A phase I study of SGI-110 combined with irinotecan followed by a randomized phase II study of SGI-110 combined with irinotecan versus regorafenib or TAS-102 in previously treated metastatic colorectal cancer patients.

Published: 23-01-2014
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This protocol is designed to determine the safety, tolerability, and efficacy of SGI-110 in combination with irinotecan in previously treated patients with metastatic colorectal cancer who progressed on irinotecan.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON47325

Source
ToetsingOnline

Brief title
CORSICA

Condition

- Other condition
- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
metastatic colorectal cancer

Health condition

Gemetastaseerd colorectaal carcinoom

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ASTEX therapeutics, Ltd,Johns Hopkins Universtity on behalf of its School of MEdicine;Baltimore;VS

Intervention

Keyword: Irinotecan, Metastatic colorectal carcinoma, Regorafenib or TAS-102, SGI-110

Outcome measures

Primary outcome

During phase I, we will be assessing the safety and tolerability of SGI-110 in combination with irinotecan, as well as determine the dose of SGI-110 that will be used in combination with irinotecan during the phase II portion of this trial.

Phase II: To improve median progression-free survival from that reported with regorafenib and TAS-102 to 4 months for SGI-110+irinotecan in previously treated metastatic colon cancer patients who have progressed on irinotecan.

Secondary outcome

In Fase I we will also be assessing the changes in global methylation and expression at the tumor level with SGI-110 and irinotecan treatment and the pharmacokinetic interactions of SGI-110 and irinotecan.

In phase II we will also evaluate the following: response rate as determined by RECIST criteria 1.1, evaluate concurrent SGI-110 and irinotecan treatment

versus regorafenib alone, assess whether SGI-110 in combination with irinotecan can improve median overall survival from the historical rate of 6.4 months, and assess for potential predictive biomarkers of response and survival using baseline tissue.

Study description

Background summary

Metastatic colorectal cancer (mCRC) is the second leading cause of cancer death. The five-year survival for all patients with metastatic disease from CRC is only 8.1%. Median survival with current generation of chemotherapies, including oxaliplatin or irinotecan as well as newer biologic therapies such as bevacizumab and cetuximab is only 20-24 months. Patients with mCRC have a 60% likelihood of responding to first-line chemotherapy and drops to 10% in the second line.
In CRC, as there are no subsequent therapy options for patients after 2nd or 3rd line therapy (based on KRAS mutational status), our group has been exploring the potential of DNMT inhibitor therapy to synergize to subsequent therapy. Ishiguro et al. first demonstrated that treatment with DAC resulted in gene re-expression of known tumor suppressor genes in CRC; moreover, in both in vitro and in vivo models, DAC treatment substantially decreased tumor growth when combined with irinotecan or SN-38 (active irinotecan metabolite) compared to either agent alone. In xenograft studies SGI-110 demonstrates promising preclinical activity in both hematologic and solid tumors.
Based on these data, we hypothesize that DNMTi therapy with SGI-110 will sensitize advanced colorectal cancer to treatment with Irinotecan.

Study objective

This protocol is designed to determine the safety, tolerability, and efficacy of SGI-110 in combination with irinotecan in previously treated patients with metastatic colorectal cancer who progressed on irinotecan.

Study design

This is a phase I/randomized phase II, open label, multi-institutional study that will be conducted in two parts. First, patients will be enrolled in a phase I study of SGI-110 combined with irinotecan in a standard 3+3 design. After the maximum tolerated dose (MTD) is determined, patients will subsequently be enrolled in a 2:1 randomized phase II study of SGI-110 and

irinotecan versus regorafenib or TAS-102.

Intervention

In phase I, patients will be tretated with SGI-110 (sc injection day 1-5) and irinotecan (125 mg/m2 IV) at day (10), 8 and 15 according to the dose escalation schedule in table 2, page 15 of the protocol.
In phase II patients in treatment arm A are treated with investigational medicine SGI-110 (sc injection day 1-5, dose determined in phase I) combined with irinotecan (125 mg/m2 IV day (1), 8 en 15). Patients in treatment arm B are treated with regorafenib (tablet 160 mg/dag, day 1-21) or TAS-102 35 mg/m2 day 1-5 and 8-12.

Study burden and risks

Besides standard patient care, additional blood sampling will be done and includes two study tumor biopsies in phase I and for a part of patients in Phase II. Side effects of systemic therapy can occur and patients can experience side effects or complications of the blood sampling and tumor biopsies. The risks of participating in the study are limited, and if successful, study treatment may benefit the subject as well. The information that we learn from this study has the potential to improve therapy for patients with refractory colorectal cancer, and may benefit individuals who are diagnosed with this disease in the future.

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

Histologically or cytologicaly confirmed adenocarcinoma of the colon or rectum,
Patients in phase I must have biopsiable diasese and be amenable to having two research biopsies.
Patients must have progressed on irinotecan therapy in the metastic setting. There are no limitation on number of prior therapies. They should have a life expectancy of greater than 12 weeks, an
ECOG of

Exclusion criteria

Chemotherapy or radiotherapy within 4 weeks prior to entering the study,
Known brain metastases,
Uncontrolled intercurrent illness,
Prior therapy with any hypomethylating agent,
Pregnancy
A history of a different malignancy unless disease-free for at least 5 years,
HIV positive individuals on HAART
Previoius treatement with regorafenb and TAS-102 (this applies to phase II only. If patients have previously received aeither regorafenib or tas-102, they must be able to receive the alternate regimen if randomized to the standard of care arm)
Hospitalization for an acute medical issue within 4 weeks prior to screening visit
Symptomatic bowel obstruction within 6 months prior to enrollment. Patients who undergo surgical correction of obstructing lesion will be eligible within 6 months.

Study design

Design

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):	10-06-2014
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	campto
Generic name:	irinotecan
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lonsurf
Generic name:	TAS-102
Product type:	Medicine
Brand name:	SGI-110
Generic name:	SGI-110
Product type:	Medicine
Brand name:	stivarga
Generic name:	regorafenib
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	23-01-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date: 06-09-2016

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date: 14-09-2016

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date: 02-03-2017

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date: 09-03-2017

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date: 03-11-2017

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date: 18-01-2018

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date: 19-06-2018

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date: 10-07-2018

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date: 22-02-2019

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date:	26-02-2019
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	EUCTR2013-003184-62-NL
ClinicalTrials.gov	NCT01896856
CCMO	NL45922.029.13