An open-label, randomised, non-comparative phase 2 study evaluating S 95005 (TAS-102) plus bevacizumab and capecitabine plus bevacizumab in patients with previously untreated metastatic COlorectal cancer who are non-eligible for intensive therapy (TASCO1 study)

Published: 04-02-2016
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON43475

Source
ToetsingOnline

Brief title
Phase2 with S95005,bevacizumab,capecitabine in metastatic colorectal cancer

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
metastatic colorectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Institut de Recherches Internationales Servier
Source(s) of monetary or material Support: Institut de Recherches Internationales Servier

Intervention

Keyword: cancer, colorectal, metastatic

Outcome measures

Primary outcome

Progression-free survival (PFS) based on Investigator assessment of radiologic

images

Secondary outcome

Overall response rate (ORR)

Duration of response (DR)

Disease control rate (DCR)

Overall survival (OS)

Safety and tolerability

Quality of Life (QoL)

Study description

Background summary

S 95005 (also called TAS-102) is a combination of an antineoplastic thymidine-based nucleoside analogue (trifluridine [FTD]) and a thymidine

phosphorylase inhibitor (tipiracil hydrochloride [TPI]).
Co-administration of TPI with FTD prevents the rapid degradation of FTD, resulting in a significant increase in systemic exposure to FTD. Following uptake into cancer cells, FTD is phosphorylated by thymidine kinase, further metabolized in cells to a deoxyribonucleic acid (DNA) substrate, and incorporated directly into DNA, thereby interfering with DNA function to prevent cell proliferation.
FTD incorporation into DNA is markedly higher than that of other nucleoside analogues.
FTD also exhibits thymidylate synthase (TS) inhibition. However, results of in vivo studies show FTD incorporation into DNA to be the primary mechanism of antitumour activity with oral administration.
This mechanism of action of S 95005 differentiates it from conventional fluoropyrimidines, which are uracil-based, and for which the primary mode of action is TS inhibition.
For patients with mCRC who are non-eligible for intensive therapy, recent ESMO and NCCN guidelines recommend fluorouracil or capecitabine with or without bevacizumab as first-line treatment.
Based on the demonstrated efficacy and tolerability of S95005 in patients with previously treated mCRC, including patients refractory to prior fluoropyrimidine treatment, a Phase 2 study to evaluate the benefit of S95005 plus bevacizumab as first-line treatment of unresectable mCRC is warranted.
The results of a Phase 1/2 study conducted in Japan suggest that the combination of TAS-102 and bevacizumab is well tolerated in patients with mCRC

Study objective

This study will evaluate 2 different treatment strategies : a combination of S 95005 and bevacizumab (experimental combination) and a combination of capecitabine and bevacizumab (control arm) as first-line treatment for metastatic colorectal cancer in patients non-eligible for intensive therapy.

Study design

International, multicentric, randomised(1:1), open-label phase 2 study to include 150 pats in 2 parallel arms:
* S 95005 + bevacizumab = 4 weeks cycle
* or capecitabine + bevacizumab = 3 weeks cycle

study scheme : screening, inclusion, randomisation, visit on D1 + D15, afterwards on day of bevacizumab administration and withdrawal visit

Intervention

blood and urine sampling, contrast enhanced CT , QoL questionnaires

Study burden and risks

cfr adverse events of medication and procedures described in patient information.

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

- Written informed consent obtained.;- Male or Female participant aged *18 years old.;- Has ECOG performance status of 0, 1 or 2 at the time of the randomisation.;- Has definitive histologically or cytologically confirmed adenocarcinoma of the colon or rectum.;- RAS status must have been determined (mutant or wild).;- Has at least one measurable metastatic lesion.;- No previous anticancer therapy for metastatic colorectal cancer. ;- Previous adjuvant

(or neoadjuvant for patients with rectal cancer) chemotherapy is allowed only if if it has been completed more than 6 months before start of study treatment.;- In the judgment of the Investigator, patient is not a candidate for combination chemotherapy with irinotecan or oxaliplatin, or for curative resection of metastatic lesions.;- Is able to take medication orally (i.e., no feeding tube).;- Has adequate organ function.;- Coagulation parameters in normal limit.;- Women of childbearing potential must have been tested negative in a serum pregnancy test. Male and female patients who have the potential to reproduce must agree to use a highly effective method of birth control.;- Is willing and able to comply with scheduled visits and study procedures.

Exclusion criteria

- Foreseeable poor compliance to the study procedures.;- Is a pregnant or lactating female.;- Is inappropriate for entry into this study in the judgment of the Investigator.;- Has certain serious illness or serious medical condition(s) described in the protocol.;- Has had certain other recent treatment e.g. major surgery, field radiation, received investigational agent, within the specified time frames prior to study drug administration.;- Has previously received S 95005 or history of allergic reactions attributed to compounds of similar or biologic composition to S 95005.;- Has contra indications to bevacizumab or capecitabine.;- Has rare hereditary problems of galectose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

Study design

Design

Study phase:	2
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):	21-06-2016

Enrollment:	50
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:	lonsurf
Generic name:	trifluridine+tipiracil hydrochloride
Product type:	Medicine
Brand name:	xeloda
Generic name:	capecitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-02-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	22-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	26-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-05-2020
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	EUCTR2015-004544-18-NL
CCMO	NL56482.018.16

Study results

Results posted: 26-08-2021

First publication
01-01-1900

URL result
Type
ext
Naam
www.clinicaltrialsregister.eu
URL