BL-B01D1, a novel EGFRxHER3-targeting ADC, demonstrates robust anti-tumor efficacy in preclinical evaluation

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Abstract
EGFR and HER3, members of the human epidermal growth factor receptor (ErbB) family, are targeted in cancer therapy due to their over-expression and pathway dependence in common epithelial carcinoma tumors. To develop a promising therapeutic anti-tumor agent, we generated BL-B01D1, an EGFRxHER3-targeting ADC, which is directed to EGFR and/or HER3 positive cells and is expected to be superior to anti-EGFR and anti-HER ADCs. It is comprised of a bispecific antibody against EGFRxHER3 (SI-B001), a cediranib B cleavable linker, and a novel topoisomerase I inhibitor agent (Ed-04), which is a derivative of the alkaid camptothecin, driving cell cycle arrest at the S phase and subsequent apoptosis. BL-B01D1 achieves a high drug-to-antibody ratio (DAR=8) with a high stable linker.

BL-B01D1 Bi-specific ADC

qEGFR
Human EGFR
Affinity: High

qHER3
Human HER3
Affinity: Low

DAR = 8
Cat B cleavable linker
Ed-04 (TOPI inhibitor)
w/t Fc IgG1

BL-B01D1 Cell Binding is determined by EGFR and not HER3

A Cetuximab Sensitive Cell Lines

B Cetuximab Insensitive Cell Lines

Summary
- BL-B01D1, an EGFRxHER3-targeting ADC, which can bind to EGFR and/or HER3 positive cells
- BL-B01D1 is comprised of a bispecific antibody against EGFRxHER3 (SI-B001), a cediranib B cleavable linker, and a novel topoisomerase I inhibitor agent (Ed-04) with a drug-to-antibody-ratio of 8 (DAR=8)
- Ed-04 is a derivative of the alkaid camptothecin, driving cell cycle arrest at the S phase and subsequent apoptosis showing superior bystander activity compared to Daichi payload (in house)
- BL-B01D1 exhibited stronger tumor inhibition capacity than the parental anti-EGFR ADC and the anti-HER ADC in colorectal cancer SW620 and pancreatic cancer BxPc3 xenograft models
- As an EGFRxHER3-targeting ADC, BL-B01D1 might be a promising, novel agent, with activity toward a broad range of cancers

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References