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Efficacy of intraperitoneal immunotherapy with the trifunctional antibody catumaxomab in addition to systemic chemotherapy in patients with peritoneal carcinomatosis from colorectal or gastric cancer

Submission date	Recruitment status	[ ] Prospectively registered
04/09/2011	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
28/10/2011	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
20/04/2017	Cancer	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims

Peritoneal carcinomatosis (PC) is a rare type of cancer that occurs in the peritoneum, the thin layer of tissue that covers abdominal organs and surrounds the abdominal cavity. PC that has spread from gastrointestinal tumours is associated with an average survival of only a few months. There is currently no standard treatment to prevent or eradicate. Various treatments have been tested including peritonectomy (surgery removing most of the peritoneum), or applying chemotherapy directly into the abdominal cavity (intraperitoneal), whether heated (hyperthermic intraperitoneal chemotherapy) or not. No effective treatment is available for patients with PC who are not eligible for surgery to remove the tumour. Chemotherapy has been used with only a small effect on preventing disease progression and symptoms. The aim of this study is t find out whether a two cycle intraperitoneal catumaxomab treatment in addition to standard intravenous chemotherapy (into a vein) is able to increase symptom and progression free survival.

Who can participate?

Patients aged 18 or over with peritoneal carcinomatosis from colorectal or gastric cancer who are not eligible for surgery

What does the study involve?

All participants are treated with intraperitoneal catumaxomab on day 0, 3, 7 and 10 after the start of treatment, followed by intravenous chemotherapy on days 30 to 90. This is followed by a second cycle of intraperitoneal catumaxomab between days 91 and 120, followed by intravenous chemotherapy between days 121 and 180. The study ends at day 270. There is an additional optional follow-up at 15 months.

What are the possible benefits and risks of participating?
The treatment may lead to survival and a reduction or delay of symptoms like ascites and bowel obstruction. Risks of participating include side effects such as fever, nausea, vomiting and abdominal pain.

Where is the study run from?
University of Witten/Herdecke (Germany)

When is the study starting and how long is it expected to run for?
October 2011 to September 2013

Who is funding the study?
Fresenius Biotech GmbH (Germany)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
10-022810-26

Study information

Scientific Title
Multicentre, open-label phase II study to evaluate the efficacy of a two cycle immunotherapy with the trifunctional bispecific antibody catumaxomab (anti EpCAM x anti-CD3) in addition to systemic chemotherapy in patients with peritoneal carcinomatosis from gastric or colorectal adenocarcinoma

Study objectives
The main hypothesis is that a two cycle intraperitoneal (i.p.) catumaxomab treatment in addition to standard intravenous (i.v.) chemotherapy is able to increase symptom and progression free survival in patients with peritoneal carcinomatosis of gastric or colorectal origin not eligible for cytoreductive surgery or with no chance to obtain macroscopic complete cytoreduction.
According to the primary endpoints this is defined as:
1. Decrease of the incidence of clinically significant malignant ascites
2. Decrease of the Incidence of intestinal obstruction with the need of surgical intervention or parenteral nutrition
3. Decrease of the incidence of Eastern Cooperative Oncology Group (ECOG) deterioration
4. Decrease of the incidence of death
Every parameter will be analysed separately in comparison to historical controls.

In addition a comprehensive immunological monitoring programme is an integrated part of this study. This programme especially focuses on investigations of the induction of anti tumour responses caused by the i.p. immunotherapy with catumaxomab.

Safety parameters like the need to discontinue catumaxomab infusion as well as frequency, relationship and intensity of clinically relevant grade III and IV adverse events will be documented and analysed.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethics Committee of Witten/Herdecke University [Ethikkommission der Universität Wittten /Herdecke, D-59448 Witten], 16/03/2011, ref: F-82/10
2. German Federal Institute for Vaccines and Biomedicines, Paul-Ehrlich-Institut, 24/02/2011, ref: 1220/01

Primary study design
Interventional

Study design
Phase II interventional multicentre open-label non-randomized single arm study in comparison to historical controls

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Peritoneal carcinomatosis from colorectal and gastric cancer (adenocarcinoma)

Interventions
Investigational medicinal product: trifunctional antibody catumaxomab (anti-EpCAM x anti-CD3)
Application of medicinal product: intraperitoneal (i.p.)

Intervention: Laparoscopy or laparotomy and exact staging of peritoneal carcinomatosis will be mandatory. Implantation of an i.p.-port or a catheter-device will be performed. Patients with laparoscopy can be treated with the first dose of catumaxomab after 3 days. Patients with

tumor debulking surgery or major resection (anterior rectum resection, gastrectomy) can also be included. In this case, treatment starts at least 10 days after surgery. Further criteria for treatment include complete enteral nutrition and no postoperative problems (i.e. anastomotic leakage, abscess formation etc.). The 1st cycle of catumaxomab is completed by 10-20-50-200 µg on day 0-3-7-10 after start of treatment. Catumaxomab treatment is followed by intravenous chemotherapy within day 30 to 90. A regimen of oxaliplatin, leucovorin, and 5-fluorouracil (FOLFOX4, FOLFOX6, or FOLFIRI) for colorectal and fluorouracil, leucovorin, oxaliplatin (FLO) or fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) for gastric cancer is recommended, but any other chemotherapy according to previous chemotherapy and decision of the medical oncologist is allowed. This is followed by a second cycle of catumaxomab i.p. immunotherapy between day 91 and 120; followed by another i.v.-chemotherapy between day 121 and day 180. Multimodal chemotherapy including biological modifiers (i.e. Cetuximab, Bevacizumab, Trastuzumab or others) is not permitted.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Catumaxomab

Primary outcome(s)
1. Decrease of the incidence of clinically significant malignant ascites
2. Decrease of the Incidence of intestinal obstruction with the need of surgical intervention or parenteral nutrition
3. Decrease of the incidence of ECOG deterioration
4. Decrease of the incidence of death
5. Every parameter will be analysed separately in comparison to historical controls

Key secondary outcome(s)
1. Safety parameters:
1.1. The need to discontinue catumaxomab infusion
1.2. Frequency, relationship and intensity of clinically relevant grade III and IV adverse events
2. Immunological monitoring:
2.1. Induction of anti-tumour response
2.2. Quality and quantity of epithelial cell adhesion molecule (EpCAM)-expression
2.3. Disseminated tumour cells and tumour stem cells within the peripheral blood during therapy
2.4. Anti-EpCAM and anti-HER2/neu humoral immune response
2.5. vascular endothelial growth factor (VEGF)-level during therapy
2.6. Induction of human anti-mouse antibodies (HAMA)
2.7. Systemic levels of catumaxomab after i.p. therapy

Completion date
30/09/2013

Eligibility

Key inclusion criteria

1. Male or female patient aged 18 years or older
2. Signed and dated informed consent
3. Patient has peritoneal carcinomatosis of colorectal or gastric adeno-carcinoma (histologically confirmed)
4. Eastern Cooperative Oncology Group (ECOG) status 1 or 2 (Karnofsky index >= 70)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Symptomatic ascites (estimated accululation of more than 1500 ml by sonography and computer tomography and puncture of more than 1500 ml)
2. Ileus or abdominal obstruction with the need of surgical intervention at inclusion or parenteral feeding (> 30% of daily calorie intake)
3. Previous use of non-humanised monoclonal mouse or rat antibodies
4. Known or suspected hypersensitivity or allergy to catumaxomab or to similar antibodies
5. Presence of any acute or chronic systemic infection
6. Pre-existing heart failure > New York Heart Association (NYHA) class II
7. Pregnancy or breast feeding
8. Other concurrent uncontrolled medical conditions
9. Previous Catumaxomab therapy
10. Medical or psychiatric conditions that compromise the patients ability to give informed consent
11. Inadequate renal function (Creatinine > 1,5 x ULN)
12. Inadequate hepatic function (AST or ALT > 2.5 x ULN or Bilirubin > 2 x ULN)
13. Inadequate bone marrow function with platelets < 100 000 cells/mm3 or absolute neutrophil count (ANC) < 1500 cells/mm3 or a proportion of < 15% of lymphocytes in differential blood count
14. Pregnant or nursing woman, or woman of childbearing potential who is not using an effective contraceptive method during the study and at least three months after the last infusion (i.e., oral or injectable contraceptives, intrauterine devices, double-barrier method, contraceptive patch, male partner sterilization or condoms)
15. Any further condition which according to the investigator results in an undue risk to the patient during participation in the present study
16. Parallel participation in another clinical trial or previously in this study
17. Treatment with another investigational product during this study or during the last 30 days prior to study start (day 0)
18. Under no circumstances must a patient be enrolled in this study more than once

Date of first enrolment
01/10/2011

Date of final enrolment
30/09/2013

Locations

Countries of recruitment
Germany

Study participating centre
University of Witten/Herdecke
Cologne
Germany
51109

Sponsor information

Organisation
University of Witten/Herdecke (Germany)

ROR
https://ror.org/00yq55g44

Funder(s)

Funder type
Industry

Funder Name
Fresenius Biotech

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration