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Press Release

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Phase II study shows trifunctional antibody Removab® (catumaxomab) well tolerated in treatment of gastric cancer

A Phase II study with the trifunctional antibody catumaxomab in the treatment of patients with gastric cancer showed the antibody was well tolerated. The primary endpoint of the study – safety and tolerability of catumaxomab administration after tumor resection – was achieved. With this study, controlled results for perioperative administration of catumaxomab are presented for the first time.

The randomized, open-label study included 55 patients with resectable gastric cancer. Tumors of all patients were removed by surgery. 28 patients were included in the catumaxomab arm and treated intraoperatively with 10µg of catumaxomab. Seven days after surgery, these patients were given 10, 20, 50 and 150µg doses of catumaxomab by intraperitoneal administration in intervals of three days. The 27 patients in the control group received no anti-tumor therapy except tumor resection within the study period.

The pattern of complications from surgery was comparable in both groups, with catumaxomab having no impact. Most of the side effects in the catumaxomab group were mild to moderate and based on the mode of action of the antibody. Side effects were mostly limited to the treatment period and were, if needed, treated symptomatically.

Secondary study endpoints were efficacy parameters, e.g. overall survival. As expected, the study showed no statistically or clinically relevant differences between the catumaxomab arm and the control group 12 months after treatment. Due to this short follow-up period and the low number of patients it was not possible to reach specific conclusions regarding the efficacy of the therapy. Other studies with similar patient populations showed a difference in overall survival just after about two years.

After finalization of the ongoing second study in patients with gastric cancer, including neoadjuvant chemotherapy prior to surgery, the safety and tolerability data of catumaxomab administration during surgery will be evaluated. Additional analyses on efficacy of the therapy are also planned.

BACKGROUND INFORMATION:

Gastric Cancer
Gastric cancer is the fifth most common type of cancer in men and the seventh most common type of cancer in women. In 2004, about 11,000 men and about 7,800 women had gastric cancer in Germany. In men the incidence peak is at the age of approx. 70, in women it is above 75. (Source: Robert Koch Institute)
The prognosis of patients depends heavily on the stage of the tumor. While five-year survival rates for patients in stage I are up to 80 %, they decline in advanced stages, with a survival rate of about 20 % for patients in stage IIIb and below 5 % for stage IV.
The only curative treatment option is the partial or complete resection of the stomach (gastrectomy) and the regional lymph nodes. If the general condition of the patient is good, the surgery can be preceded by a neoadjuvant chemotherapy to reduce the size of the tumor, which led to a significant improvement of five-year survival to 36 % in a first Phase III study (MAGIC). If tumor tissue remains after the surgery, an additive chemotherapy is administered which might enable a second successful resection. In case of inoperable tumors or distant metastases, a palliative chemotherapy can be administered to alleviate the symptoms and prolong life.

Second Phase II Gastric Cancer Study GC03
In the second study IP-CAT-GC-03, a single-arm trial, gastrectomy follows chemotherapy (neoadjuvant). The primary endpoint of the study is safety and tolerability of the trifunctional antibody catumaxomab. The secondary endpoints are efficacy parameters such as overall survival and disease-free survival.

Trifunctional Antibodies
Trifunctional antibodies are proteins that activate different cell types of the immune system simultaneously and target tumor cells specifically. Trifunctional antibodies therefore are very effective in destroying cancer cells and show a therapeutic effect even at very low doses. They are being developed by TRION Pharma GmbH.

Mode of action of trifunctional antibody catumaxomab
The therapeutic objective of trifunctional antibodies is to generate a stronger immune reaction against tumor cells. Catumaxomab has two different antigen binding sites: While one arm of the antibody recognizes and binds to T-cells, the other arm binds EpCAM (epithelial cell adhesion molecule) that is overexpressed in many types of epithelial cancers. Immune effector cells with Fc receptors (macrophages, monocytes, dendritic cells and natural killer cells) can also bind the Fc region of intact trifunctional antibodies. This simultaneous binding subsequently results in the costimulation and activation of T-cells and accessory cells, enabling the generation of a strong immune response against tumor cells. Preclinical data also suggest a potential long-lasting effect to prevent cancer recurrence. Apart from removab two other trifunctional antibodies targeting other cancer antigens are currently undergoing clinical development.

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