Treatment of PERItoneal dissemination in Stomach Cancer patients with cytOreductive surgery and hyperthermic intraPEritoneal chemotherapy

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Primary objective:- to study the safety, tolerability and feasibility of gastrectomy combined with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) after neoadjuvant systemic chemotherapy as primary treatment option for…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON41435

Source
ToetsingOnline

Brief title
PERISCOPE-study

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified
- Gastrointestinal therapeutic procedures

Synonym
adenocarcinoma of the stomach, gastric cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Onderzoeksfonds / KWF / instituten zelf

Intervention

Keyword: Gastric cancer, Hyperthermic intraperitoneal chemotherapy, peritoneal dissemination, positive cytology

Outcome measures

Primary outcome

Treatment related toxicity (graded according to the NCI Common Toxicity

Criteria version 4.0)

Secondary outcome

- postoperative morbidity and mortality

- pharmacokinetic parameters (systemic, intraperitoneal fluid concentrations of

oxaliplatin and docetaxel)

- cytoreductive completeness score

- patterns of tumour recurrence

- disease free and overall survival

Study description

Background summary

Patients with gastric cancer have a poor prognosis, this is partly because these patients often develop peritoneal metastases. Peritoneal metastases in gastric cancer give serious symptoms and a poor quality of life. Additionally, patients with peritoneal metastases have a poor prognosis, usually between 3 to 6 months. Cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (HIPEC) is a relatively new treatment that is already used successfully in patients with peritoneal metastases of colorectal cancer. At HIPEC the inside of the abdomen is perfused with heated chemotherapy during the

operation, after the removal of cancerous growth. This happens to kill any remaining invisible cancer cells. The HIPEC is an addition to the normal operation of cancer. Although this treatment is applied to colon cancer, there is little known about this treatment in Western gastric cancer patients. In Asia, where stomach cancer is much more common, this treatment is already extensively used successfully. The present study aims to develop a HIPEC treatment in gastric cancer patients.

Study objective

Primary objective:
- to study the safety, tolerability and feasibility of gastrectomy combined with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) after neoadjuvant systemic chemotherapy as primary treatment option for advanced gastric cancer with tumour positive peritoneal cytology (C+) and/or limited peritoneal carcinomatosis (P+).

Secondary objectives:
- to determine the maximum tolerated dose of intraperitoneal docetaxel in combination with a fixed dose regimen of intraperitoneal oxaliplatin in gastric cancer patients undergoing gastrectomy combined with cytoreductive surgery and HIPEC after neoadjuvant systemic chemotherapy.
- to investigate the pharmacokinetics of intra-operative hyperthermic intraperitoneal chemotherapy after gastrectomy and cytoreductive surgery in patients with advanced gastric cancer and peritoneal dissemination.
- to identify genetic profiles predictive of tumour response in patients with advanced gastric cancer and peritoneal dissemination undergoing gastrectomy combined with cytoreductive surgery and HIPEC.
- to determine the two-year disease free and overall survival of advanced gastric cancer patients with tumour positive peritoneal cytology (C+) and/or limited peritoneal carcinomatosis (P+) treated with cytoreductive surgery and HIPEC.

Study design

A multicenter, open label, dose-escalation phase I-II study aimed to evaluate the safety, tolerability and feasibility of HIPEC with oxaliplatin and docetaxel after neoadjuvant systemic chemotherapy in advanced gastric cancer patients with tumour positive peritoneal cytology (C+) and/or limited peritoneal carcinomatosis (P+). This will be accomplished by enrolling 20-30 patients meeting the inclusion criteria, using a 3+3 design. Safety will be assessed by toxicity graded according to the NCI Common Toxicity Criteria version 4.0.

Intervention

Diagnostic investigations
All patients with locally advanced (T3-T4, any N) gastric adenocarcinoma and no evidence of distant metastasis with limited peritoneal dissemination or positive peritoneal cytology treated with neoadjuvant chemotherapy will be scheduled for surgery.

At laparotomy, the presence and extent of peritoneal tumour deposits will be recorded. Any peritoneal fluid is sampled for cytology. When a potentially radical resection of the primary tumour can be achieved, a total or partial gastrectomy with a D2 lymph node dissection is performed. In patients with limited peritoneal carcinomatosis, cytoreductive surgery (CRS) is done with the objective to leave no macroscopic tumour behind.

HIPEC procedure
Intraperitoneal chemoperfusion is performed using an open HIPEC technique. At an intraperitoneal temperature of 41-42 °C, 460 mg/m2 oxaliplatin is added to the perfusate. After 30 minutes, the perfusion fluid is drained from the abdomen. In successive patients a dose-escalation study will be performed with 0-50-75-100-125-150 mg/m2 docetaxel is administered in the peritoneal cavity for 90 minutes.

Study burden and risks

The group of patients in which this treatment will be carried out have a poor prognosis. This treatment offers these patients a potential life extension. The burden of this study is the risk of complications of this treatment. Since it is a partly experimental treatment in gastric cancer patient a strict patient selection of patients has been chosen to only treat patients in which we expect effect of the treatment. Furthermore, there are 7 additional blood tests are carried out around the HIPEC treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Biopsy proven adenocarcinoma of the stomach (including tumours at the oesophagogastric junction provided that the bulk of the tumour is located in the stomach for which the intended surgical treatment is a gastric resection and not a resection of the oesophagus and cardia)
• T3-T4 tumour based upon CT-scan and/or EUS results
• Tumour positive peritoneal cytology and/or peritoneal carcinomatosis limited to the upper abdominal cavity (above the transverse colon) and/or at the most at one location in the lower abdominal cavity (e.g., Douglas* pouch, ovarian metastasis, Sister Mary Joseph nodule) confirmed by diagnostic laparoscopy or laparotomy
• Treated with three courses of neoadjuvant chemotherapy consisting of a curative or palliative regimen, with the last course ending within 6 weeks prior to inclusion
• Age >= 18 years
• WHO performance status 0-1
• ASA classification I-III
• Adequate bone marrow, hepatic and renal function, i.e., minimal acceptable laboratory values at start of the study inclusion:
a. ANC >= 1.5 x 10^9 /L
b. Platelet count >= 100 x 10^9 /L
c. Serum bilirubin <= 1.5 x ULN, and ALAT and ASAT <= 2.5 x ULN
d. Creatinine clearance >= 50 ml/min (measured or calculated by Cockcroft-Gault formula).
• Negative pregnancy test (urine/serum) for female patients of childbearing potential
• Life expectancy >= 3 months allowing adequate follow up
• Able and willing to undergo blood sampling for pharmacokinetics
• Written informed consent

Exclusion criteria

• Distant metastases (e.g., liver, lung, para-aortic lymph nodes) or small bowel dissemination
• Signs of local irresectability
• Recurrent gastric cancer
• Metachronous peritoneal carcinomatosis
• Prior resection of the primary gastric tumour
• Pregnancy, breast feeding or active pregnancy ambition
• Unreliable contraceptive methods. Patients enrolled in this trial must agree to use a reliable contraceptive method throughout the study
• Uncontrolled infectious disease or known Human Immunodeficiency Virus HIV-1 or HIV-2 type
• A known history of hepatitis B or C with active viral replication
• Recent myocardial infarction (< 6 months) or unstable angina.
• Uncontrolled diabetes mellitus
• Any medical condition not yet specified above that is considered to possibly, probably or definitely interfere with study procedures, including adequate follow-up and compliance and/or would jeopardize safe treatment
• Known hypersensitivity for any of the applied chemotherapeutic agents and/or their solvents

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-08-2014
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Oxaliplatin
Generic name:	Oxaliplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	docetaxel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-01-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-07-2013
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-09-2013
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-01-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-04-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-06-2015
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	30-03-2017
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 21196
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-000138-37-NL
CCMO	NL42799.031.13
OMON	NL-OMON21196