A FEASIBILITY STUDY OF SGM-101, A FLUOROCHROME-LABELED ANTI-CARCINOEMBRYONIC ANTIGEN MONOCLONAL ANTIBODY FOR THE INTRAOPERATIVE DETECTION OF COLORECTAL BRAIN METASTASES

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This study has been transitioned to CTIS with ID 2024-510767-30-00 check the CTIS register for the current data. 1. To determine the feasibility of SGM-101 for intraoperative imaging of colorectal brain metastases - Concordance between fluorescent...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON56091

Source
ToetsingOnline

Brief title
SGM-101 in colorectal brain metastases

Condition

- Metastases
- Nervous system neoplasms malignant and unspecified NEC
- Nervous system, skull and spine therapeutic procedures

Synonym
Colorectal brain metastases

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: SurgiMab

Intervention

Keyword: Brain metastases

Outcome measures

Primary outcome

Concordance between intraoperative fluorescence assessment of resected lesions

and their histopathologic result.

Secondary outcome

- Tumor to background ratio (TBR) for fluorescence in malignant and benign

tissue

- To assess the correlation between fluorescent tissue in the resection plane

and observed residual tumor or tumor progression on the routinely performed

postoperative MRI scans.

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

Brain metastasectomy is an important treatment option for brain metastases of colorectal origin. A microscopic complete resection (R0) is crucial to improve the overall survival. Unfortunately achieving a R0 resection can be challenging and is based upon preoperative imaging and intraoperative inspection and palpation to discriminate between malignant and normal tissue. To aid the surgeon in discriminating between tumor tissue and normal tissue, real-time intraoperative imaging techniques are developed. Particularly the use of tumor-specific markers coupled to fluorescent imaging moieties shows great promise for improving intraoperative staging and increase the proportion of radical (R0) resections.
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) (1). The hypothesis is that, following preoperative IV administration of SGM-101 in patients with brain metastases of colorectal origin, 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.
A recent study in colorectal cancer patients showed that additional malignant lesions were detected and resected using NIR fluorescence imaging in 6 out of 17 patients (35%) (2). Moreover, an expansion on this study (unpublished data) showed no SGM-101 related adverse events up to 15 milligrams in 75 patients. There were no trends or clinically relevant changes in vital signs, ECGs or laboratory parameters reported. Any changes in the laboratory results reported in the follow-up moments are related to the surgical procedure. Best imaging results (according to the tumor to background ratio) were achieved with 10 milligrams injected 3 to 5 days prior to surgery.
In order to increase intraoperative tumor visibility we propose a study to determine the feasibility of SGM-101 for intraoperative imaging of colorectal brain metastases. Moreover, the safety of SGM-101 will be monitored.

Study objective

This study has been transitioned to CTIS with ID 2024-510767-30-00 check the CTIS register for the current data.

1. To determine the feasibility of SGM-101 for intraoperative imaging of colorectal brain metastases
- Concordance between fluorescent signal and tumor status of resected tissue
- Concordance between the fluorescent signal and the resection margin with the use of neuronavigation
If it appears that the malignantly resected tissue is fluorescent and the tumor margin based on fluorescence is similar or even more accurate than the tumor

margin based on neuronavigation (calibrated with the preoperative MRI scan), then the fluorescent agent SGM-101 can be considered feasible for the intraoperative detection of colorectal brain metastases.
2. To assess the correlation between fluorescent tissue in the resection plane and observed residual tumor or tumor progression on the routinely performed postoperative MRI scans.
3. To determine the Tumor-to-background ratio (TBR);
4. To determine the tolerability and safety of SGM-101

Study design

This is a feasibility study of patients undergoing surgery for colorectal brain metastases. The study will consist of a total of 10 patients with brain metastases in which the feasibility of 10 mg SGM-101 will be explored during surgery. The selected dose is based on the pre-clinical and phase I/II results.

Intervention

10 mg intravenous SGM-101 will be administered over 30 minutes 3 to 5 days prior to surgery.
The imaging system that will be used in the study is a dedicated camera system from Quest Medical Imaging (QMI); the Quest Spectrum Platform, that is optimized for measurements in the NIR-spectrum. For this device ample experience for intra-operative imaging exists at HMC.

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.

As proven with extensive knowledge of the Leiden University Medical Center, the presence of a camera system in the operating room is not novel and should create little problem with maintaining a sterile field. Although neurosurgeons at the Haaglanden Medical Center already have some experience with fluorescence surgery, trained researchers from the Leiden University Medical Center will operate the camera themselves. The Quest Spectrum Platform Camera will be used initially prior to surgical excision to record the localization of tumors and post-excision to document the 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 have been no adverse events with this system or similar systems.

While SGM-101 appears to specifically localize both colorectal and pancreas 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 cancer and in particular of brain metastases may not be known before surgery but most patients will likely have CEA expressing tumors.
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. During administration of SGM-101, the infusion bag will be wrapped in aluminium foil. In addition, exposure to excitation light (laser and LED light) will be limited to necessary exposure to properly perform the study-related handlings and surgery. Previous research with SGM-101 has shown that limited exposure to excitation light does not result in decreased fluorescence signal and is therefore negligible.

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 without the system.

Based on 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, this suggests that toxicity associated with its use should be minimal.
Nevertheless SGM-101 will be administered under medical supervision of a medical doctor at the LUMC with measures to deal with any potential adverse reactions.

The potential benefits of SGM-101 cancer imaging in brain metastases of

colorectal origin are:
- Lesion removal with greater precision;
- Intraoperative detection of irradical resection (margins).

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. Signed informed consent prior to any study-mandated procedure;
2. Patients aged over 18 years old;
3. 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.
4. Has the ability to communicate well with the Investigator in the Dutch language and willing to comply with the study restrictions.

5. Diagnosed with brain metastasis of colorectal origin and scheduled for a resection.

Exclusion criteria

6. History of any anaphylactic reaction;
7. Previous use of SGM-101;
8. Other malignancies either currently active or diagnosed in the last 5 years, except adequately treated in situ carcinoma of the cervix and basal or squamous cell skin carcinoma;
9. Patients pregnant or breastfeeding (pregnancy should be ruled out by a pregnancy test within two weeks prior to administration of the conjugate);
10. Any condition that the investigator considers to be potentially jeopardizing the patient*s well-being or the study objectives (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and 12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-04-2024
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Near-infrared fluorescence imaging system
Registration:	Yes - CE outside intended use
Product type:	Medicine
Brand name:	SGM-101
Generic name:	Fluorochrome labeled anti-carcinoembryonal antigen (CEA) monoclonal antibody

Ethics review

Approved WMO Date:	13-05-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	09-11-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-12-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-09-2024
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
EU-CTR	CTIS2024-510767-30-00
EudraCT	EUCTR2020-003804-15-NL
ClinicalTrials.gov	NCT04755920
CCMO	NL74956.058.21