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.

References
1 Klöner M et al. Blood 2012; 119: 6226
3 Topp M et al. J Clin Oncol 2011; 29: 2493
4 Nagarsen D, Baeuerle PA. Exp Cell Res 2011; 317: 1255
5 Lutterbuese R et al. Proc Natl Acad Sci USA 2010; 107: 12605 – 12610
9 Brischwein K et al. J Immunother 2007; 30: 798 – 807
12 Dreier T et al. Intl J Cancer 2002; 100: 690 – 697

Bibliography
DOI http://dx.doi.org/10.1055/s-0032-1324899
Arzneimittelforschung 2012; 62, Suppl. 1: S3–S3
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