A randomized phase II study of pulsatile high-dose sunitinib versus TAS-102 in patients with metastatic colorectal carcinoma (mCRC).

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27160

Source
Nationaal Trial Register

Brief title
SUNRISE-CRC

Health condition

Metastastic colorectal cancer

Sponsors and support

Primary sponsor: Radboud UMC
Source(s) of monetary or material Support: ZonMW - Oncode

Intervention

Outcome measures

Primary outcome

The primary objective of this study is to improve progression free survival (PFS), of patients

with metastatic colorectal carcinoma (mCRC) treated with high-dose sunitinib once every 2 weeks to 5 months, compared to the reported 2 months for TAS-102 monotherapy.

Secondary outcome

Secondary objectives include: overall survival (OS), the safety and efficacy of the treatment, the quality of life in the two study arms, the value of blood and biopsy based markers for response to sunitinib or TAS-102.

Study description

Background summary

Study design: A prospective, open-label, randomized, mono-center, phase II clinical trial (with registration intent).

The purpose of this study is to compare progression free survival rates of metastasized colorectal cancer patients refractory or intolerant to systemic therapy with fluoropyrimidine, irinotecan, oxaliplatin, anti-VEGF therapy and anti-EGFR therapy (for tumours with wild-type KRAS)); randomized for treatment with TAS-102 (standard-arm) or High Dose Intermittent Sunitinib (700 mg once every 2 weeks). The investigators hypothesis is that treatment with the experimental arm (sunitinib) will provide an improvement in progression free survival in this patient group with an improvement in quality of life. .

Study objective

The investigators hypothesize a clinically relevant increase in PFS by 3 months; from 2 months as reported for TAS-102 to 5 months in patients treated with sunitinib. They further hypothesize that this will result in a meaningful improvement in Quality of Life (QoL).

Study design

After study inclusion, patients will be randomized (1:1) via a centralized randomization system to receive either oral sunitinib (700 mg once every 2 weeks) or TAS-102 (35 mg per square meter, twice daily, 5 days a week, with 2 days of rest, for 2 weeks, followed by a 14-day rest period). Patients will receive treatment until disease progression or discontinuation due to unacceptable toxic effects, withdrawal of consent, or other reason.

Intervention

A: TAS-102 (Lonsurf) 35 mg per square meter, twice daily, 5 days a week, with 2 days of rest, for 2 weeks, followed by a 14-day rest period.
B: Experimental: High Dose Intermittent Sunitinib 700 mg once every 2 weeks.

Contacts

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Eligibility criteria

Inclusion criteria

Inclusion Criteria:
• Signed (by the patient or legally acceptable representative) and dated Informed Consent Form (ICF).
• Histological or cytological confirmed, documentation of incurable locally advanced or metastatic, colorectal adenocarcinoma, not amenable for potentially curative treatment (i.e. inoperable).
• Indication for treatment with TAS-102; progressive on (or intolerant to) therapy including fluoropyrimidine, irinotecan, oxaliplatin, anti-VEGF therapy and anti-EGFR therapy (for tumours with wild-type KRAS)).
• Evaluable disease by RECIST version 1.1 criteria (see appendix III).
• Age ≥ 18 years.
• Eastern Cooperative Oncology Group (ECOG) Performance Status of ≤ 3.
• Normal 12-lead ECG (clinically insignificant abnormalities permitted).
• No signs of clinical thyroid abnormalities (suppletion or blocking drugs permitted).
• Adequate bone marrow function
• Adequate liver function
• Albumin higher than 25 g per L
• Serum creatinine ≤1.5 x ULN
• Pregnant or breast-feeding subjects: Women of childbearing potential must have a negative pregnancy test performed within 7 days of the start of treatment. For fertile men or women of childbearing potential: documented willingness to use a highly effective means of contraception (e.g., hormonal methods [implants, injectables, or combined oral contraceptives], intrauterine devices, sexual abstinence, or vasectomized or surgically sterilized partner). Contraception is necessary for at least 6 months after receiving the study medication.

Exclusion criteria

Exclusion Criteria:
• Previous treatment with sunitinib and/or TAS-102 for mCRC.
• Evidence of significant uncontrolled concomitant disease, such as cardiovascular disease (including stroke, New York Heart Association Class III or IV cardiac disease or myocardial infarction within 6 months prior to screening, unstable arrhythmia, clinically significant valvular heart disease and unstable angina); pulmonary disease (including obstructive pulmonary disease > GOLD 2 and inadequately treated symptomatic bronchospasm), and uncontrolled central nervous system, renal, hepatic, endocrine, or gastrointestinal disorders; or a serious non-healing wound or fracture.
• Extensive prior radiotherapy in the rectum, pelvis or in more than 3 vertebrae in the spine (less than 3 vertebrae are considered a small radiation field and eligibility will be decided on an individual basis from the PI).
• Poorly controlled hypertension despite adequate blood pressure medication. Blood pressure must be ≤160/95 mmHg at the time of screening on a stable antihypertensive regimen. Blood pressure must be stable on at least 2 separate measurements.
• Instable seizure disorders requiring anticonvulsant therapy.
• Major surgery, other than diagnostic surgery, within 4 weeks prior to day 1, without complete recovery.
• Uncontrolled bleeding disorders, and/or active bleeding.
• Known active bacterial, viral, fungal, mycobacterial, or other infection. (including HIV and atypical mycobacterial disease, but excluding fungal infection of the nail beds.)
• Known hypersensitivity to sunitinib, TAS-102, or to its excipients.
• Presence of any significant psychiatric disorder(s) that would interfere with the patient's compliance.
• Chemotherapy, radiotherapy, or other anti-cancer therapy within the previous 4 weeks; no nitrosoureas or mitomycin C within the previous 6 weeks; no investigational agents within the previous 4 weeks.
• Clinically significant history of liver disease, including viral or other hepatitis, current alcohol abuse, or cirrhosis.
• Untreated or active central nervous system (CNS) metastases.
• Predisposing colonic or small bowel disorders in which the symptoms are uncontrolled as indicated by baseline of > 3 loose stools daily despite medication.
• Unresolved bowel obstruction
• Any evidence of a disease or condition that might affect compliance with the protocol or interpretation of the study results or render the patient at high risk from treatment complications.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-10-2019
Enrollment:	60
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Ethics review

Positive opinion

Date:	10-10-2019
Application type:	First submission

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
NTR-new	NL8081
Other	METc VU Medisch Centrum : METc 2018.136

Study results