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PROCEEDINGS ABSTRACT

The utility, effectiveness, and challenges of the use of antibody–drug conjugates in targeted cancer therapy: a narrative review

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Cancer remains one of the leading causes of morbidity and mortality worldwide, with approximately 20 million new cases and 9.7 million deaths reported in 2022. Global projections indicate that the annual incidence of cancer could exceed 35 million cases by 2050 due to population growth, ageing, and increasing exposure to risk factors such as smoking and obesity. Although surgery, radiotherapy, and conventional chemotherapy remain fundamental treatment modalities, their clinical utility is often limited by inadequate tumour selectivity, systemic toxicity, and the emergence of drug resistance. The aim of this narrative review was to summarise the utility, therapeutic effectiveness, and current challenges associated with antibody–drug conjugates (ADCs) in targeted cancer therapy, while highlighting recent innovations that may enhance their clinical impact. ADCs represent an important advancement in precision oncology by combining the high specificity of monoclonal antibodies with the cytotoxicity of anticancer agents. These agents function through selective binding to tumour-associated antigens expressed on malignant cells, followed by the receptor-mediated internalization and intracellular release of payloads. This targeted delivery strategy allows ADCs to maximize antitumour activity while minimizing exposure of healthy tissues. ADCs frequently employ humanised IgG1 antibody backbones, providing prolonged circulation times and additional immune-mediated mechanisms such as antibody-dependent cytotoxicity and complement activation. Clinical effectiveness of ADCs has been demonstrated across a growing range of haematological malignancies and solid tumours. By late 2024, approximately 15 ADCs had received approval from the United States FDA for various oncological indications. Notable examples include gemtuzumab ozogamicin for acute myeloid leukaemia and trastuzumab deruxtecan for human epidermal growth factor receptor 2 (HER2)-positive and HER2-low breast cancer. These successes have established ADCs as a major therapeutic platform. Despite their promise, several challenges continue to limit the broader application of ADCs: drug delivery efficiency remains relatively low, with only a small proportion of the administered dose reaching tumour tissues, while clinically significant toxicities (including interstitial lung disease, neutropenia, and ocular adverse effects) may compromise the treatment outcomes and contribute to trial discontinuation. Additional barriers include complex manufacturing processes, high production costs, and limited accessibility in resource-constrained settings. Moreover, the emergence of acquired resistance through antigen downregulation, epitope alterations, and enhanced drug efflux mechanisms further complicates long-term treatment success. In order to overcome these limitations, next-generation

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ADC technologies are being actively developed. These include bispecific ADCs capable of targeting multiple antigens simultaneously, probody–drug conjugates that are designed for selective activation within the tumour microenvironment, degrader–antibody conjugates utilising targeted protein degradation strategies, and immune-stimulating ADCs enhancing antitumor immune responses. These innovations, together with advances in site-specific conjugation and combination therapies involving immune checkpoint inhibitors, are expected to improve the safety, efficacy, and clinical utility of ADCs. The latter are, therefore, likely to remain central to the continuing evolution of personalised and targeted cancer treatment.

Keywords

antibody–drug conjugates; cancer therapy; monoclonal antibodies; precision medicine; targeted drug delivery

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Conflicts of interest statement

None to declare.

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