SGM-101 tumor-targeted fluorescence endoscopy to enable discrimination of malignant from benign tissue in rectal polyps with suspected T1 adenocarcinoma or high grade dysplasia: a feasibility study

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This study has been transitioned to CTIS with ID 2024-510769-41-00 check the CTIS register for the current data. The main objective is to investigate the feasibility of a tumour-targeted fluorescent tracer SGM-101, combined with the use of the CE-...

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

Summary

ID

NL-OMON53334

Source
ToetsingOnline

Brief title
SGM-T1

Condition

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

Synonym
polyp, rectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: subsidies A.Vahrmeijer;J.Boonstra,Surgimab S.A.S.

Intervention

Keyword: Early rectal cancer, Fluorescence Imaging, Oncology, Polyp

Outcome measures

Primary outcome

Phase I/2: Primary endpoint is the ex-vivo fluorescence TDR (T1RC/HGD to LGD ratio).

Secondary outcome

- Ex-vivo NIR-fluorescence tumour-to-background ratio (TBR) and dysplasia-to-background ratio (DBR) (ex-vivo TDR already encountered within main objective) on whole specimen (Quest open camera, PEARL), bread loafs (Quest open camera and PEARL) and slides (dedicated 700nm microscopy scanner)
- In-vivo TDR, TBR and DBR, as measured with the Quest spectrum laparoscope.
- The accuracy of SGM-101 to discriminate T1RC/HGD from LGD ex-vivo on whole specimen (Quest open camera, PEARL), bread loafs (Quest open camera and PEARL) and slides (dedicated 700nm microscopy scanner). A TDR of >=1,5 is defined as true positive. A TDR of <1.5 is defined as false negative. The accuracy is defined as the percentage of patients that are true positive. Same analysis will be performed for TBR and DBR.
-The accuracy of SGM-101 to discriminate T1RC/HGD from LGD in-vivo with the

Quest laparoscope. Accompanying endpoint is the percentage of true positives (fluorescent spot in- vivo correlated to T1RC/HGD at pathology), false negatives (no fluorescent hotspot in vivo, T1RC/HGD component at pathology), false positives (fluorescent hotspot in-vivo, no T1RC/HGD at pathology) and true negatives (no fluorescent hotspot in vivo, no T1RC/HGD at pathology).

- The correlation between in-vivo TBR/TDR and Kudo level (SM1 vs SM2/3)

- The agreement of resection margins status (R0 vs R1) assessed by fluorescence and histopathology. A resection margin is classified positive when there is a fluorescent hotspot visible in the wound bed or on the specimen.

- The ratio of tissue CEA expression of T1RC/HGD divided by LGD, to TDR. The amount of CEA expression is determined by immunohistochemistry and quantified using the immunoreactive score (IRS)[28]. The ratio is calculated by dividing the IRS of T1RC/HGD by the IRS of LGD, after which this ratio is correlated to the TDR.

Study description

Background summary

Selection of patients with early rectal cancer, T1 rectal cancer (T1RC) or high-grade dysplasia (HGD), for local resection is based on endoscopic imaging, endorectal ultrasound and/or MRI. However, all these imaging modalities have their limitations in the accurate detection of small areas of cancer in large rectal polyps [1-4]. Fluorescent guided endoscopy may offer the opportunity to aid in detecting these small cancerous areas in colorectal polyps.

Detection of T1RC or HGD in large rectal polyps is essential to select patients for the appropriate (endoscopic) resection technique [5]. Completely benign polyps, solely containing low-grade dysplasia (LGD), could be resected by piecemeal endoscopic mucosal resection (pEMR), a fast technique on which almost all endoscopists are trained. However, for rectal polyps with T1RC or HGD,

curative resection must be achieved by en-bloc resection techniques such as endoscopic submucosal dissection (ESD) or endoscopic intermuscular dissection (EID) [5]. These techniques are more complex and expensive and only a small number of endoscopists are trained on these techniques [2]. pEMR of lesions with HGD or T1RC must be avoided because they may result in irradical resections (R1) or in inconclusive histological margin assessment since the polyp is not resected en-bloc [2]. Often, this leads to unnecessary additional abdominal surgical resections.
Furthermore reported sensitivities for optical diagnosis of T1RC in a polyp are low, varying from 20.8% to 77.8% [3, 4, 6]. Because of the limited accuracy of optical diagnosis, the current Dutch guideline suggest that rectal polyps >3cm should be resected in an en-bloc manner, although it has been demonstrated that only 10.2% of rectal polyps >3cm contain a malignant component [6]. Similarly, in recent studies it was shown that 10-15% of entirely benign polyps were removed by abdominal surgery rather than endoscopically. This has major implications for the patient since surgical resection is associated with considerable morbidity [7]. Therefore, we are in need of a technique that provide the endoscopist with real-time information about specific molecular features of the tumor to differentiate between benign polyps with LGD amenable for pEMR and those that contain HGD or T1RC that require en-bloc resection.
Tumor targeted fluorescence-guided surgery (FGS) has emerged as a technique with the potential to enable real-time lesion visualization based on specific molecular features rather than on morphology [8]. Recently it was shown that carcinoembryonic antigen (CEA) is overexpressed in approximately 75% of HGD/T1RC [9]. Additionally, expression in LGD was (nearly) absent in 66% of low-grade dysplastic tissue and in 98% of normal rectum tissue, making it a suitable marker for distinguishing T1RC and HGD from LGD and normal tissue. CEA can be targeted by SGM-101, an anti-CEA antibody attached to a fluorophore which has been studied in several clinical studies for patients with colorectal cancer undergoing surgery [10-14]. We hypothesize that the use of SGM-101 during endoscopy aids the endoscopist in discriminating benign polyps with solely LGD from polyps containing HGD/T1RC.

Study objective

This study has been transitioned to CTIS with ID 2024-510769-41-00 check the CTIS register for the current data.

The main objective is to investigate the feasibility of a tumour-targeted fluorescent tracer SGM-101, combined with the use of the CE-marked fluorescence-laparoscope of Quest Medical Imaging, to discriminate between normal, LGD and malignant tissue (HGD, T1RC) in patients with suspected T1/HGD rectal cancer.
It consists of two phases for which primary objectives are defined separately:
Phase I: Dose optimization phase to determine the optimal dose of SGM-101
Phase II: feasibility assessment of tumor-targeted fluorescence endoscopy with the use of SGM-101 in discriminating normal, LGD and malignant tissue (HGD,

T1RC).

Study design

This is a single center prospective, non-randomized phase 2 proof of concept study, on the performance of SGM-101 to discriminate HGD/T1RC from LGD in patients that will be scheduled for endoscopic local en-bloc resection in the Leiden University Medical Centre (LUMC).

Intervention

In total 20 patients will be included. The first 3 patients with large rectal polyps in the distal and mid-rectum scheduled for a local endoscopic en-bloc resection, will receive a single dose of 10mg SGM-101 4 days (+-1) prior to surgery, the optimal dose in our previous study in patients undergoing surgery for advanced colorectal cancer [12]. During abdominal surgery, visualization of the tumor can be hampered by overlying colon and other tissue. During endoscopic intraluminal imaging, the tumor can directly be visualized, and a smaller dose of SGM-101 could suffice. Therefore, the consecutive 3 patients will receive 5mg 4 days (+-1) prior to endoscopy. If after analysis of the first 6 patients normal tissue and LGD are oversaturated as assessed by intensity and TBR then the next group will consist of 3 patients receiving 2mg. In the unlikely event that no adequate differentiation can be achieved between tumor (T1RC/HGD) and dysplasia (LGD) in the first 6 patients due to low maximum fluorescence intensity and a low TDR, dose-escalation to 15mg SGM-101 will be considered. The remaining patients will receive the dose of the group that provided the highest T1RC/HGD to LGD ratio - from now on defined as tumor-to-dysplasia ratio (TDR). If no difference between these treatment groups is observed, we will continue with the lowest dose. If uncertainty about the optimal dose persists after this first interim analysis, a second interim analysis will be conducted after 13 patients have been included (10 patients in one dosing group and 3 patients in the other). Based on the findings from this analysis, the dose for the remaining 7 patients can be adjusted to 2 mg, 5 mg, 10 mg, or 15 mg. Imaging will be performed with the CE-marked Quest Spectrum system intraluminally and on the back table, respectively with the laparoscope and open imaging camera. Under propofol sedation a standard transanal minimal invasive surgery (TAMIS) seals port (Applied medical) will be placed and fluorescent imaging will be performed using the Quest Spectrum laparoscope. After careful fluorescent imaging, a local endoscopic en-bloc resection will be performed according standard care [15]. Postoperative, ex-vivo imaging will be performed with the Quest open Camera and the Pearl Trilogy fluorescence imager (LI-COR, Lincoln, Nebraska). The resection specimen is pinned on cork for standard assessment by the pathologist. Additional formalin-fixed paraffin-embedded (FFPE) slides will be analyzed with a dedicated 700nm NIR-fluorescence scanner to allow for macro- and microscopic histological evaluation and the accompanied difference in SGM-101 fluorescence distribution

between T1RC/HGD, LGD and normal rectum tissue.

Study burden and risks

Patients will need to make one extra visit to the LUMC for infusion of SGM-101 4 days (+-1) prior to their intervention. This admission comprises of infusion (45 minutes) and observation (3 hours). In over its >5 years of use, SGM-101 has not caused drug related adverse effects in >250 patients, suggesting that toxicity associated with its use should be minimal. A standard TAMIS seals port will be placed and fluorescent imaging will be performed using the Quest Spectrum laparoscope. The procedure will be extended by approximately 30 minutes. In this study, no action will be taken on fluorescence. The risks for the patients are therefore deemed negligible.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Patient must have suspected HGD/T1RC and scheduled for a local endoscopic en-bloc resection. The rectum is defined as the area between the linea dentata and 10cm ab ano.
2. Age > 18 years old
3. Patients should be capable and willing to give signed informed consent before study specific procedures.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study

1. Prior participation in this study
2. Previous administration of SGM-101
3. Patients with a history of anaphylactic shock
4. Patients pregnant or breastfeeding, lack of effective contraception in male or female patients with reproductive potential
5. Any condition that the investigator considers to be potentially jeopardizing the patients* well-being or the study objectives.

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):	25-01-2024

Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Quest Spectrum Platform imaging system v2/3.0
Registration:	Yes - CE outside intended use
Product type:	Medicine
Brand name:	SGM-101
Generic name:	Fluorochrome-labeled anti-carcino-embyonicantigen (CEA) monoclonalantibody

Ethics review

Approved WMO Date:	06-03-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	23-08-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-10-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	20-09-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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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	CTIS2024-510769-41-00
EudraCT	EUCTR2023-000171-13-NL
CCMO	NL83765.058.23