Mini Review

Pharmaceutical BIOPROCESSING

Technology Considerations for Production of Antibodies and Antibody-Drug Conjugates In Cancer Therapy

Anna Dobrev*

Department of Pharmacy, Finland

*Author for correspondence: dobrevanna@rediff.com

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Abstract

The cornerstone for the therapeutic antibody field's explosive growth and development is the capacity of monoclonal antibodies to bind to a target antigen with high specificity and either neutralise or boost its activity. Traditional immunoglobulin antibodies have recently undergone additional engineering for improved efficacy and safety, and technological advances in the field have made it possible to design and produce engineered antibodies that can mediate therapeutic functions that were previously not possible by conventional antibody formats. Bispecific antibodies and antibody-drug conjugates, each with several approved medications and dozens more in the clinical research stage, serve as examples of this more recent generation of therapeutic antibody forms. The technological underpinnings and difficulties of bispecific antibodies and antibody-drug conjugates are covered in this review, with a focus on clinically validated formats and recent advancements in the field, many of which are anticipated to significantly expand the current therapeutic arsenal against cancer and other diseases with unmet medical needs [1-5].

Keywords: Bi specific antibody • Antibody drug conjugate • Cancer therapy

Introduction

ADCs are typically made up of a monoclonal antibody (mAb) that has been covalently linked to a cytotoxic substance by a chemical linker. One of the hotspots for the study and creation of anticancer medications, it combines the benefits of highly specific targeting capacity and highly potent killing impact to produce accurate and efficient elimination of cancer cells. There have been 14 ADCs that have achieved market approval globally thus far since the first ADC, Mylotarg® (gemtuzumab ozogamicin), was licenced by the US Food and Drug Administration (FDA) in 2000. Additionally, more than 100 ADC candidates are now being studied in clinical phases. A new age of targeted cancer therapy is being pioneered by this class of novel anti-cancer medications, also referred to as "biological missiles". Here, we reviewed the background and general mechanism of action of ADCs before briefly going over the molecular features of some of their most important constituents and the ways by which they affect the activities of ADCs. Additionally, we evaluated the authorised ADCs and other interesting candidates in phase 3 clinical trials and talked about the present issues and potential outcomes for the next generation's development, which offers insights for the investigation and creation of innovative cancer therapies utilising ADCs [6-8].

In order to deliver a powerful cytotoxic payload to target antigens expressed on cancer cells, antibody-drug conjugates (ADCs) use the monoclonal antibody (mAb)'s specificity. Wider therapeutic windows, improved pharmacokinetic/pharmacodynamic features, and a unique possibility to deliver medicines to tumour cells all come from ADCs. More than 80 ADCs are currently undergoing clinical development around the world, and nine ADCs have already received FDA approval. We give a summary of the biology and chemistry of each ADC design component in this study. We briefly go through the main routes implicated in ADC resistance as well as the clinical experience with licenced ADCs. The developing class of anticancer therapeutic agents known as antibody-drug conjugates (ADCs) combines the deadly efficacy of chemotherapy medications with the selectivity of targeted therapy. New linker technology combined with

innovative, highly potent cytotoxic payloads has made it possible to create ADCs that are both safer and more efficient. T-DM1 and brentuximab vedotin, two ADCs that have recently been licenced, are already making their mark in the field of cancer treatment. Phase I and II trials are investigating a wide variety of ADCs, and preliminary data are encouraging. More ADCs will probably become viable treatment choices as single agents or in conjunction with chemotherapy as we gain a better knowledge of what makes an effective ADC [9].

Discussion

Antibodies used for therapeutic purposes work by attaching to and neutralising extracellular target molecules. The benefits of therapeutic antibodies include the capacity to inhibit protein-protein interactions, which is typically not possible with small-molecule medications, and strong and specific binding to the target antigen, maximising efficacy and safety. However, just like with the majority of other treatment approaches, complex disorders like cancer are rarely cured by simply blocking one particular disease-causing component with an antibody. Few diseases are entirely dependent on a single target and its signalling pathways and treatment resistance is frequently caused by sick cells downregulating the target molecule and/or developing compensatory mechanisms. Therapeutic antibodies function by binding to and neutralising extracellular target molecules. Therapeutic antibodies have several advantages over small-molecule drugs, including the ability to block protein-protein interactions and strong, precise binding to the target antigen, which maximises efficacy and safety. Complex diseases like cancer are rarely healed by just blocking one single disease-causing component with an antibody, just like with the bulk of other therapeutic strategies. Few diseases are solely dependent on one target and its signalling pathways, and treatment resistance is typically brought on by sick cells downregulating the target molecule and/or evolving compensatory mechanisms.

One of the anticancer medications with the quickest growth is antibody-drug conjugates (ADC). This method uses a mAb attached to a lethal payload via a chemical linker that is directed at a target antigen expressed on the surface of the cancer cell, limiting systemic exposure and toxicity. ADCs are intricate molecules that need special consideration for a number of factors. ADCs' safety and effectiveness are largely determined by the choice of an appropriate target, a mAb, a cytotoxic payload, and how the antibody is coupled to the payload. Increased understandings of the mechanism of action of ADCs, mechanistic pathways involved in ADC resistance, and numerous methodologies to optimise ADC design are all provided in this paper. It also provides an overview of the systemic examination of each component of an ADC design [10].

Conclusion

Even though only four ADCs have received clearance, the ADC design has significantly advanced. ADCs are a frontier for the upcoming generation of therapeutic therapies for a number of diseases because of the adaptability of antibodies, the discovery of new antigens and cytotoxic payloads, and the increasing complexity of methodologies. To increase the effectiveness of an ADC design, each component must be thoroughly evaluated. Additionally, a more thorough knowledge of the molecular mechanisms underlying ADC resistance would help to rationally design ADCs and improve treatment outcomes. There are currently over 60 ADCs in clinical development, and the clinical data generated by these next-generation ADCs will be crucial for understanding the molecular foundation of ADC design. Combination medicines have the power to lower drug resistance, boost medication efficacy, and reduce tumour metastasis, growth, and survival rates for cancer. The results of research show that when combined with other medications, ADC has even better efficacy and is less hazardous. AXL-107-MMAE and BRAF/MEK is one example of an ADC combo therapy. According to the study's findings, AXL-107-MMAE alone has less of an impact than it does when combined with BRAF/MEK. Combining these inhibitors strengthens each one's ability to block the spread of drug-resistant tumour cell colonies. Similar to this, Schönfeld and associates improved the efficacy of indatuximab ravtansine (BT062) when used in combination with other therapies for multiple myeloma. Indatuximab ravtansine research in both *vivo* and *in vitro* demonstrated excellent anticancer effects.

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