Claudin 18.2 targeting antibody-drug conjugate (ADC) prepared by AbClick linker

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The antibody-drug conjugate (ADC) is composed of a tumor-specific antibody, a cytotoxic payload, and a linker that facilitates the connection between the antibody and payload. Conjugation of drugs to antibodies has presented a significant challenge due to the complex nature of antibodies as large biomacromolecules. The method of drug conjugation onto the antibody greatly influences the pharmacokinetic properties of the ADC. Traditional protein conjugation often relies on the utilization of Cys and Lys residues. However, the abundance of these residues within an antibody molecule results in a complex mixture through conventional conjugation. To address this challenge, we have successfully developed a novel site-selective antibody-cross linker called AbClick®, which selectively acylates the ε-NH_2 group of K248 on off-the-shelf antibodies. This selective conjugation is achieved by utilizing an IgG Fc-binding peptide (FcBP) fused with active esters through an appropriate spacer. By employing this innovative linker, we have successfully prepared an ADC targeting claudin 18.2, incorporating the potent microtubule inhibitor MMAE with a drug-to-antibody ratio (DAR) of 2. Our in vitro studies have demonstrated that the prepared ADC exhibits comparable or superior anticancer activity compared to the unmodified drug, MMAE. Moreover, in an SNU601 xenograft mice model, it has demonstrated remarkable in vivo anticancer efficacy, with a minimum effective dose (MED) range of 1.0 to 1.5 mg/kg.

In this conference, we will present a comprehensive account of the AbClick® technology, including a thorough evaluation of the biological activity of our ADC targeting claudin 18.2.

toward artificial photosynthesis or anti-cancer drugs.