The OCEANS II trial: Fluorescence guided surgery with indocyanine green for better visualization of small intestine neuroendocrine tumors: a feasibility study

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The aim of the study is to investigate whether SI-NETs can be visualized with indocyanine green (ICG) and near-infrared (NIR) fluorescence imaging (FLI).

Ethical review	Approved WMO
Status	Pending
Health condition type	Neoplastic and ectopic endocrinopathies
Study type	Interventional

Summary

ID

NL-OMON56479

Source
ToetsingOnline

Brief title
The OCEANS II trial

Condition

- Neoplastic and ectopic endocrinopathies
- Gastrointestinal therapeutic procedures

Synonym
hormone producing tumors, Neuro-endocrine tumors

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Fluorescence guided surgery, Indocyanine green, Neuro-endocrine tumors, Small bowel

Outcome measures

Primary outcome

The primary objective of this study is to assess feasibility of intraoperative visualization of small intestine neuroendocrine tumors (SI-NET). Feasibility is defined as a Tumor-to-Background Ratio (TBR) of >= 1.5 in at least 60% of the patients. TBR will be assessed based on in vivo measurements on the primary SI-NET.

Secondary outcome

- To asses the ex vivo TBR of the primary SI-NET

- To assess the TBR of (lymph node) metastases;

- To assess the number of extra (occult) lesions found and their fluorescence intensity;

- To assess fluorescence signal on the pathology slides;

- To assess the optimal dose of ICG to visualize the primary tumor.

Study description

Background summary

Neuroendocrine tumors of the small intestine (SI-NETs) are rare tumors.
Patients often do not present until distant metastases are already present in

the abdomen. Curative surgery is no longer possible for these patients. The clinical problem is that it is often difficult to diagnose these distant metastases. For this reason, the guidelines state to operate with a laparotomy, after which it becomes clear that distant metastases are present. It is decided not to continue the operation.

Near-infrared (NIR) fluorescence imaging (FLI) can be used to improve visualization of tumors and vital structures during surgery. A previous study showed that FLI using methylene blue (MB) is an effective method to detect metastases of SI-NETs. However, primary SI-NETs and multiple primaries could not be detected with NIR FLI using MB. Indocyanine green (ICG) can be a possible alternative of MB in detecting both primary SI-NETs and metastases. Therefore, this study aims to investigate whether a combination of intravenous indocyanine green and fluorescence imaging can visualize neuroendocrine tumors. If this is possible, in the future it can be assessed with fluorescence by means of laparoscopy whether distant metastases are present in the abdomen. In this way, a group of patients can be sparred from an unnecessary laparotomy. Moreover occult metastases can be identified for resection when curation is possible.

Study objective

The aim of the study is to investigate whether SI-NETs can be visualized with indocyanine green (ICG) and near-infrared (NIR) fluorescence imaging (FLI).

Study design

This is an open-label dose escalation study to investigate whether small intestine NETs can be visualized with ICG and NIR FLI. A maximum of 31 patients will be included who are eligible for resection of the SI-NET in the Erasmus MC. ICG will be administered at least 18 hours prior to surgery. During the operation standardized pictures of the primary tumor will be taken. The Tumor-to-Background ratio (TBR) will be measured on each photo. This is a way to measure the fluorescence intensity. Furthermore, pictures will be taken of the (lymph node) metastases. Surgical policy will not be changed based on fluorescent imaging. Biopsies will be taken (if possible) of fluorescence lesions that are not clinically suspected for tumor.

The first part of the study is the dose finding part. The first 3 patients will receive the middle dose of 2.5 mg/kg. Standardized fluorescence images will be taken and the TBR will be determined. In case of a TBR of 2.0 or higher, the next 3 patients will receive the lowest dose of 1.0 mg/kg. In case of a TBR of lower then 2.0, the next 3 patients will receive the highest dose of 4.5 mg/kg. Hereafter, an interim analysis will be performed to assess the optimal dose. The last 20 patients will receive the optimal dose.

All patients of the first part of de study will first undergo laparoscopy to investigate whether the primary tumor is visible, followed by the regular laparotomy. In case of an adequate laparoscopic detection of the primary tumor, an additional group of 5 laparoscopic patients will be added to the second part of the study.

Intervention

Patients will be administered to the hospital a day prior to surgery and will receive a single intravenous dose of ICG at least 18 hours prior to surgery (1.0 mg/kg, 2.5 mg/kg or 4.5 mg/kg).
The abdomen of the first 6 patients will first be inspected using the laparoscope via the laparotomy wound to visualize the primary tumor. No extra incisions will be made. Hereafter, laparotomy will be performed an standardized pictures with the NIR camera will be made of the primary tumor(s) and (lymph node) metastases.

Study burden and risks

Indocyanine green is a near-infrared fluorescence imaging reagent approved by the European Medicines Agency (EMA) in doses of max. 5.0 mg/kg. In this study, the maximum dose will be 4.5 mg/kg and therefor the risks of side effects will be minimal. Possible side effects will be, among others, hypersensitivity reactions. For this reason, we excluded patients known with clinically significant allergy or anaphylactic reactions to any of the components of the agent, including iodine. In addition, precautionary measures were taken, including supervised administration by qualified staff and availability of adequate medications in case of a hypersensitivity reaction. Regardless of the findings during surgery, the surgical plan will not be altered and therefore the patient risks are minimal and the patients benefits are none.

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

- Patients with lesions on the 68Ga-DOTATATE-PET-CT scan suspected for a SI-NET;
OR
- Patients with biopsy proven SI-NET;

AND
- With the primary SI-NET in situ;
- >= 18 years old;
- Obtained informed consent according to ICH/GCP, and national/local regulations.

Exclusion criteria

- Patients known with an allergy for iodine, intravenous contrast or shellfish;
- Patients with hyperthyroidism;
- Patients pregnant or breastfeeding;
- Patients with an ASA classification of 4 or higher;
- Incapacitated subjects;
- Any condition that the investigator, surgeon or anaesthesiologist considers to be potentially jeopardizing the patient*s well-being or the study objectives.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2024
Enrollment:	31
Type:	Anticipated

Ethics review

Approved WMO

Date:	12-02-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL84703.078.23