Multicenter, semi-blinded, randomized, controlled, parallel arms clinical study on the performance of SGM-101, a fluorochrome-labeled anti-carcinoembryonic antigen (CEA) monoclonal antibody, for the delineation of primary and recurrent tumor and metastases in patients undergoing curative surgery for colorectal cancer.

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The primary objective of this clinical trial is to assess the performance of SGM-101 in theintraoperative detection of resection margins and metastases in patients undergoing curativesurgery for colorectal cancer. SGM-101 will be administered as a...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON54662

Source
ToetsingOnline

Brief title
SGM-CLIN03

Condition

- Gastrointestinal conditions NEC

Synonym
colorectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: SurgiMab
Source(s) of monetary or material Support: SurgiMab

Intervention

Keyword: anti-carcinoembryonic antigen, delineation, SGM-101, tumor

Outcome measures

Primary outcome

Primary efficacy endpoint P1 (detection rate):

The detection rate is agregated at the patient level and corresponds to the

rate of patients who have

at least one zone of interest identified under NIR only (not detectable under

WL) and pathologically

confirmed as cancer [WL negative, NIR positive, pathology positive].

Key secondary efficacy endpoint P2 (conservative surgery benefit):

The key secondary efficacy endpoint is agregated at the patient level and

corresponds to the rate of

patients who have more [WL positive, NIR negative, pathology negative lesions]

(NIR true negatives)

than [WL negative, NIR positive, pathology negative] (NIR false positive)

lesions, i.e. a net benefit in

numbers of negative lesions wrongly resected.

Secondary outcome

Assessment at the zone of interest level: For each zone of interest, a

fluorescence outcome will

be derived as either

• positive (if the use of fluorescence led to a change in the surgical plan or

post-surgery

management of the patient that was beneficial, e.g. identification and

resection of a

metastatic lesion not visible with normal light, i.e. [WL negative, NIR

positive, pathology

positive], identification of R2 margins*)

• negative (if the use of fluorescence led to a change in the surgical plan

that was potentially

deleterious, e.g. resection of some fluorescent tissue that was considered as

normal with

normal light and is confirmed as non-tumorous by pathology, i.e. [WL negative,

NIR positive,

pathology negative])

• neutral (if the use of fluorescence did not result in a change in the

surgical plan, or if it

induced a change in the plan that was neither beneficial nor detrimental).

Study description

Background summary

Technological advances have been made in cancer diagnostics and therapeutics during the last years to compensate for the high rate of death due to cancer over the world. Although modern surgical advancements have improved surgical oncology, adequate tumor visualization remains a limitation preventing total removal of cancer tissue. Surgeons rely primarily on white light reflectance, which limits the differentiation between healthy tissue and tumor and can lead to residual cancer cells inadvertently left behind [1]. Oncologic surgeons agree that advances in fluorescence imaging using targeted probes to enhance the visual capability of the operating surgeon beyond that of white-light reflectance would provide a major opportunity to improve outcomes [2]. The goal of administration of SGM-101 is to provide oncologic surgeons with an intraoperative imaging tool that will offer them pseudo-color distinction between tumor and adjacent normal tissue thus allowing them to visualize and delineate tumors overexpressing CEA, particularly colorectal tumors and their metastases.

Study objective

The primary objective of this clinical trial is to assess the performance of SGM-101 in the intraoperative detection of resection margins and metastases in patients undergoing curative surgery for colorectal cancer. SGM-101 will be administered as a single intravenous dose, at the optimal dose and according to the schedule determined in the Phase I/II studies.

To analyze the clinical benefit resulting from the use of Fluorescence Guided Surgery (FGS) during the surgical procedure, with SGM-101 as the intraoperative imaging agent, in terms of additional cancer lesions resected.detected with the goal to achieving R0

resection

Study design

This is a randomized, multicenter, semi-blinded parallel-group, Phase III study on the performance of
SGM-101, a fluorochrome-labeled anti-carcino-embryonic antigen (CEA) monoclonal antibody, for
the delineation of primary tumor, recurrent disease and metastases in patients undergoing curative
surgery for colorectal cancer.
The focus of this trial is on the evidence needed for an indication of improved visualization based on
the concordance between histopathology and tissue fluorescence. The control is standard operating
conditions or what can be called white light surgery, and each patient in the SGM-101 arm is his own
control. Indeed surgeons will have the possibility to turn the near-infrared camera on and off when
they need during the procedure, several times if necessary. Moreover there is no possibility to blind
the surgeons in such an imaging procedure as they will know immediately if the patient has received
SGM-101 when turning-on the near-infrared light.
300 patients will be randomized with an unbalanced randomization ratio of 4:1 (SGM-101 guided
surgery: saline injection and standard surgical treatment). The randomization will be stratified
according to two stratification variables:
• tumor location-and-type with the following five categories:
o cT4 colon cancer
o cT3/4 rectal cancer
o recurrent colon cancer
o recurrent rectal cancer
o peritoneal metastasized colorectal cancer
• geographical region with two categories
o USA
o Europe.
The objective of the control arm is to assess the influence of the fluorescence on the surgical
approach and thus on the safety of each patient. Indeed, for clear ethical reasons, no surgeon shall
deliberately minimize the initial resection knowing that the SGM-101 fluorescence would constitute
a back-up security on visible defects. Nor shall he be more aggressive in the presence of
fluorescence. There will be very clear instructions to follow standard of care

tumor assessment (that
has to be done in white light at the beginning of every surgical intervention).
In the SGM-101 arm
the surgeons will have the possibility to assess the presence of additional
tumor lesions by use of
fluorescence but in no case shall they modify their initial global evaluation
routine. Documentation
of patients* short-term outcome in both arms shall give sufficient information
on a possible
surgeons* bias to use an overly-aggressive approach (too much resection) caused
by fluorescence.

Intervention

Eligible and consenting patients will be randomized 4:1 to one of two groups (A
and B).
• Group A: SGM-101 injection followed by conventional then fluorescence tumor
assessment.
• Group B: Saline injection followed by standard surgical treatment -
conventional tumor
assessment
SGM-101 is a CEA-specific chimeric antibody conjugated with a NIR emitting
fluorochrome,
developed as an intraoperative imaging agent for the delineation and/or
detection of tumors.
The SGM-101 active ingredient is a covalent conjugate of the SGM-Ch511 anti-CEA
chimeric
monoclonal antibody with the fluorochrome BM-104 (Figure 1). The BM-104
fluorochrome is
conjugated to free amino groups of the antibody via a stable heterobifunctional
linker and an amide
bond.

Study burden and risks

The issues of possible concern with the use of the SGM-101 and accompanying
imaging system are:
• Presence of a camera in the operating room;
• Phototoxicity from the light source;
• Nonspecificity of localization;
• Failure to bind to receptors;
• Fading of the chromophore (photobleaching);
• Inability to excite SGM-101 or to record emission;
• Adverse reactions to SGM-101;
• Adverse events resulting from unnecessary tissue resection.
To maintain a sterile field, the camera will be used initially prior to

surgical excision to record the
localization of tumors and post-excision to document the status and does not interfere with sterility
requirements. Standard hospital procedures to ensure sterilization or masking of the equipment will
be employed.
There is a potential for phototoxicity from any light source. The degree of risk is related to the power
of the beam and the extent of exposure. Controls will be in place to ensure exposure is limited to
what is necessary to capture the images needed.
While SGM-101 appears to specifically localize to colorectal carcinomas, there is a possibility that
some patients will have CEA-negative tumors and will not benefit from the use of this agent. The CEA
expression of CRC may not be known before surgery but most patients (>90%) will have CEA
expressing tumors. In the case where the tumor would not express CEA, SGM-101 would be
eliminated with no risk for the patient.
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 resulting in altered binding.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Patients aged over 18 years old;
2. Patients should be scheduled for curative colorectal cancer surgery of primary cT4 colon cancer or primary cT3/4 rectal cancer, recurrent colorectal cancer or peritoneal metastasized colorectal cancer;
3. Female patients should not be of child-bearing potential (i.e., women with functioning ovaries who have a documented tubal ligation or hysterectomy, ovariectomy or women who are post-menopausal) nor breastfeeding. Women of child-bearing potential, including women with a documented tubal ligation, will be
included provided that they have a negative highly sensitive urine pregnancy test or a negative
serum pregnancy test at the day of the injection and agree to practice adequate contraception
for 30 days prior to administration of investigational product, and 3090 days after completion
of injection. A postmenauposal state is defined as no menses for 12 months without an
alternative medical cause. A high follicle stimulating hormone (FSH) level in the postmenopausal
range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy. However, in the absence of 12 months of
amenorrhea, a single FSH measurement is insufficient.
Acceptable forms of highly effective contraception methods are methods that can achieve a failure
rate of less than 1% per year when used consistently and correctly are considered as highly
effective birth control methods. Such methods include:
• Combined (estrogen and progestogen containing) hormonal contraception associated with

inhibition of ovulation:
o Oral;
o Intravaginal;
o Transdermal.
• Progestogen-only hormonal contraception associated with inhibition of ovulation:
o Oral;
o Injectable;
o Implantable.
• Intrauterine device (IUD) 2;
• Intrauterine hormone-releasing system (IUS) 2;
• Bilateral tubal occlusion 2;
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• Male sterilization (with the appropriate post-vasectomy documentation of the absence of
sperm in the ejaculate). For female subjects on the study, the vasectomized male partner
should be the sole partner for that subject.
• True abstinence: When this is in line with the preferred and usual lifestyle of the subject and
only if defined as refraining from heterosexual intercourse during the entire period of risk
associated with the study treatments. Periodic abstinence (e.g. calendar, ovulation,
symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of
contraception
4. Patients should be capable and willing to give informed consent before study specific procedures.

Exclusion criteria

1. Other malignancies, either currently active or diagnosed in the last 5 years, except for adequately treated in situ carcinoma of the cervix and basal or squamous cell skin carcinoma;
2. Primary appendiceal cancer;
3. Laboratory abnormalities defined as:
- Aspartate AminoTransferase, Alanine AminoTransferase, Gamma Glutamyl Transferase) or Alkaline Phosphatase levels above 5 times the ULN or;
- Total bilirubin above 2 times the ULN or;

- Serum creatinine above 1.5 times the ULN or;
- Platelet count below 100 x 109/L or;
- Hemoglobin below 4 mmol/L (females) or below 5 mmol/l (males);
4. 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;
5. Use of another investigational drug during 4 weeks before the Injection Day.
6. Any condition that the investigator considers it would potentially jeopardize the patient*s well-being or the study objectives, such as severe anaphylactic reaction in medical history, previous allergic reaction to SGM-101 or to any excipient present in the product or known hypersensitivity to murine proteins.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-05-2019
Enrollment:	150
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	SGM-101
Generic name:	fluorochrome-labeled anti-carcinoembryonic antigen (CEA) monoclonal antibody

Ethics review

Approved WMO Date:	09-01-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-04-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-12-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	01-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	09-05-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-07-2021
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2018-000151-40-NL
CCMO	NL68489.058.18