Development of a docetaxel, oxaliplatin, capecitabine combination schedule in patients with advanced cancer of the stomach or the gastro-esophageal junction.

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

Summary

ID

NL-OMON33562

Source
ToetsingOnline

Brief title
The D-Doccs study

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
Advanced adenocarcinoma of the stomach or the gastro-esophageal junction; advanced gastric cancer or cancer of the gastro-esophageal junction

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Farmaceutische industrie (unrestricted educational grant),Sanofi-aventis

Intervention

Keyword: capecitabine, docetaxel, gastric cancer, oxaliplatin

Outcome measures

Primary outcome

Determination of MTD and DLT of DOCCS in patients with advanced cancer of

stomach or gastro-esophageal junction.

Secondary outcome

- Determination of preliminary clinical activity of DOCCS

- Pharmacokinetic parameters for determination of the pharmacokinetic of DOCCs

- Determination of circulating tumor cells before start of treatment and after

cycle 1, and to correlate changes with clinical outcome

- Determination of platinum DNA adducts in gastric- and tumortissue, 24 h after

start oxaliplatin (optional)

Study description

Background summary

Surgical resection is the primary curative treatment option in gastric cancer, with or without the combination of adjuvant chemotherapy. If surgery is not applicable anymore, such as in advance disease, chemo(radio)therapy is indicated. However, the survival advantage appears to be marginal and there is no established standard regime, although the ECF schedule, with response rate about 45% and median overall survival of 9 months, has been popular in Europe. The current poor prognosis of gastric cancer underscores the need for new and better treatment modalities, taking into account the toxicity profile and the

administration logistics.
Docetaxel has been shown to be active in the treatment of gastric cancer and is approved for the treatment of unresectable advanced adenocarcinoma of the stomach and gastroesophagheal junction in combination with cisplatin and 5-FU. Oxaliplatin has a favorable toxicity profile compared to cisplatin, which makes it an attractive alternative. The same accounts for replacement of 5-FU by capecitabine, with the extra advantage of the patient-convenient route of administration. Oxaliplatin and capecitabine both in multiple studies have shown activity in the treatment of gastric cancer.
Based on the extensive experience with combination chemotherapy for gastric cancer and existing data of the 3 study drugs, we expect to be able to develop a tolerable chemotherapy combination schedule with docetaxel, oxaliplatin and capectibine (DOCCS) in therapeutic dosage.

Study objective

The primary objective of the study is assessment of the dose limiting toxicity (DLT) and maximal tolerated dose (MTD) of docetaxel, oxaliplatin and capecitabine given in combination in patients with advanced cancer of the stomach or the gastro-oesophageal junction.

Secondary objectives are:
a) To determine preliminary clinical activity of the DOC combination
b) To establish the effect of functional genetic polymorphisms on the pharmacokinetics and pharmacodynamics of the DOC combination
c) To assess the frequency of circulating tumor cells detectable in patients with advanced cancer of stomach or gastro-esophageal junction prior to initiation of systemic therapy and after one course of therapy and to correlate these changes with radiological findings and clinical outcome.
d) To assess the feasibility of the analysis of pt-DNA adducts in tissue using ICP-MS and to determine the minimal amount of tissue needed, and to determine whether there is a relationship between the amount of pt-DNA adducts in gastric-, tumor tissue and PBMCs 24 hours after start of the first administration of oxaliplatin. (optional)

Study design

Non-comparitive, phase I, dose-escalation, multicenter study

Intervention

Treatment consists of:
- Docetaxel as a 1-hour i.v. infusion in a 250 ml 0.9% NaCl solution on day 1, followed by
- Oxaliplatin as a 2-hour i.v. infusion in a 500 ml 5% glucose solution on day 1,

- Capecitabine p.o. BID on days 1 - 14 in a cycle of 21 days

In total 6 dose levels are defined with escalation of just one study drug at a time per dose level. The first 3 patients will start in dose level 1. If no or minimal (grade 0 or 1) toxicity is observed during the first course including 1 week after the last patient has completed course 1, the next three patients may proceed to dose level 2. The same accounts for subsequent dose levels. No intrapatient dose escalation will be applied.
If at any dose level one of the 3 patients develops significant toxicity, up to an additional 3 patients (up to a total of 6) will be treated at the same dose level. If 2 or more out of 6 exhibit dose limiting toxicity, the maximum tolerated dose (MTD) will be considered to be the dose given at the previous lower dose level. This will be the advised dose for the combination schedule of docetaxel, oxaliplatin and capecitabine. Finally, a minimum of 14 and a maximum of 25 patients will be treated at the MTD.

Study burden and risks

Several blood samples will be obtained during course 1, which is associated with a minimal risk. The total number of venapunctures and blood sampling procedures will be reduced to a minimum, to minimise the patients burden. Gastric- and tumortissue sampling is optional. The inconvenience will be minimised by throat anaesthesia and, if the patient wishes so, sedation. Biopsies taken during gastroscopy may leed to small bleedings, however, these bleedings generally stop immediately.

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

1. Patients with advanced, histologically confirmed, adenocarcinoma of the stomach or the gastroesophageal junction
2. Previous (neo)adjuvant chemotherapy with epirubicin, cisplatin, 5-FU or capecitabine is allowed provided that a relapse occurred > 12 months after chemotherapy. Otherwise patients should be chemonaive.
3. Measurable or evaluable non-measurable disease
4. Age 18 years or older
5. Able to swallow and retain oral medication
6. Able and willing to undergo blood sampling for pharmacogenetic and pharmacokinetic analysis, and circulating tumor cells analysis
7. Life expectancy of at least 3 months allowing adequate follow up of toxicity evalution and antitumor activity
8. Minimal acceptable safety laboratory values
a. ANC of 1.5 x 109 /L or higher
b. Platelet count of 100 x 109 /L or higher
c. Haemoglobin level of 6.0 mmol/l or higher - transfusion is permitted
d. Hepatic function as defined by serum bilirubin of less 1.5 x ULN or less, ALT and AST and alkaline phosphatase 2.5 x ULN or less
e. Renal function as defined by serum creatinine 1.5 x ULN or less or creatinine clearance more than 50 ml/min (by Cockcroft-Gault formula).
9. Able and willing to give written informed consent
10. WHO performance status of 0, 1 or 2

Exclusion criteria

1. Known CNS or leptomeningeal metastases (a CT or MRI scan should be done if there is a clinical suspicion of CNS metastases)

2. History of another primary cancer, except curatively treated in situ cervical cancer or resected non-melanoma skin cancer
3. Uncontrolled infectious disease or known HIV, hepatitis B or hepatitis C patients
4. Patients with known alcoholism, drug addiction and/or psychotic disorders in the history that are not suitable for adequate follow up
5. Women who are pregnant or breast feeding
6. Women of childbearing potential who refuse to use a reliable contraceptive method throughout the study
7. Any other medical condition that would interfere with study procedures and/or decrease safety of the protocol treatment.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2007
Enrollment:	35
Type:	Anticipated

Medical products/devices used

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

Product type:	Medicine
Brand name:	Xeloda
Generic name:	Capecitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-06-2007
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-08-2009
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-04-2010
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-002626-30-NL
CCMO	NL17610.031.07