Near-infrared fluorescence imaging with IndoCyanine Green for the intraoperative identification of Gastrointestinal stromal cell tumours: a pilot study

Published: 24-02-2020
Last updated: 12-04-2024

The primary objective is to achieve intraoperative detection of histologically or cytologically proven GIST and metastases with ICG and NIR fluorescence imaging. The primary end-point is the diagnostic value of ICG in detecting GIST with NIR...

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

Summary

ID

NL-OMON50040

Source
ToetsingOnline

Brief title
NITGIST

Condition

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

Synonym
GIST, stromal neoplasm

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Gastrointestinal stromal cell tumour, intraoperative identification, Near-infrared fluorescence imaging IndoCyanine

Outcome measures

Primary outcome

-number of detections of GIST and metastases through near-infrared imaging.

Secondary outcome

-tumor to background ratio will be determined, which is defined as the

fluorescence signal in the tumor compared to the fluorescence signal of the

surrounding tissue

Study description

Background summary

1.1 General
Gastrointestinal stromal cell tumours (GIST) are the most common mesenchymal neoplasms and account for 1% of primary gastrointestinal tumours. Estimations of the incidence range from 6.8 to 14.5 per million. The mean age of diagnoses is 64 years. In 85% GISTs are discovered after symptomatic clinical presentation (i.e. bleeding, pain). However, GISTs can be asymptomatic and found by chance.

Although disagreement persists about the treatment of GISTs <2cm, consensus exists that GISTs >2cm require treatment. Surgical resection is the preferred treatment modality if no sequalae is expected. Adjuvant therapy with Imatinib is indicated when sequalae are expected after surgery, to significantly improve survival. GISTs arise as a result of mutations in proto-oncogenes C-kit and PDGFR and are frequently identified by expression of the KIT protein. Imatinib is an inhibitor of receptor tyrosine kinase, product of the KIT proto-oncogene.

Secondary progression of the disease is usually observed after 24-30 months after resection, whereupon second-line treatment with Sunitinib is recommended. Surgery could be an alternative for switching to second-line treatment, since it has been shown that cytoreductive surgeries, including peritoneal lesions and liver resections, can provide survival benefit12.

Since resectability of GISTs depends upon tumour location, size and extent of spread, optimal staging and tumour identification are to be pursued. We suspect intraoperative imaging of GISTs to be useful to achieve optimal margin status in resection and cytoreductive surgery.

1.2 Intraoperative imaging
Intraoperative imaging leads to better intraoperative tumour identification and tumour demarcation in various types of tumours resulting in more radical resections and less iatrogenic harm13. Yet more progress is to be made as intraoperative imaging in gastrointestinal stromal tumours (GIST) has not been researched. Especially imaging of endoluminal GISTs is expected to contribute to improve intraoperative tumour localization. Given that GISTs frequently metastasize to liver and peritoneum, intraoperative imaging could improve staging and cytoreductive surgery of GISTs.

With the use of indocyanine green (ICG) (a well-known NIR fluorophore) and near-infrared (NIR) fluorescence imaging systems, tumours can be identified intraoperatively14. The exogenous light penetrates several millimetres in tissue and therefore has the possibility to make non-superficial structures visible. This technique could possibly also enable fluorescence imaging of GISTs.

1.3 Purpose of the study
It is necessary to demonstrate in a pilot study that primary GISTs and metastasis can be visualized with ICG and NIR fluorescence camera systems. The ultimate aim is to optimize surgery and the treatment of GISTs to improve patient outcomes (i.e. survival).

Study objective

The primary objective is to achieve intraoperative detection of histologically or cytologically proven GIST and metastases with ICG and NIR fluorescence imaging. The primary end-point is the diagnostic value of ICG in detecting GIST with NIR fluorescence imaging.
Furthermore, the signal in tumour tissue compared to the signal of the surrounding tissue, i.e. tumour-to-backgroundratio (TBR) will be determined.
* Primary objective: to assess the diagnostic value of ICG in intraoperative GIST and metastases detection

* Efficacy endpoint: tumor to background ratio will be determined, which is defined as the fluorescence signal in the tumor compared to the fluorescence

signal of the surrounding tissue

Study design

This is an open-label pilot study consisting of 10 patients diagnosed with GIST, locally or metastasized, and scheduled to undergo an elective open or laparoscopic resection in Leiden University Medical Center (LUMC) and Erasmus Medical Center (EMC). Screening will coincide with routine pre-operative screening. Patients will receive a single dose injection of 10mg ICG at an given moment during the hospitilisation prior to surgery or during surgery. The timing of administration will be determined according to a step-up, step-down procedure. The first administration will be given intra-operatively since this has proven to be most effective for peritoneal metastasis in other tumours. During surgery the surgeon will perform standard of care surgery and a NIR fluorescence imaging system will be used to record the GIST under fluorescence.

Intervention

Patients will receive a single dose injection of 10mg ICG at an given moment during hospitalization and prior to surgery or during surgery. This will be done on the surgical ward at the LUMC. During surgery the surgeon will perform standard of care surgery and a NIR fluorescence imaging system will be used to record the GIST under fluorescence.

Study burden and risks

The use of ICG for diagnostic purposes is very safe. Within the LUMC ICG is frequently used by the departments of anaesthesiology, ophthalmology and surgery. However, it cannot be excluded that hypersensitivity reactions may occur. Such reactions are generally mild and transient in nature and can be treated effectively.
Adverse events can be: headache, pruritus, urticarial, faeces discoloration (green), diaphoresis and anaphylactic reaction have been registered as adverse events of intravenous ICG. These events are uncommon. In two studies a treatment for adverse event was necessary in <0,01%.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300 RC
NL

Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300 RC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Patients diagnosed with GIST by histology or cytology scheduled to undergo an elective open or laparoscopic resection
* Patients > 18 years of age

Exclusion criteria

* History of an allergy or hypersensitivity to sodium iodide, iodine or ICG
* Patients with hyperthyroidism and patients with an autonomous thyroid adenoma
* Patients pregnant or breastfeeding
* Patients with severe renal insufficiency (eGFR <30)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-06-2020
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Verdye
Generic name:	Indocyanine green
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	24-02-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	18-08-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	15-01-2021
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	EUCTR2019-003119-77-NL
CCMO	NL67828.058.18

Study results

Actual enrolment: 7