Feasibility of adjuvant treatment with S-1 and oxaliplatin in patients with resectable esophageal cancer

Published: 20-11-2014
Last updated: 21-04-2024

The primary objective is to assess the feasibility of administering adjuvant S-1 and oxaliplatin in patients with esophageal cancer after neoadjuvant chemoradiotherapy with paclitaxel and carboplatin and esophagectomy

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON47475

Source
ToetsingOnline

Brief title
SOX

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
esophageal cancer; esophagus tumour

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Nordic

Intervention

Keyword: Adjuvant, Chemotherapy, Esophageal cancer, Feasability

Outcome measures

Primary outcome

The percentage of patients completing the preplanned number of 6 cycles of SOX.

Secondary outcome

- Percentage of patients completing 6 cycles of S-1 (with or without oxaliplatin)
- Dose modifications (i.e. delays, dose reductions, or interruptions) for S-1
- Dose modifications (i.e. delays, dose reductions, or interruptions) for oxaliplatin
- Dose intensity of S-1.
- Dose intensity of oxaliplatin
- Toxicity
- Disease free survival
- Overall survival

Exploratory:

- Assessment of pharmacokinetics of S1 in relation to safety and efficacy.
- Potential biomarker development based on assessment of archived tumor tissue and blood samples and the proposed mechanism of action of study drugs.

Study description

Background summary

Esophageal cancer is the 8th most common cancer and ranks sixth on the list of cancer mortality causes. The outcome is poor with an overall 5-year survival of 10% worldwide. The incidence is rising, due to the rising incidence of adenocarcinoma. The outcome of resectable esophagus cancer can be improved by a multimodality treatment. Perioperative chemotherapy of gastric cancer has been proven beneficial, however the benefit of adjuvant therapy after neo-adjuvant chemoradiation followed by surgery in esophageal cancer is unknown. Also, adjuvant treatment after major gastrointestinal surgery may be hard to complete. Given the need for improvement of treatment outcomes of esopheal cancer and the benefits of perioperative chemotherapy in gastric cancer, in this study we will assess the feasibility of SOX as adjuvant treatment in patients with esophageal cancer.

Study objective

The primary objective is to assess the feasibility of administering adjuvant S-1 and oxaliplatin in patients with esophageal cancer after neoadjuvant chemoradiotherapy with paclitaxel and carboplatin and esophagectomy

Study design

Prospective single arm feasibility study

Intervention

Adjuvant treatment with six courses of S-1 and oxaliplatin.

Study burden and risks

The main question of this study is feasibility of adjuvant chemotherapy of esophageal tumors after surgery. Literature studies show that additional treatment with chemotherapy around surgery from gastric cancer has a positive effect on disease-free survival. If it is shown that it is feasible to administer adjuvant therapy after surgery future studies can be examine whether this affects the survival positively. Also, this study and additional research on tumor tissue and blood may provide useful information for future patients.

It is possible that the patient experiences side effects of the chemotherapy used. The side effects have been extensively studied in patients treated for other types of cancer and this form of chemotherapy is generally well tolerated. Nevertheless, if side effects are severe these can lead to

hospitalization.

The patient should come to the hospital six times over a period of 18 weeks for the administration of oxaliplatin as wellas medical check ups. He/she also takes in two of the three weeks of treatment tablets twice daily .

Before starting a treatment cycle blood samples will be drawn (about 5 ml each time). Furthermore, additional blood sampling will be performed in the first two cycles (123 ml in total, about 7-8 tablespoons) to measure the uptake and degradation of S-1 in the body and to investigate factors that could predict side effects and efficacy of the treatment. These additional blood samples are taken in the hospital before the intake of S-1 and a half hour, one hour, one and a half hours, three hours, five hours and eight hours thereafter. An additional sample is taken in the first or second week after start of treatment in cycle 1 and 2.

Both the blood test and the IV insertion can be painful and lead to bruising at the puncture site.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Macroscopic radically resected adenocarcinoma of the esophagus
- Completed neoadjuvant treatment with paclitaxel 50 mg/m2 and carboplatin AUC <= 2 on and radiotherapy to a total dose of 41.4 Gy in 23 fractions of 1.8 Gy, 5 fractions per week, with maximun one missed dose of systemic therapy, not due to haematological toxicity
- Being able to start within 16 weeks after esophagectomy
- Age * 18 years
- WHO performance status 0-1
- Adequate bone marrow function (Hb * 6.0 mmol/L, absolute neutrophil count *1.0 x 109/L, platelets * 100 x 109/L), renal function (serum creatinine * 1.5x ULN and creatinine clearance, Cockroft formula, *30 ml/min), liver function (serum bilirubin * 2 x ULN, serum transaminases * 3 x).
- Negative pregnancy test in women with childbearing potential.
- Expected adequacy of follow-up.
- Written informed consent.

Exclusion criteria

- Any history or clinical signs of metastasis
- A second malignancy interfering with the prognosis of current esophageal carcinoma
- Known dihydropyrimidine dehydrogenase (DPD) deficiency or treatment within 4 weeks with DPD inhibitors, including sorivudine or its chemically related analogues such as brivudine.
- - Significant cardiovascular disease < 1 yr before start of the study (as determined by the investigator, for example: symptomatic congestive heart failure, myocardial ischemia or infarction, unstable angina pectoris, serious uncontrolled cardiac arrhythmia, arterial thrombosis, cerebrovascular event, significant pulmonary embolism).
- Chronic active infection.
- Any other concurrent severe or uncontrolled disease preventing the safe administration of study drugs.
- Any impairment of gastrointestinal function or *disease that may significantly impair the absorption of oral drugs (i.e. uncontrolled nausea, vomiting, diarrhoea (defined as ³CTC grade 2), malabsorption syndrome, bowel obstruction, or inability to swallow tablets).

- Concomitant treatments: concomitant (or within 4 weeks before randomisation) administration of any other experimental drug under investigation; concurrent treatment with any other anti-cancer therapy.
- Continuous use of systemic immunosuppressive agents (except the use of corticosteroids as anti-emetic prophylaxis/treatment).

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-02-2015
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Eloxatin
Generic name:	oxaliplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Teysuno
Generic name:	S-1
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	20-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2014-003603-30-NL
CCMO	NL49889.018.14