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BiTE Antibodies for Cancer Therapy

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Bispecific antibodies can transiently link tumor cells with otherwise inactive cytotoxic T cells in patients for induction of potent redirected lysis of tumor cells. One example is blinatumomab (MT103), a CD19/-CD3-bispecific BiTE for the treatment of human B cell-derived 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 has commenced a pivotal study for the treatment of adult patients with therapy-refractory acute lymphocytic leukemia (ALL). A phase 2 study in ALL patients has shown an 80% complete molecular response rate at a dose level of 15 micrograms/squaremeter per day. Blinatumomab has also shown high response rates in non-Hodgkin's lymphoma (NHL) patients with follicular and mantle cell lymphoma, and first signs of efficacy in patients with diffuse large B cell lymphoma. Centrally confirmed complete and partial responses according to Cheson criteria were seen in NHL patients treated at a dose of 60 micrograms/squaremeter/day. The presentation will update on the clinical development of blinatumomab in leukemia and lymphoma.

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 or stem 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. A series of new BiTE antibodies for solid tumor treatment are being developed in collaboration with large biopharma partners, including MedImmune/AstraZeneca, Bayer Schering Pharma, Boehringer Ingelheim and Sanfi-aventis.