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Tolerability and efficacy of the trifunctional antibody removab® (anti-EpCAM x anti-CD3) in patients with malignant ascites due to ovarian cancer: Results of a phase I/II study

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Introduction

Malignant ascites in patients with gynecological malignancies is associated with poor prognosis and poor quality of life. The bispecific trifunctional antibody removab® (anti-EpCAM x anti-CD3) belongs to a new class of intact antibodies that has been developed for targeted therapy of epithelial tumors. The two binding sites of removab® are directed against epithelial tumor cells (EpCAM+) and T-cells (CD3+) thus recruiting T-cells in the direct environment of tumor cells. Simultaneously, mediated by the intact Fc-fragment removab® binds to FcγI/IIIR+ accessory cells (e.g. macrophages, natural killer cells, dendritic cells) that are mandatory for the induction of a tumor-specific immune response.

Patients and methods

In an open-label multicenter phase I/II-dose escalating study, a total of 23 patients with ovarian cancer and symptomatic ascites at FIGO stage III-IV were treated intraperitoneally with removab®. The patients had received a median of 3 (1–8) previous therapies. Their mean age was 62 (42–80) years. The treatment consisted of up to 5 intraperitoneal applications of the antibody within 13 days using increasing dosages.

Results

The intraperitoneal treatment with removab® was able to stop the production of ascites in 22 of 23 patients. These patients were ascites-free at the end of the study (day 37). Immunocytochemical quantification of tumor cells in the ascites fluid showed a dramatic reduction of EpCAM+ cells (>log 5). In addition, clinically significant improvement of the quality of life was observed. The majority of adverse events was mild to moderate. The most common side effects observed in the study were fever (82.6%), nausea (60.9%), vomiting (56.5%), and abdominal pain (30.4%). The MDT (maximal tolerated dose) was reached at the increasing dosages of 10 μg–20 μg–50 μg–200 μg–200 μg.

Conclusion

In conclusion, intraperitoneal treatment with removab® was safe, well tolerated and showed encouraging efficacy in patients with malignant ascites due to ovarian cancer. Thus, the new concept of the anti-EpCAM x anti-CD3 anti-

body might offer a promising treatment option for patients with epithelial tumors.