The OCEANS trial: fluorescence guided surgery with methylene blue for better visualization of small intestine neuroendocrine tumors: a feasibility study.

Published: 03-03-2021
Last updated: 08-04-2024

The aim of the study is to investigate whether SI-NET's can be visualized with Methylene Blue (MB) and near-infrared (NIR) fluorescence imaging.

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

Summary

ID

NL-OMON56617

Source
ToetsingOnline

Brief title
The OCEANS 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, Methylene blue, Neuro-endocrine tumors, Small bowel

Outcome measures

Primary outcome

The primary outcome is the Tumor to Background ratio (TBR). This is determined

on the primary tumor. A TBR> 2.0 is defined as 'feasible'. If this is the case

in at least 60% of the tumors, the method is defined as a success.

Secondary outcome

Determine the TBR of (lymph node) metastases

Determine the number of occult lesions found

Determine the optimal dose of MB

Determine the optimal time frame for the administration of MB

Determine confirmation of your signal with fluorescence microscopy

Study description

Background summary

Neuroendocrine tumors of the small intestine (SI-NET) 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 and then palpate and visualize the entire abdominal cavity. It is common for a patient to undergo a laparotomy, after which it becomes clear that distant metastases are present. It is decided not to continue the operation.

The aim of this study is to investigate whether a combination of intravenous methylene blue 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-NET's can be visualized with Methylene Blue (MB) and near-infrared (NIR) fluorescence imaging.

Study design

This is an open-label dose escalation study to investigate whether small intestinal NETs can be visualized with MB and NIR. 17 patients will be included who are eligible for resection of the SI-NET in Erasmus MC. Methylene blue will be administered after the laparotomy. In the 10 minutes after that, a standardized picture of the primary tumor will be taken every minute. The Tumor to Background ratio will be measured on each of these photos. Furthermore, pictures will be taken of the (lymph node) metastases. Surgical policy will not change based on fluorescent imaging. Biopsies will be taken (if possible) of fluorescence lesions that are not clinically suspected for metastases.

First, two groups of 5 patients will be included. The first group will receive 0.5 mg / kg MB, the second group will receive 1.0 mg/kg. After these 10 patients, an interim analysis will be performed to assess the optimal dose. The last 7 patients will receive this optimal dose.

Intervention

After the laparotomy, 0.5 - 1.0 mg / kg MB will be administered. In the 10 - 15 minutes after that, images will be made of the tumor and possibly of the (lymph node) metastases with a NIR camera.

Study burden and risks

The burden is deemed as 'nil'. MB is administered after anesthesia, so the patient will not notice this. The operation takes about 15 minutes longer for the study. After surgery, the study is finished for the patient. Methylene blue is safe and registered as a medicine. Some patient groups have a higher risk of toxicity and are therefore excluded (see exclusion criteria). In addition, this toxicity has been reported in higher doses. MB is registrered for doses up to 7 mg / kg. In this study, a maximum of 1.0 mg / kg will be used.

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 Galium-68-dotatate PET/CT scan suspected for a Small intestine Neuro-endocrine tumor (SI-NET);
OR
- Patients with biopsy proven SI-NET;

AND
- With the primary SI-NET in situ
- >= 18 years of age;
- Before patient registration, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion criteria

- Patients taking the following medication 30 days or less prior to surgery: selective serotonin reuptake inhibitors (SSRI*s), serotonin noradrenalin reuptake inhibitors (SNRI*s), tricyclic antidepressants (TCA*s), bupropion, or buspiron.
- Use of serotonergic party drugs (MDMA, ecstasy, GHB, cocaine) 30 days or less prior to surgery.
- Patients diagnosed with Glucose-6-Phosphate Dehydrogenase (G6DP) deficiency;
- Patients with a clinical significant history of allergic reaction to MB
- Patients who are pregnant or breastfeeding, female from childbearing potential without adequate contraceptives.
- 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:	Recruitment stopped
Start date (anticipated):	12-04-2021
Enrollment:	17
Type:	Actual

Ethics review

Approved WMO

Date:	03-03-2021

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	NL75203.078.20