing traditional treatment plans for inoperable or metastatic breast cancer. Presented as a late-breaking abstract at ESMO, results from the TROPION-Breast01 phase 3 trial found that datopotamab deruxtecan, an ADC jointly developed by AstraZeneca and Daiichi Sankyo, demonstrated a statistically significant and clinically meaningful improvement in progression-free survival compared to 'investigator's choice' of chemotherapy in patients with inoperable or metastatic hormone receptor-positive, HER2-low or negative breast cancer previously treated with endocrine-based therapy and at least one systemic therapy.[6]

Both sets of findings are considered practice-changing because ADCs have previously had later-stage labels for use. Now, with earlier integration into the treatment plan, some patients may be able to reduce chemotherapy treatment dosages and related systemic toxicities.

Early dose optimisation and access to new treatments

Along with ADCs, there is a magnitude of newer therapies that are under evaluation in combination for potential in the efficacious treatment of varying cancers, especially in historically difficult-to-treat forms. However, with the potential that patients may receive these novel therapies for longer periods of time, consideration of patients' quality of life is vital during development. For example, a newer therapy which extends survival by several years but results in the patient experiencing prolonged grade 2 toxicity requires a different approach to the assessment of treatment tolerability.

A key discussion at ESMO, the FDA's Project Optimus initiative is designed to guide trial sponsors to reform typical oncology



R&D efforts by evaluating dose optimisation earlier in trial programmes.[7,8] This initiative has the goal of helping to select a targeted dose that prioritises efficacy but also considers the full impact of toxicity and potentially debilitating symptoms for individuals. Navigating the Project Optimus guidance to better meet qualitative needs of patients alongside survival is paramount for regulators, trial sponsors, investigators and patients alike. There is no one-size-fits-all approach for early dose optimisation, especially as complexities increase when evaluating therapies in combination. The industry is still exploring strategies and innovative methodologies to dose optimisation in collaboration with scientific, regulatory and patient advocacy groups.

In addition to Project Optimus, the FDA's Project FrontRunner initiative encourages sponsors to determine when it may be appropriate to develop and seek approval for new cancer therapies for advanced and metastatic cancers in earlier clinical settings rather than testing in those patients who have been heavily pre-treated and have both less likelihood of response and tolerance for toxicity.[9] For example, R&D efforts regarding immunotherapies, such as PD-1/PD-L1 checkpoint inhibitors, in combinations are demonstrating positive results in the neoadjuvant and adjuvant settings. At ESMO, phase 3 data findings from the CheckMate-77T trial showed that adding Bristol Myers Squibb's PD-1 inhibitor, Opdivo (nivolumab), pre- and post-surgery along with pre-surgical chemotherapy reduced risk of tumour recurrence, progression or death by 42% in patients with stage 2 to 3b non-small cell lung cancer and significantly improved event-free survival.[10]

Expanding access to viable treatment options

When aiming to offer patients living with various forms of cancer increased survival and improved quality of life, a focus on research to address cancers and diseases of high unmet medical needs is key. Below are a few noteworthy examples from ASH 2023 of the industry's commitment to exploring additional ways to meet patient needs.

Since acute myeloid leukaemia typically impacts cells that are not completely developed and can progress rapidly, it can be challenging for patients to function without debilitating symptoms, making traditional chemotherapy treatment difficult to endure.[11] Presented at ASH, the QuANTUM-First global phase 3 trial was the first study to report longitudinal patient-reported outcomes of an FLT3-inhibitor (quizartinib) as a first-line therapy for newly diagnosed acute myeloid leukaemia. Results found that patients treated with quizartinib alongside standard chemotherapy who achieved complete remission, remained in remission longer, continued the treatment longer and reported better quality of life than those treated with standard chemotherapy plus placebo.[12] With additional research, investigators will gauge the benefit of survival from first-line therapy use. Also, in aiming to gauge other monotherapies outside of chemotherapy and related antineoplastic agents commonly used for treatment of blood cancers, efficacy and safety results from an open-label, first-in-human, phase 1/2 dose-escalation study of SAR443579, an investigational CD123 targeting NKp46/CD16-based natural killer cell engager (NKCE), combined with the BCL2 inhibitor Venclexta (venetoclax) for the treatment of acute myeloid leukaemia and high-risk myelodysplasia were shared at the ASH meeting. To examine the NKCE as a monotherapy treatment for these blood cancers, early-stage results showed durable clinical efficacy and favourable safety profile.[13] SAR443579 has received FDA Fast Track Designation for acute myeloid leukaemia, which is exciting news given the limited treatment options for this patient community.

The industry is also showing commitment to tackling long-standing treatment challenges for non-malignant conditions such as sickle cell disease, a rare and potentially life-threatening blood disorder. ASH 2023 attendees were genuinely pleased to hear about the FDA approval of the first two cell-based gene therapies for the treatment of patients 12 years of age and older with recurrent vaso-occlusive events.[14] Sickle cell most commonly affects African Americans and people of African descent, Hispanic-Americans and those of Middle Eastern, Indian and Mediterranean descent. So, this advance in gene therapy and editing gives promise to potentially underserved patient communities and opens opportunities to continue exploration of this innovative space. Also, demonstrating the value of improved access to a commonly used disease-modifying treatment called hydroxyurea for sickle cell disease for paediatric patients in Sub-Saharan Africa, research presented at ASH said 87% of the 635 children enrolled in the REACH trial remained under the treatment eight years later due to dose optimisation efforts.[15] Hydroxyurea was given safely and effectively and was feasible for children in this region, which underscores that more extensive access to this relatively low-cost drug is possible.

Expanding on nuances in innovation

The oncology industry and broader healthcare ecosystem are moving away from drug-centred development and

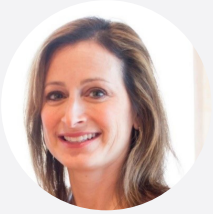
increasingly focusing on patient-centred approaches to improve health outcomes and expand treatment access to all regardless of location or circumstance. As cancer care continues to shift in this direction, the nuances in oncology R&D will only grow, aiming to provide more tailored care options to better suit everyone in their individual journeys.

The extensive number of positive results from clinical trial programmes coming out of these critical annual oncology gatherings is a strong indication of the collective commitment stakeholders worldwide are investing into optimising cancer care and ensuring R&D efforts reflect what patients need in the real world. Looking ahead to 2024 and beyond, the momentum to accelerate viable cancer care therapies that shift clinical practice for improved patient outcomes will remain high, and stakeholders will eagerly await news of more advances coming out of this year's global oncology gatherings.

References:

1. *Visit: iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-oncology-trends-2023*
2. *Visit: esmo.org/meeting-calendar/past-meetings/esmo-congress-2023*
3. *Visit: hematology.org/Meetings/Annual-Meeting*
4. *Visit: esmo.org/oncology-news/fda-approves-enfortumab-vedotin-ejfv-with-pembrolizumab-for-locally-advanced-or-metastatic-urothelial-cancer?*
5. *Visit: prnewswire.com/news-releases/european-medicines-agency-validates-type-ii-variation-application-for-padcev-enfortumab-vedotin-with-keytrudapembrolizumab-for-first-line-treatment-of-advanced-bladder-cancer-302045751.html*
6. *Visit: oncologypro.esmo.org/meeting-resources/esmo-congress/datopotamab-deruxtecan-dato-dxd-vs-chemotherapy-in-previously-treated-inoperable-or-metastatic-hormone-receptor-positive-her2-negative-hr-her2*
7. *Visit: oncologypro.esmo.org/meeting-resources/esmo-congress?event_resources_filter_form%5Bsearch%5D=Project%20optimus*
8. *Visit: fda.gov/about-fda/oncology-center-excellence/project-optimus*
9. *Visit: fda.gov/about-fda/oncology-center-excellence/project-optimus*
10. *Visit: oncologypro.esmo.org/meeting-resources/esmo-congress/checkmate-77t-phase-iii-study-comparing-neoadjuvant-nivolumab-nivo-plus-chemotherapy-chemo-vs-neoadjuvant-placebo-plus-chemo-followed-by-surge*
11. *Visit: lls.org/leukemia/acute-myeloid-leukemia*
12. *Visit: ash.confex.com/ash/2023/webprogram/Paper189035.html*
13. *Visit: ash.confex.com/ash/2023/webprogram/Paper173162.html*
14. *Visit: fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease*
15. *Visit: ashpublications.org/ashnewsdaily/news/7642/Sickle-Cell-Disease-in-Resource-limited-Settings*

José Luis García is senior medical strategy director, Oncology Center of Excellence, at **IQVIA**. Bringing more than 12 years of clinical oncology experience and nearly two decades in cancer research to his current role at IQVIA, José is currently responsible for overseeing the development of innovative and evidence-driven delivery strategies and solutions for oncology trial programmes, with a specialised focus on brain tumour, liver tumour, gastrointestinal and melanoma studies. Alongside having extensive clinical experience in medical oncology and related patient care, José has served as principal investigator for various clinical and translational phase 1-4 oncology studies and has supported new and expanded existing drug life cycles through his work in medical affairs in the pharmaceutical industry.



Dr Sari Heitner Enschede, senior medical director and Hematology-Medical Strategy lead, Oncology Center of Excellence at **IQVIA**. Sari has worked in the pharmaceutical industry for 18 years with five years at IQVIA, providing strategic guidance to customers for haematology studies and programmes and expert consultation and leveraging of professional networks for haematology-specific partnerships. Her previous experience at AbbVie/Abbott entailed leading global clinical trials in haematologic malignancies for phases 1-4, with key roles in product safety, regulatory agency communications and the launch of its BCL2 inhibitor Venetoclax. Prior to transitioning into the pharmaceutical industry, Sari is an experienced haematologist who served as assistant professor in Medicine in the Department of Hematology-Oncology at Rush University in Chicago, US.

Matt Simmons is senior director, Oncology Strategy, at **IQVIA Biotech**. Matt provides strategic guidance to the oncology operational teams as well as consultative oversight for biopharma and biotech sponsors developing therapeutics to treat cancer. He has more than 25 years of experience across all phases of drug development with large and small pharma, CROs, consulting and software companies, as well as managing a leading oncology phase 1 clinical research unit in London.