

Clinical Studies With Trifunctional Antibodies

August 2007

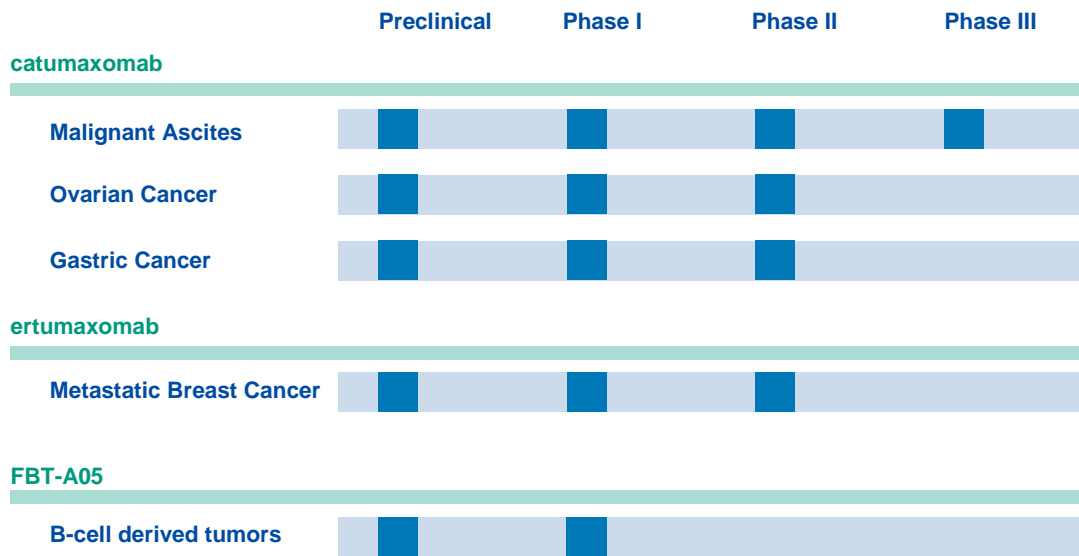


Clinical studies with trifunctional antibodies I

Trifunctional antibodies represent a new concept for targeted anticancer therapy. This new antibody class has the capability to redirect T cells and accessory cells (e.g. macrophages, dendritic cells [DCs] and natural killer [NK] cells) to the tumor site. According to preclinical data, trifunctional antibodies seem to activate immune cells, which can trigger a complex anti-tumor immune response.

Currently, three trifunctional antibodies (catumaxomab, ertumaxomab, FBT-A05) with distinct tumor antigen specificities are in clinical stages of development. These studies are being conducted by Fresenius Biotech in collaboration with its partner TRION Pharma.

Development Status of Trifunctional Antibodies



Status 08/2007

Catumaxomab: Targeting epithelial tumors via EpCAM

Catumaxomab is a trifunctional antibody with binding specificities for human EpCAM (Epithelial Cell Adhesion Molecule), which is overexpressed on carcinoma cells, and for human CD3 antigen, expressed on all T lymphocytes. Via its intact Fc region, catumaxomab also has the potential to recruit accessory cells that are essential for a complex immune response.

The anti-tumour potential of catumaxomab is presently being investigated in different tumour indications, such as ovarian cancer, malignant ascites caused by various primary tumours, and gastric cancer.

Ertumaxomab: Targeting HER2 positive tumors

Ertumaxomab is a trifunctional antibody with specificities for the human epidermal growth factor receptor 2 (HER2) and the human CD3 antigen. HER2 is overexpressed in a variety of cancers such as breast and lung cancer. Similar to catumaxomab, ertumaxomab also has the potential to recruit accessory cells.

Ertumaxomab is currently undergoing clinical testing for safety and efficacy in patients with metastatic breast cancer.

FBT-A05: Targeting B-cell derived CD20+ tumors

FBT-A05 is a trifunctional antibody with specificities for the human CD20 protein and the human CD3 antigen. CD20 is specifically expressed on B-cells and is used as therapeutic target for B-cell derived tumors such as chronic lymphocytic leukemia (CLL).

Currently, FBT-A05 is being investigated in a phase I/II study in CLL patients.

Malignant Ascites

IP-REM-AC-02-US

- Title:** A single-arm, open-label, phase II study to assess the safety and efficacy of the trifunctional antibody catumaxomab (anti-EpCAM x anti-CD3) administered intraperitoneally in ovarian cancer patients with recurrent symptomatic malignant ascites
- Patients:** Patients with recurrent and symptomatic malignant ascites caused by ovarian, peritoneal, or fallopian tube cancer requiring therapeutic puncture.
- Antibody:** catumaxomab (anti-EpCAM x anti-CD3)
- Study sites:** USA
- Contact:** Fresenius Biotech North America
Tel: +1-866-491-8137
Email: clinicaltrials@fresenius-biotech.com

IP-REM-AC-01

- Title:** Two-arm, randomized (2:1), open-label phase II/III study in EpCAM positive cancer patients with symptomatic malignant ascites using paracentesis plus the tri-functional antibody catumaxomab (anti-EpCAM x anti-CD3) versus paracentesis alone
- Patients:** Patients with recurrent and symptomatic malignant ascites caused by tumors of epithelial origin requiring therapeutic puncture.
- Antibody:** catumaxomab (anti-EpCAM x anti-CD3)
- Study sites:** Europe
- Contact:** Fresenius Biotech GmbH
Tel: +49-(0)89-306 593-17
Email: clinicalstudies@fresenius-biotech.com
- Status:** **No longer recruiting**

Gastric Cancer

IP-REM-GC-02

- Title:** Multicenter, open-label and randomized phase II study to evaluate safety and efficacy of the trifunctional bispecific antibody catumaxomab (anti-EpCAM x anti-CD3) in patients after curative resection of a confirmed gastric adenocarcinoma compared with surgery alone
- Patients:** Patients with advanced resectable gastric adenocarcinoma with serosal infiltration (T3/T4, N+/-, M0 or T2b, N+/-, M0)
- Antibody:** catumaxomab (anti-EpCAM x anti-CD3)
- Study sites:** Europe
- Contact:** Fresenius Biotech GmbH
Tel: +49-(0)89-306 593-17
Email: clinicalstudies@fresenius-biotech.com
- Status:** **No longer recruiting**

IP-CAT-GC-03

- Title:** Multicenter, open-label phase II study to evaluate the safety and efficacy of the trifunctional antibody catumaxomab (anti-EpCAM x anti-CD3) in patients with gastric adenocarcinoma after neoadjuvant chemotherapy and curative resection
- Patients:** Patients with advanced resectable gastric adenocarcinoma with serosal infiltration (T3/T4, N+/-, M0 or T2, N+, M0)
- Antibody:** catumaxomab (anti-EpCAM x anti-CD3)
- Study sites:** Europe
- Contact:** Fresenius Biotech GmbH
Tel: +49-(0)89-306 593-17
Email: clinicalstudies@fresenius-biotech.com

Ovarian Cancer

IP-CAT-OC-01

- Title:** An open-label, single-arm, phase II safety and tolerability study of catumaxomab (anti-EpCAM x anti-CD3) in women with advanced epithelial ovarian cancer after a complete response to chemotherapy
- Patients:** Patients with ovarian, fallopian-tube, or primary peritoneal cancer, FIGO stage IIb – IV who experienced a complete response to chemotherapy
- Antibody:** catumaxomab (anti-EpCAM x anti-CD3)
- Study sites:** USA
- Contact:** Fresenius Biotech North America
Tel: +1-866-491-8137
Email: clinicaltrials@fresenius-biotech.com

IP-CAT-OC-02

- Title:** Multicenter, single-arm, phase II study of the tri-functional antibody catumaxomab (anti-EpCAM x anti-CD3) administered intra- and postoperatively in patients with epithelial ovarian cancer
- Patients:** Patients with primary ovarian cancer, FIGO stage Ia– IV
- Antibody:** catumaxomab (anti-EpCAM x anti-CD3)
- Study sites:** Germany
- Contact:** Fresenius Biotech GmbH
Tel: +49-(0)89-306 593-17
Email: clinicalstudies@fresenius-biotech.com

Metastatic Breast Cancer

FBT-IVREXBC 02

- Title:** Phase II study of the trifunctional antibody anti-HER2/neu x anti-CD3 ertumaxomab for hormone therapy refractory patients with Her-2/neu 1+ or 2+ expressing advanced or metastatic breast cancer
- Patients:** Her2/neu 1+ or 2+ positive metastatic or advanced breast cancer patients not qualifying for treatment with trastuzumab and failing anti-hormonal therapies
- Antibody:** ertumaxomab (anti-Her2/neu x anti-CD3)
- Study sites:** Europe
- Contact:** Fresenius Biotech GmbH
Tel: +49-(0)89-306 593-17
Email: clinicalstudies@fresenius-biotech.com

IV-ERT-BC-03

- Title:** Phase II study for repeated dosing of the trifunctional bispecific anti-HER-2/neu x anti-CD3 antibody ertumaxomab in patients with HER-2/neu 1+ or 2+/FISH negative expressing advanced or metastatic breast cancer (stage IIIb/IV) progressing after endocrine treatment
- Patients:** Her2/neu 1+ or 2+ positive metastatic or advanced breast cancer patients not qualifying for treatment with trastuzumab and failing anti-hormonal therapies
- Antibody:** ertumaxomab (anti-Her2/neu x anti-CD3)
- Study sites:** Europe
- Contact:** Fresenius Biotech GmbH
Tel: +49-(0)89-306 593-17
Email: clinicalstudies@fresenius-biotech.com

IV-ERT-BC-04

- Title:** Phase II study of the trifunctional bispecific anti-HER-2/neu x anti-CD3 antibody ertumaxomab in patients with HER-2/neu overexpressing (3+ or 2+/FISH+) metastatic breast cancer progressing after trastuzumab treatment
- Patients:** Patients with metastatic or advanced breast cancer overexpressing Her2/neu (3+ or 2+/FISH+) and progressed after trastuzumab therapy
- Antibody:** ertumaxomab (anti-Her2/neu x anti-CD3)
- Study sites:** USA
- Contact:** Fresenius Biotech GmbH
Tel: +49-(0)89-306 593-17
Email: clinicalstudies@fresenius-biotech.com

Chronic Lymphocytic Leukemia (CLL)

IV-A05-LL-01

- Title:** Phase I/II dose escalation study of the trifunctional bispecific anti-CD20 x anti-CD3 antibody FBT-A05 in patients with recurrent or refractory chronic lymphocytic leukemia
- Patients:** B-CLL patients with confirmed positive CD20 status and recurrent or refractory disease following at least one prior treatment and need for further therapy
- Antibody:** FBT-A05 (anti-CD20 x anti-CD3)
- Study sites:** Germany
- Contact:** Fresenius Biotech GmbH
Tel: +49-(0)89-306 593-17
Email: clinicalstudies@fresenius-biotech.com

The clinical trials are conducted in collaboration with TRION Pharma.

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