

Special Thematic Issue for Current Drug Safety**Safety and Adverse Effects of Antibody Drug Conjugates (ADC)***Guest Editor: Pollen K.Yeung*

Aims & Scope: Biological agents are increasingly used in drug therapy ranging from cancer to chronic diseases such as cardiometabolic diseases, inflammation, osteoporosis and neurological disorders. One type of these agents is the antibody drug conjugates (ADCs) which are gaining momentum for treatment of cancer. These biologics are designed to harness the specificity of targeted therapy and combining it with the potent cytotoxic effect of a small molecule. ADCs have complex molecular structures, including the key components of a highly-selective monoclonal antibody (mAb) directed against a cancer antigen (target), a potent cytotoxic small molecule referred to as payload, and a linker connecting these two components. The linker is designed to maintain stability of the ADC in circulation and only release the payload once the ADC is internalized into cancerous target cells. Thus in theory, ADC should be more specific and better tolerated than the cytotoxic small molecule drugs. While the concept of ADCs is theoretically simple, designing a successful ADC with an improved therapeutic index has been quite challenging. At the moment there are only a limited number of ADCs approved for treatment of solid and hematologic malignancies, although many more are currently under development in various stages of clinical trials.

For most ADCs currently in clinical development, dose limiting toxicities (DLTs) are often off-target which is not directly linked to the anti-tumor effect. Since the small molecule payload is a non-specific cytotoxic agent, once it is cleaved (intentionally or not) from the mAb, it can cause the same typical chemotherapy toxicities including hematologic and non-hematologic adverse effects such as hepatotoxicity. Thus an ideal ADC should not release the payload prematurely in systemic circulation before hitting the target which could result in serious toxicities. Thus stability and payload-driven toxicity is clearly a key factor when designing an ADC, and this insight should be considered carefully together. With increasing knowledge of linker technology, cancer type, molecular target including expression and distribution in the body, and profiles of probable concomitant anticancer or supportive therapies, it is possible to select the optimal ADC dose and administration regimen for the intended patient population.

Although treatment with the ADC in cancer chemotherapy is not yet widespread, we envisage use of these specialty biologic agents will grow steadily in the future particularly for the advanced form of cancers. It is imperative we need to report and document their adverse effects and toxicities which will provide valuable knowledge to help design the next generation of ADCs with much improved safety and efficacy profiles for targeted chemotherapy.

Keywords: Antibody Drug Conjugates, dose limiting toxicities, Biological agents, cardiometabolic diseases.

Schedule:

- ◇ Manuscript submission deadline: July 30, 2020
- ◇ Peer Review Due: August 30, 2020
- ◇ Revision Due: Sept 30, 2020
- ◇ Announcement of acceptance by the Guest Editors: Depending on the date of the revision (if any)
- ◇ Final manuscripts due: Depending on the date of the revision (if any)
- ◇ Final date of Submission of Special issue: December 20, 2020.

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