T Cell Engaging BiTE Antibodies for Cancer Therapy

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Bispecific antibodies can transiently link tumor cells with otherwise inactive polyclonal T cells for induction of a surface target antigen-dependent redirected lysis of tumor cells. One example is blinatumomab, a CD19/-CD3-bispecific BiTE for the treatment of human B cell malignancies. Blinatumomab and other BiTE antibodies were shown to activate T cells in a highly conditional manner that is strictly dependent on the presence of target cells. Blinatumomab is in phase 1 dose escalation study for the treatment of patients with therapy-refractory non-Hodgkin's lymphoma (NHL), and concluded a phase 2 study in patients with B-precursor acute lymphocytic leukemia (ALL). Centrally confirmed complete and partial responses have been observed with blinatumomab in 12 out of 12 NHL evaluable patients treated at 0.06 mg/m^2 per day, and a complete molecular response in 16 out of 20 evaluable ALL patients treated at 0.015 mg/m^2 per day.

MT110 is a novel BiTE antibody recognizing the pan-carcinoma antigen EpCAM (CD326), which is expressed on a large variety of human adenocarcinoma, and on cancer-initiating cells derived thereof. MT110 is a in phase 1 study with gastrointestinal, lung, breast, prostate, ovarian, and esophageal cancer patients. A murine EpCAM/CD3-specific version of the BiTE antibody, called muS110, has shown a robust therapeutic window in mice with no damage to EpCAM-expressing normal epithelia. Additional BiTE antibodies specific for EGFR, CD33, EphA2, CEA, Her-2/neu, FAP-alpha, IGF-1R and c-Met have been generated and shown to have a high potency of redirected target cell lysis. Conversion of anti-EGFR antibodies cetuximab and panitumumab into BiTE antibodies generated molecules engaging at high potency T cells for lysis of colorectal cancer cells expressing KRAS and BRAF mutations, and provided evidence for a therapeutic window in primate studies.

Four BiTE programs have been partnered with large biopharma companies including MedImmune, Bayer Schering Pharma, Sanofi-Aventis and Boehringer Ingelheim.

Selected publications:

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For more references, abstracts and poster presentations, please visit www.micromet-inc.com