S-1 versus capecitabine in the first line treatment of metastatic colorectal cancer patients, the SALTO randomised phase III study of the Dutch Colorectal Cancer Group. A safety evaluation of oral fluoropyrimidines.

Published: 18-06-2013
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The primary objective is to determine the incidence of HFS in first line treatment with S-1 compared to capecitabine in patients with metastatic colorectal cancer. Secondary objectives include a comparison of efficacy.

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

Summary

ID

NL-OMON41674

Source
ToetsingOnline

Brief title
SALTO

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
Bowel Cancer, Colorectalcancer

Research involving

Human

Sponsors and support

Primary sponsor: Dutch Colorectal Cancer Group
Source(s) of monetary or material Support: Dutch Colorectal Cancer Group,Nordic Pharma

Intervention

Keyword: Chemotherapy, Colorectal cancer, Fluoropirimidine, Hand-footsyndrome

Outcome measures

Primary outcome

To assess the incidence of HFS in first line treatment with S-1 compared to

capecitabine in patients with metastatic colorectal cancer.

Secondary outcome

To evaluate and assess:

* Incidence of grade 3 hand-foot syndrome

* Incidence of other toxicities

* Progression-free survival

* Response rate

* Overall survival

Study description

Background summary

Nowadays, standard 1st-line treatment for patients with metastatic colorectal cancer currently consists of fluoropyrimidine-containing chemotherapy plus bevacizumab.
It has been shown that first-line fluoropyrimidine monotherapy is a valid alternative for combination chemotherapy in the majority of metastatic colorectal cancer patients. Upfront combination chemotherapy is only indicated

in patients in whom tumour shrinkage is the primary goal or who are less likely to be eligible for salvage treatments. Bevacizumab is considered as part of the first-line standard treatment, and has also shown a benefit when added to fluoropyrimidine monotherapy. However bevacizumab may not be indicated in all patients.

Study objective

The primary objective is to determine the incidence of HFS in first line treatment with S-1 compared to capecitabine in patients with metastatic colorectal cancer. Secondary objectives include a comparison of efficacy.

Study design

The study is a two-arm randomised phase III trial. Eligible patients will be randomised after informed consent has been obtained.
Patients will be randomised 1:1 to receive capecitabine (arm A) or S-1 (arm B). Bevacizumab may be added according to the choice of the investigator. Patients will be followed 3-weekly at the outpatient clinic, toxicity will be assessed according to study protocol guidelines. Patients will be evaluated every 3 cycles for response. Upon disease progression patients will be treated according to the local investigators choice.

Intervention

Teysuno 2dd versus Capecitabine 2dd with or without bevacizumab

Study burden and risks

A patient diary has to be completed each cycle.

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

* Histological proof of colorectal cancer.;* Distant metastases (patients with only local recurrence are not eligible);* Unidimensionally measurable disease (*1 cm on spiral CT scan or *2 cm on chest X-ray; liver ultrasound is not allowed). Serum CEA may not be used as a parameter for disease evaluation.;* In case of previous radiotherapy, at least one measurable lesion should be located outside the irradiated field.;* Age * 18 years ;* Planned first line treatment with capecitabine monotherapy with or without bevacizumab. ;* WHO performance status 0-2 (Karnofsky PS *70%);;* Laboratory values obtained within 2 weeks prior to randomisation:;* adequate bone marrow function (Hb * 6.0 mmol/L, absolute neutrophil count *1.5 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 ULN without presence of liver metastases or * 5x ULN with presence of liver metastases).;* Life expectancy > 12 weeks.;* Negative pregnancy test in women with childbearing potential.;* Expected adequacy of follow-up.;* Institutional Review Board approval.;* Written informed consent.

Exclusion criteria

* Prior adjuvant treatment for stage II/III colorectal cancer completed within 6 months prior to randomisation.;* Any prior adjuvant treatment after resection of distant metastases.;* Any prior systemic treatment for advanced disease.;* History or clinical signs/symptoms of CNS metastases.;* History of a second malignancy <5 years with the exception of adequately treated carcinoma of cervix or basal/squamous cell carcinoma of skin.;* Previous intolerance of capecitabine.;* Known dihydropyrimidine dehydrogenase (DPD) deficiency or treatment within 4 weeks with DPD inhibitors, including sorivudine or its chemically related analogues such as brivudine.;* Planned radical resection of metastases after downsizing by systemic

treatment.;* Significant cardiovascular disease < 1 yr before randomisation (symptomatic congestive heart failure, myocardial ischemia or infarction, unstable angina pectoris, serious uncontrolled cardiac arrhythmia, arterial thrombosis, cerebrovascular event, pulmonary embolism).;* Any significant cardiovascular events during previous fluoropyrimidine therapy.;* 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 ^{3}CTC 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 immunosuppressive agents (except the use of corticosteroids as anti-emetic prophylaxis/treatment).;In case of treatment with bevacizumab:;* Uncontrolled hypertension, i.e. consistently > 150/100 mmHg.;* Use of * 3 antihypertensive drugs.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-01-2014
Enrollment:	160
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin

Generic name: Bevacizumab

Registration: Yes - NL intended use

Product type: Medicine

Brand name: Teysuno

Generic name: Tegafur Oteracil Gimeracil

Registration: Yes - NL outside intended use

Product type: Medicine

Brand name: Xeloda

Generic name: Capecitabine

Registration: Yes - NL intended use

Ethics review

Approved WMO
Date: 18-06-2013

Application type: First submission

Review commission: METC Amsterdam UMC

Approved WMO
Date: 06-09-2013

Application type: First submission

Review commission: METC Amsterdam UMC

Approved WMO
Date: 17-12-2013

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 20-12-2013

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 24-02-2014

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 01-04-2014

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 03-04-2014

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 19-12-2014

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 06-03-2015

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 13-05-2015

Application type: Amendment

Review commission: METC Amsterdam UMC

Not approved
Date: 18-05-2015

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 18-09-2015

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	EUCTR2013-002147-28-NL
CCMO	NL45030.018.13