Phase II Study of Docetaxel, Oxaliplatin, Capecitabine with Bevacizumab and Trastuzumab in case of human epidermal growth factor receptor 2 (HER2)-positivity in Patients with Locally Advanced or Metastatic Gastric Cancer or Adenocarcinoma of the Gastro-oesophageal Junction (B-DOCT study)

Published: 08-10-2010
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Primary: Progression free survival.Secondary: Toxicity, overall survival, response rate, duration of response, translational research.

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

Summary

ID

NL-OMON39414

Source
ToetsingOnline

Brief title
B-DOCT study

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym

locally advanced or metastatic gastric cancer or adenocarcinoma of the gastro-oesophageal junction, metastatic gastric cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: NKI-AVL

Intervention

Keyword: biological, chemotherapy, gastric cancer, metastatic

Outcome measures

Primary outcome

Progression free survival.

Secondary outcome

Toxicity, overall survival, response rate, duration of response, translational

research.

Study description

Background summary

It is estimated that in the Netherlands each year approximately 900 patients with gastric cancer or adenocarcinoma of the gastro-oesophageal junction are candidates for chemotherapy. Randomized studies comparing chemotherapy versus best supportive care have shown that survival and quality of life are prolonged with chemotherapy. However, no chemotherapy regimen is clearly superior with regard to prolongation of survival. Therefore, tolerability of treatment and ease of administration (outpatient compared to inpatient) are important considerations for the development of novel treatment schedules.
This is an open-label, multicentre, phase II trial designed to evaluate the efficacy and safety of bevacizumab in combination with docetaxel, oxaliplatin and capecitabine chemotherapy (B-DOC) as first-line therapy in patients with inoperable locally advanced or recurrent and/or metastatic adenocarcinoma of the stomach or gastro-oesophageal junction. In case of HER2 positive inoperable locally advanced or recurrent and/or metastatic adenocarcinoma of the stomach

or gastro-oesophageal junction trastuzumab is added to this regimen (B-DOCT). Stabdard treatment in the Netherlands consists in most clinics of epirubicin, capecitabine and oxaliplatin or cisplatin.

Study objective

Primary: Progression free survival.
Secondary: Toxicity, overall survival, response rate, duration of response, translational research.

Study design

National multicenter open non-comparative fase II study.
Treatment:
Cycles of 3 weeks with
• Docetaxel 50 mg/m2 i.v. day 1, max. 6 cycles
• Oxaliplatin 100 mg/m2 i.v. day 1, max. 6 cycles
• Bevacizumab 7.5 mg/kg i.v. day 1, until progression
• Capecitabine 850 mg/m2 (after 6 cycles 1000 mg/m2) orally bid, day 1-14, until progression.
In case of HER2 positivity of the de tumor, addition of
• Trastuzumab 6 mg/kg i.v. day 1 (at 1st administration 8 mg/kg) , until progression.
Duration of administration: oxaliplatin plus docetaxel 4 h, bevacizumab 1st administration * h and thereafter * h, trastuzumab 1st administration 1* h and thereafter * h.
90 patients.

Intervention

Treatment with docetaxel, oxaliplatin, capecitabine, bevacizumab and, in case of HER2 positivity also trastuzumab.

Study burden and risks

Risk: AEs of the (combination of the) study drugs.
Burden: The burden for the patient will not be notably different from the burden during regular treatment. Only the translational research (4 blood samples during cycle 1-3 and one further sample every following cycle, during progression, combined with regular blood samples -if possible-) is a clear additional burden.

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. Histologically confirmed adenocarcinoma of the stomach or gastro-oesophageal junction with inoperable locally advanced or recurrent and/or metastatic disease not amenable to curative therapy.
2. Measurable/evaluable disease, according to the Response Evaluation Criteria in Solid Tumours (RECIST), assessed using imaging techniques (CT or MRI)
3. ECOG Performance status 0, 1 or 2
4. Life expectancy of at least 3 months
5. Male or female age >= 18 years
6. Assessment of HER2 status (primary tumour or metastasis) by the central laboratory prior to initiation of study treatment (Dual SISH, Ventana).
7. LVEF >= 50% assessed by multigated radionucleotide angiography (MUGA) or cardiac ultrasound.

Exclusion criteria

1. Previous chemotherapy for advanced/metastatic disease (prior peri-operative chemotherapy is allowed if at least 6 months has elapsed between completion of this therapy and enrolment into the study)
2. Patients with increased risk of gastro-intestinal perforation in response to treatment due to deep ulceration of the tumour through the wall of the distal oesophagus and/or stomach, as assessed by endoscopy.
3. Previous radiotherapy on the abdomen
4. Other malignancy within the last 5 years, except for carcinoma in situ of the cervix, or basal cell carcinoma
5. Patients with active (significant or uncontrolled) gastrointestinal bleeding
6. Residual relevant toxicity resulting from previous therapy (with the exception of alopecia), e.g. neurological toxicity >= grade 2 NCI-CTCAE
7. Creatinin clearance <50 mL/min
8. Neutrophil count <1.5 × 109/L, or platelet count <100 × 109/L
9. Serum bilirubin >1.5 × upper limit of normal (ULN); or, AST or ALT >2.5 × ULN (or > 5 × ULN in patients with liver metastases); or, alkaline phosphatase >2.5 × ULN (or >5 × ULN in patients with liver metastases, or >10 × ULN in patients with bone but no liver metastases); or, albumin <25 g/L
10. Known dihydropyrimidine dehydrogenase (DPD) deficiency.
11. History of documented congestive heart failure; angina pectoris requiring medication; evidence of transmural myocardial infarction; poorly controlled hypertension (systolic BP >180 mmHg or diastolic BP >100 mmHg); clinically significant valvular heart disease; or high risk uncontrollable arrhythmias.
12. Patients with dyspnoea at rest due to complications of advanced malignancy or other disease, or who require supportive oxygen therapy.
13. Patients receiving chronic or high dose corticosteroid therapy. (Inhaled steroids and short courses of oral steroids for anti-emesis or as an appetite stimulant are allowed)
14. Major surgery within 4 weeks of start of study treatment,
15. Known hypersensitivity to any of the study drugs
16. History or clinical evidence of brain metastases
17. Serious uncontrolled systemic intercurrent illness, e.g. infections or poorly controlled diabetes
18. Positive serum pregnancy test in women with childbearing potential
19. Subjects with reproductive potential not willing to use an effective method of contraception
20. Any investigational drug treatment within 4 weeks of start of study treatment
21. Radiotherapy within 4 weeks of start of study treatment (2 week interval allowed if palliative radiotherapy given to bone metastastic site peripherally and patient recovered from any acute toxicity)
22. Therapeutic use of oral coumarin-derived or LMWH anticoagulants or NSAIDs.
23. Continuous use of immunosuppressive agents (for the use of corticosteroids see #12).

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-03-2011
Enrollment:	90
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin
Generic name:	bevacizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Eloxatin
Generic name:	oxaliplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Herceptin
Generic name:	trastuzumab
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:	08-10-2010
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	19-01-2011
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	23-08-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-10-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-11-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	15-11-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-01-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	27-01-2014
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
Other	clinicaltrials.gov. NCT01359397
EudraCT	EUCTR2010-022699-30-NL
CCMO	NL33964.031.10