Multicenter, open-label, controlled, parallel arms clinical study on the performance of SGM-101, a fluorochrome-labeled anti-carcino-embryonic antigen (CEA) monoclonal antibody, for locally advanced or recurrent rectal cancer patients undergoing curative surgery.

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This study has been transitioned to CTIS with ID 2024-510768-21-00 check the CTIS register for the current data. This study aims to investigate if fluorescence guided surgery performed with SGM-101 can improve R0 resection rates and allows to find...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON56317

Source
ToetsingOnline

Brief title
SGM-101 in Locally Advanced and Recurrent Rectal Cancer

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

- Gastrointestinal therapeutic procedures

Synonym
Rectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: KWF,Quest Medical Imaging,SurgiMab

Intervention

Keyword: Fluorescence Guided Surgery, Rectal cancer

Outcome measures

Primary outcome

The primary objective is based on the clinical benefit of FGOS combined with SGM-101 as the intraoperative imaging agent. The corresponding endpoint is the rate of patients with R0 resections.

Secondary outcome

- To determine the effect of fluorescence guided surgery combined with SGM-101 on intra-operative decision making. The corresponding endpoint is the clinical benefit at the patient level; a *positive* change in surgical plan or post-surgical management. Moreover, standard of care surgery will be compared to fluorescence guided surgery and assessing if the latter allowed to remove any additional histopathologically confirmed malignant lesions and/or to resect less non-malignant tissue.

- To determine the performance of SGM-101 in the intra-operative detection of rectal cancer. The corresponding endpoint will be the tumor-to-background ratio. In addition, the concordance between fluorescent signal and

histopathologic results will be defined.

- To compare intra-operative fluorescence imaging with SGM-101 and histopathology. The corresponding endpoints will be the rate of false negatives, false positives, true negatives and true positives.
- To determine the changes in surgical planning due to FGOS combined with SGM-101 on mortality and postoperative complications caused by the surgical procedure. The corresponding endpoints are 30-day mortality and 30-day complication rates in order to substantiate the benefit/risk assessment of the use of SGM-101.
- To determine the effect of fluorescence guided surgery combined with SGM-101 on overall and disease-free survival, and to determine the effect on local recurrence rates. The corresponding endpoints will be the 2-year overall survival, 2-year disease-free survival and 2-year local recurrence free survival.

Tolerability / safety endpoints

- Treatment-emergent (serious) adverse events ((S)AEs).
- Concomitant medication
- Vital signs (pulse rate, systolic blood pressure, diastolic blood pressure and body temperature)

Study description

Background summary

In the next decade approximately 5000 patients per year will develop rectal cancer each year. the treatment of locally advanced and locally recurrent rectal cancer has evolved from a merely surgical approach to a multimodality treatment strategy. However, surgery remains the cornerstone of treatment. Since an incomplete resection (R+) is associated with high local recurrence rates and diminished disease free and overall survival, achieving a resection with clear margins (R0) is key. Besides, discriminating between tumor remnant and fibrotic tissue, caused by neoadjuvant treatment, is often difficult with preoperative magnetic resonance imaging (MRI) and peroperative visual and tactile feedback.
The compound that will be studied in this study is SGM-101, a CEA-specific chimeric antibody conjugated with a NIR emitting moiety developed by SurgiMab (Montpellier, France). The hypothesis is that, following preoperative IV administration of SGM-101 in patients with (recurrent) rectal cancer, SGM-101 will bind to CEA expressing cancer cells and these cells can then be visualized with a NIR fluorescence imaging system, thereby increasing the chance of complete resection and additional resections.
Near-infrared fluorescence-guided oncologic surgery (FGOS) with the use of a tumor specific tracer (SGM-101) developed by Surgimab can provide valuable intra-operative information about tumor location and extensiveness, which can be difficult to detect with conventional visual and tactile feedback. Hence, this information could aid in intra-operative decision making and therewith foster complete resection margins and less extensive surgery. Subsequently, this may drastically improve patient care by improving oncologic outcome.

Study objective

This study has been transitioned to CTIS with ID 2024-510768-21-00 check the CTIS register for the current data.

This study aims to investigate if fluorescence guided surgery performed with SGM-101 can improve R0 resection rates and allows to find additional malignant tissue in locally advanced and recurrent rectal cancer, or to achieve a *positive* change in surgical plan or post-surgical management and thereby improve patient related outcomes.

Study design

This is a national phase III, multicenter, open label clinical trial on the performance of SGM-101, a fluorochrome-labeled anti-carcino-embryonic antigen (CEA) monoclonal antibody, for the delineation of locally advanced and recurrent rectal cancer. Patients will be followed for a total duration of two years postoperatively.

Intervention

The proposed dose is 10 mg to be administered intravenously over 30 minutes 4 (+/-1) days prior to surgery. During surgery a fluorescence imaging device will be used to intraoperatively visualize tumor tissue.

Study burden and risks

The issues of possible concern with the use of the SGM-101 and accompanying imaging system are:
- Adverse reactions to SGM-101.
- Failure to bind to receptors;
- Fading of the chromophore (photobleaching);
- Inability to excite SGM-101 or to record emission;
- Presence of a camera in the operating room;
- Phototoxicity from the light source;
- Nonspecificity of localization;

Based on the experience with SGM-101 and other fluorescent probes, it cannot be excluded that adverse reactions, such as hypersensitivity reactions, may occur. However as discussed in paragraph 1.1, binding of anti-CEA antibodies to their target does not trigger the activation of cell signalling pathways and radiolabelled anti-CEA antibody, in over its 9 years of use, did not cause adverse effects, suggesting that toxicity associated with its use should be minimal. Nevertheless, SGM-101 will be administered under the supervision of a medical doctor with measures to deal with any potential adverse reactions.

There is no evidence to date of a failure of SGM-101 to bind to CEA in pre-clinical models, so this remains a theoretical concern. Possible mechanisms would be competitive antagonism with another ligand or a change in the molecule or receptor to hinder binding.

Like all chromophores, excitation by appropriate wavelength of light will result in molecular activation in which a different wavelength of light is emitted. This is an active process which changes the excitability of the molecule leading to photobleaching. Since white light contains all wavelengths of light, extended room light exposure could also lead to bleaching. Exposure to the excitation light source, e.g., a laser or LED source, will be limited during the procedure.

The risk that the imaging system will not excite SGM-101 or record an image after emission is minimal. An external source of SGM-101 can be used to check that the system is working. In the event of such failure, the surgeon continues as he/she would have without the system.

As proven with extensive knowledge of the Leiden University Medical Center and Catherina Hospital Eindhoven research team the presence of a camera system in the operating room is not novel and should create little problem with maintaining a sterile field. In this case, the camera will be used initially

prior to surgical excision to record the localization of tumors and post-excision to document the remaining status. As such, it needs not be intrusive during the procedure. Standard hospital procedures to ensure sterilization or masking of the equipment will be employed.

There is limited potential for phototoxicity from any light source. The degree of risk is related to the power of the beam and the extent of exposure. The power of the beam in this study is low and potential phototoxicity is negligible. There has been no adverse events reported with this system or similar systems.

While SGM-101 appears to specifically localize in colorectal carcinomas, there is a possibility that some patients will have CEA-negative tumors and will not benefit from use of this agent. The CEA expression of colorectal or pancreas cancer may not be known before surgery but most patients (>90%) will likely have CEA expressing tumors.

In this protocol, we propose different steps in order to prevent unnecessary tissue resection and subsequent potential adverse events. Resections only take place when both surgically feasible and clinically significant as judged by the surgeon. Moreover, in case of discordance between clinical inspection and NIR fluorescence imaging, it will be possible to obtain a frozen section for ad-hoc histopathology assessment at the discretion of the surgeon.

Despite these precautionary measures, an adverse event caused by unnecessary tissue resection may still occur. It is important to realize that the potential adverse reactions from unnecessary tissue resection are no other than complications expected during standard resections for colorectal cancer.

An unnecessary tissue resection is defined as resection of suspected malignant tissue (either by white light inspection or near infrared inspection), confirmed by the pathologist as non-malignant tissue. This makes a necessary tissue resection: resection of suspected malignant tissue (either by white light inspection or near infrared inspection), confirmed by the pathologist as malignant tissue.

Following on these two definitions, an unnecessary resection can occur during conventional (without SGM-101/NIR inspection) surgery and in our experimental group. As mentioned above, adverse reactions caused by an unnecessary resection are the same as adverse reactions from necessary resections. Such as bleeding (from the wound bed), hollow organ perforation and surgical site infection.

The potential benefits of SGM-101 cancer imaging in colorectal cancer are:
- Improved staging of the tumor;
- Differentiation between tumor and fibrosis allowing prevention of unnecessary removal of non-tumor tissue
- Removal of more lesions, otherwise invisible to the naked eye;

- Intraoperative detection of irradical resection (margins) and thus allowing re-resection and adequate application of IORT

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

1. Patients aged over 18 years old;
2. All women of child bearing potential and all males must practice effective contraception during the study and be willing and able to continue contraception for at least 30 days after their last dose of study treatment.
3. Patients should be scheduled and eligible for surgery because of a clinical diagnosis of T3 with a threatened CRM or T4 rectal cancer (locally advanced) or recurrent rectal cancer. (UICC. TNM classification of diseases for oncology. 3rd ed. Geneva: World Health Organization; 2000)

4. Patients should be capable and willing to give signed informed consent before study specific procedures.

Exclusion criteria

1. Other malignancies, either currently or in the past five years, except adequately treated in situ carcinoma of the cervix and basal or squamous cell skin carcinoma.
2. Patients with a history of, or recently diagnosed with, peritoneal metastases (even those diagnosed during surgery)
3. Patient with a history of a clinically significant allergy.
4. Patients pregnant or breastfeeding lack of effective contraception in male or female patients with reproductive potential;
5. Laboratory abnormalities defined as:
a. Aspartate AminoTransferase, Alanine AminoTransferase, Gamma Glutamyl Transferase) or Alkaline Phosphatase levels above 5 times the or;
b. Total bilirubin above 2 times the ULN or;
c. Serum creatinine above 1.5 times the ULN or;
d. Platelet count below 100 x 109/L or;
e. Hemoglobin below 4 mmol/L (females) or below 5 mmol/l (males);
f. Known positive test for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAG) or hepatitis C virus (HCV) antibody or patients with untreated serious infections;
6. Any condition that the investigator considers to be potentially jeopardizing the patients* well-being or the study objectives.
7. Previous administration of SGM-101

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-11-2019
Enrollment:	203
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	SGM-101
Generic name:	Fluorochrome labeled anti-carcino-embryonal antigen (CEA) monoclonal antibody

Ethics review

Approved WMO Date:	18-07-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-08-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-02-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	08-05-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-02-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28772
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EU-CTR	CTIS2024-510768-21-00
EudraCT	EUCTR2019-001748-23-NL
CCMO	NL69838.056.19
Other	NL7653
OMON	NL-OMON28772