

BGB-B2033, a novel 4-1BB/GPC3 bispecific antibody, exhibits potent in vitro and vivo antitumor activity in preclinical model

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Abstract

4-1BB (CD137) is a key costimulatory immunoreceptor expressed on activated T-cells and natural killer cells, making it a promising therapeutic target in cancer. Glypican-3 (GPC3), a membrane-bound heparan sulfate proteoglycan, is overexpressed in approximately 70% to 80% of hepatocellular carcinomas, and extensively expressed in a variety of other solid tumors. GPC3 is recognized as an attractive drug target in precision cancer therapy as it is highly expressed in multiple tumors while minimally expressed in adult normal tissues. BGB-B2033 is a novel immunoglobulin G (IgG)-based bispecific antibody targeting 4-1BB and GPC3 and is under clinical development for the treatment of advanced or metastatic solid tumors in humans.

BGB-B2033 binds to its target proteins with high specificity and affinity. Potent and GPC3-dependent functional activities were demonstrated using peripheral blood mononuclear cell (PBMC)-based immune cell activation and cytotoxicity assays. In humanized 4-1BB knock-in mice bearing human GPC3-expressing tumors, BGB-B2033 exhibited potent, dose-associated single-agent efficacy in Hepa1-6/hGPC3 orthotopic tumor model, as well as synergistic antitumor activity in combination with antiPD-1 antibody.

In conclusion, BGB-B2033 is a potent therapeutic agent with strong anti-tumor activity in both in vitro and in vivo studies. The phase 1 study of BGB-B2033, alone or in combination with Tislelizumab is ongoing (NCT06427941).