Immunotherapy with BiTE® Antibodies: Lessons Learned from Blinatumomab

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T cell-engaging bispecific antibodies can transiently link with otherwise inactive cytotoxic T cells in patients' tumor cells and induce redirected potent lysis of tumor cells. One example for this is blinatumomab (AMG 103), a CD19/-CD3-bispecific BiTE® antibody used to treat acute lymphocytic leukemia (ALL) and non-Hodgkin's lymphoma (NHL), which is in an advanced stage of clinical development. Two other BiTE® antibodies, AMG 211/MEDI-565 (CEA/CD3-specific) and AMG 110 (EpCAM/CD3-specific), are in the early stages of clinical development to treat solid tumors. Blinatumomab and all other BiTE® antibodies have been shown to activate T cells in a highly conditional manner that was strictly dependent on the presence of target cells, effect the serial lysis of target cells by T cells, induce T cell proliferation, and act at sub-nanomolar concentrations. The mode of action of BiTE® will be described in detail and compared to other treatment modalities. Phase 2 studies investigating monotherapy using blinatumomab in patients with minimal residual (n = 20) or relapsed ALL (n = 36) have shown complete response rates in the range of 50–80% at a dose level of 15 micrograms/square meter/day. In a Phase 1 study (n = 76), the BiTE® antibody blinatumomab has also shown high response rates in relapsed or refractory NHL patients with follicular mantle cell lymphoma or diffuse large B cell lymphoma at a dose level of 60 micrograms/square meter/day (n = 28). An overview of the clinical program and insights into the immunopharmacology, safety profile, and clinical activity of blinatumomab will be provided.

Conflict of Interest: Prof. Zugmaier is employed by AMGEN Research (Munich) GmbH

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