ABZENA

Linking Antibody to Drug with ThioBridge™ Conjugation Technology for Better ADCs

ThioBridge™

Antibody-drug conjugates (ADCs) are a powerful approach to targeted cancer treatment, combining monoclonal antibodies (mAbs) with potent drugs. However, first-generation conjugation technologies used in ADC development have limitations such as inconsistent drug-to-antibody ratios (DAR) and unstable linkers. Abzena's ThioBridge™ conjugation technology offers a solution by providing a more uniform DAR profile, stable linker attachment, and improved pharmacokinetic properties.

ThioBridge™ Delivers Next-Gen Results

ThioBridge™ provides several benefits for ADC development, offering a controlled, uniform, and specific attachment of linker payloads to support the stability and optimal function of the antibody. We can demonstrate ThioBridge™ versus maleimide stability ex vivo using rat serum (Figure 1).

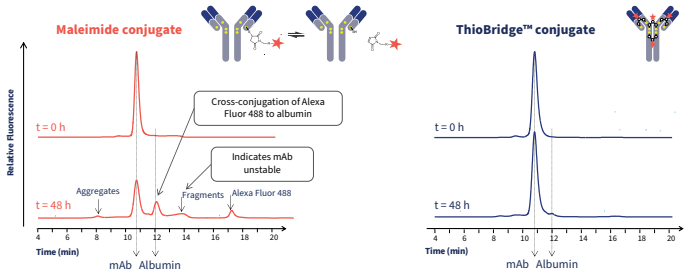

Figure 1. Size-exclusion chromatography (SEC) analysis of the stability of ThioBridge™ vs maleimide conjugation.

Analytical size-exclusion chromatography (SEC) analysis revealed that the ThioBridge™ conjugate maintained its stability, with no loss of AlexaFluor488, while the maleimide conjugate showed payload loss.

The ThioBridge™ conjugation process is straightforward and tolerant of different reaction conditions. After reducing the interchain disulfides, the ThioBridge™ reagent is added to the antibody, followed by purification. The resulting ADC can be analyzed to determine the DAR.

Studies have shown the superiority of ThioBridge™ ADCs in terms of stability, potency, and efficacy. ThioBridge™ conjugation maintains stability in serum, exhibits higher potency in mouse tumor models (Figure 2), and demonstrates improved stability in non-human primates. Different ThioBridge™ linker-payload combinations have shown enhanced tumor volume reduction compared to other conjugation technologies.

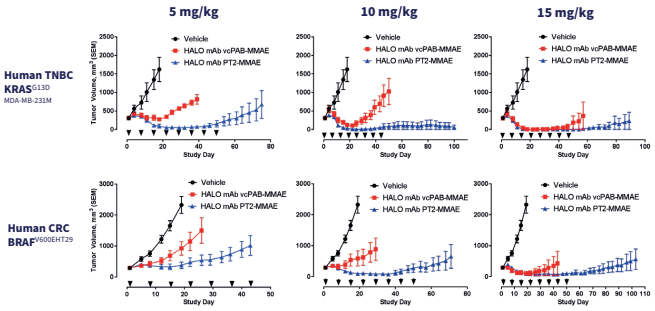

Figure 2. Comparing the potency of the ADC HTI-1511, generated via ThioBridge™ conjugation with a maleimide ADC (HALO mAb vc-PAB- MMAE) in a mouse model.*

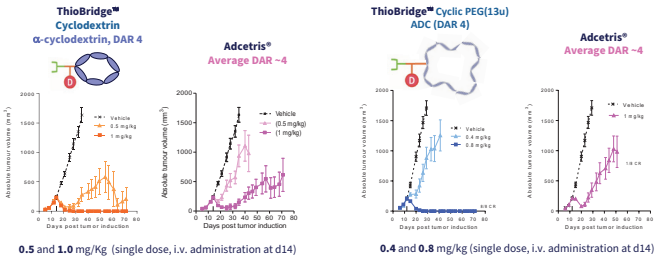

Figure 3. Comparing the potency of ThioBridge™ alpha-cyclodextrin ADC (DAR 4) and ThioBridge™ Cyclic PEG(13u) ADC (DAR 4) in a Karpas-299 mouse xenograft model.

ThioBridge™ can work with different linker architectures such as alpha-cyclodextrin and cyclic PEG ADCs to increase potency and result in superior tumor reduction compared to existing ADCs (Figure 3). ThioBridge™ ADCs with different payload release mechanisms have also shown superior efficacy.

Conclusions

Abzena's ThioBridge™ conjugation technology offers significant advantages for ADC development. It provides a uniform DAR profile, stable linker attachment, and optimized pharmacokinetic properties. ThioBridge™ enables precise control over drug loading and attachment sites, supporting efficient production and profiling of ADCs.

***Huang,L. et al. (2016). AACR Annual Meeting, Poster #1472. Data presented at PEGS 2016;** Engineering a Tumor-Specific, Next-Generation Anti-EGFR ADC Development Candidate, Christopher D. Thanos, Ph.D. Sr. Director Biotherapeutics Discovery