Antibody-Drug Conjugates in Oncology: Revolutionizing Cancer Treatment

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In the ever-evolving field of cancer treatment, a powerful novel approach is changing the landscape: antibody-drug conjugates (ADCs). These cutting-edge therapies offer renewed hope for patients and groundbreaking opportunities for pharmaceutical and biotech companies. In this blog, we will explore the essence of ADCs, successes, challenges, and their promising future.

What are Antibody-Drug Conjugates?

Imagine a therapy that can precisely target and eliminate cancer cells while sparing healthy tissue – this is the promise of ADCs. These innovative treatments combine the targeting ability of monoclonal antibodies with the potent, cell-killing power of cytotoxic drugs by maximizing efficacy while minimizing side effects.

Understanding how ADCs work involves delving into their three components:

1. **Monoclonal Antibody:** Targets specific cancer cell antigens.
2. **Linker:** Attaches the drug to the antibody and releases it inside the cancer cell.
3. **Cytotoxic Drug:** Kills the cancer cell with minimal impact on healthy cells.

Breakthroughs in the ADCs Therapies

ADCs are not just theoretical – they influence patients' lives. Here are some of the latest and most impactful examples:

Enfortumab Vedotin (Padcev®) Approved for advanced urothelial cancer, Padcev® targets Nectin-4, a protein highly expressed in bladder cancer. In a pivotal phase II clinical trial, Padcev® demonstrated an overall response rate (ORR) of 44%, with 12% of

patients achieving a complete response (CR) and with a median duration of response (DOR) of 7.6 months, providing significant benefits for patients who progressed on other therapies (Chang, et al., 2011).

Trastuzumab Deruxtecan (Enhertu®) For HER-2-positive breast cancer, Enhertu® offers a new lifeline. In the DESTINY-Breast01 trial, Enhertu® achieved an ORR of 60.9%. The median duration of response was 14.8 months, and the median progression free survival (PFS) was 16.4 months. These impressive results have made Enhertu® a crucial option for patients with previously treated metastatic disease (Modi, et al., 2020).

Moxetumomab Pasudotox (Lumoxiti®) Used for Hairy Cell Leukemia, Lumoxiti® targets CD22 and has provided substantial clinical benefits. In clinical trials, Lumoxiti® achieved an ORR of 75%, with 30% of patients experiencing a durable CR lasting at least six months. These outcomes highlight Lumoxiti's® effectiveness in treating this rare blood cancer (Kreitman, et al., 2018).

Sacituzumab Govitecan (Trodelvy®) Approved for triple-negative breast cancer, Trodelvy® targets Trop-2 and has shown remarkable improvements in progression-free survival. In the ASCENT trial, Trodelvy® demonstrated an objective response of 35%, with a median PFS of 5.6 months compared to 1.7 months for chemotherapy. The median OS was also significantly improved at 12.1 months versus 6.7 months for chemotherapy (Bardia, et al., 2021).

Polatuzumab Vedotin (Polivy®) Polivy® is combined with Bendamustine and Rituximab for relapsed or refractory diffuse large B-cell lymphoma. Polivy® targets CD79b and has demonstrated significant clinical benefit. In the GO29365 trial, the addition of Polivy® to Bendamustine and Rituximab resulted in a complete response rate of 40% compared to 18% without Polivy®, underscoring its effectiveness (Sehn, et al., 2020).

Some Key Oncology Acronyms		
Acronym	Meaning	Explanation
OS	Overall Survival	The duration from randomization to death. The "gold-standard" primary endpoint.
PFS	Progression-Free Survival	The duration from randomization to the first sign of disease progression or death.
ORR	Overall Response Rate	The proportion of patients in a study whose cancer shrinks or disappears after treatment.
CR	Complete Response	The absence of any detectable signs of a tumor.
DOR	Duration of Response	The period during which a tumor remains responsive to treatment without increasing in size or spreading.

Market Insights and Commercial Potential

The market for ADCs is expanding rapidly, driven by their proven efficacy and continuous innovation in biotechnology. Currently, several ADCs have received approval, with many more in various stages of clinical development. Key players in the market include both established pharmaceutical giants and innovative biotech firms. Recent market entries have demonstrated significant commercial potential, with ADCs like Trastuzumab Deruxtecan (Enhertu®) achieving substantial market penetration and strong sales.

Future growth projections for the ADC market are robust. The increasing incidence of cancer, combined with the growing demand for targeted therapies, suggests that the ADC market will continue to expand. Additionally, advances in ADC technology, such as improved linker stability and novel cytotoxic agents, are expected to enhance the therapeutic window of these drugs, making them more attractive to investors and clinicians.

Navigating the challenges of ADCs

Despite their promise, ADCs face several hurdles:

1. **Antigen Selection:** Finding the right target antigen abundantly expressed on cancer cells but minimally on healthy cells is crucial for efficacy and safety.

2. **Drug Resistance:** Cancer cells can develop resistance to ADCs by altering antigen expression or using drug efflux mechanisms, posing significant challenges.

3. **Toxicity Management:** Even with targeted delivery, off-target effects and systemic toxicity can occur, requiring precise dose optimization and vigilant patient monitoring.

Collaborative Efforts in ADC Development

ADC development is a collaborative effort involving academic institutions, biotech firms, pharmaceutical companies, and contract research organizations (CROs). These partnerships are crucial for advancing ADC technology and bringing new therapies to market. Academic researchers often provide the foundational science and early-stage discoveries that drive ADC innovation. Biotech firms typically focus on translating these discoveries into viable therapeutic candidates. At the same time, pharmaceutical companies bring the necessary resources and expertise to conduct large-scale clinical

trials and navigate the regulatory landscape.

CROs play a vital role in this ecosystem by providing specialized services that support the development and commercialization of ADCs. These services include clinical trial management, regulatory consulting, data management, and more by leveraging the expertise of CROs, biotech and pharmaceutical companies can streamline their development processes, reduce cost, and accelerate the time-to-market for their ADC products.

Moreover, incorporating the patient's voice into ADC development is crucial to understanding the full impact of these therapies.

Global regulatory agencies, including the FDA and EMA, emphasize integrating patient perspectives in drug development through frameworks that ensure treatments align with patient needs and experiences (FDA, 2022) Electronic Patient-Reported Outcomes (ePROs), such as the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the Functional Assessment of Cancer Therapy (FACT-G), play a vital role in capturing patient's perspectives on their quality of life, beyond the clinical outcome measured by clinical outcomes by healthcare providers.

By utilizing ePROs, researchers can gain insights into the side effects, physical and emotional well-being, and overall treatment experience from the patient's point of view, ensuring that the development of ADCs is aligned with improving not only survival but also the quality of life of cancer patients. Signant Health has a broad experience in Health-related Quality of Life (HRQoL) patient-reported measures and offers advice on best practices to optimize their implementation in clinical studies.

Conclusion

ADCs represent a major advancement in cancer therapy, offering new hope for patients. Signant Health was key in 40% of FDA oncology drug approvals and 38% of EMA approvals in 2023. Explore the transformative potential of ADCs with us—contact us to learn how we can support your oncology studies.

About the Author

Dr. Figueroa is a Clinical Scientist with the eCOA Science Team at Signant Health, where she leverages her extensive expertise in electronic Clinical Outcome Assessments (eCOA) across diverse therapeutic areas, including oncology, dermatology, and infectious diseases. With over a decade of translational research experience, Dr. Figueroa is dedicated to advancing the field of clinical trials and improving patient outcomes through innovative methodologies and strategic insights. Her work at Signant Health focuses on integrating cutting-edge eCOA technologies to enhance the accuracy and reliability of clinical data, ultimately contributing to more effective and patient-centric healthcare solutions.

References

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