A pilot study to assess the safety and feasibility of fluorescent sentinel lymph node identification in colon carcinoma using Indocyanine green and nanocolloid

Published: 10-02-2020
Last updated: 17-01-2025

Primary objective:The primary aim of this pilot study is to assess safety and feasibility of SLN identification using submucosal peritumoral ICG-nanocolloid injections.Secondary objectives:Secondary objectives are assessing detection rate and...

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

Summary

ID

NL-OMON49141

Source
ToetsingOnline

Brief title
FLUOR*ICG*SLN(pilot)

Condition

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

Synonym
colon carcinoma, Intestinal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Meander Medisch Centrum
Source(s) of monetary or material Support: Meander medisch Centrum

Intervention

Keyword: Colon carcinoma, Fluorescence, Indocyanine green nanocolloid, Sentinel lymph node

Outcome measures

Primary outcome

The primary outcome parameters are identification rate of SLN with

ICG-nanocolloid, defined as the number of patients with one or more SLNs

identified/total number of procedures, secondly the rate of adverse events

related towards ICG-nanocolloid will be measured. This is defined as the number

of adverse events related towards ICG-nanocolloid/total number of procedures.

Secondary outcome

Secondary outcome parameters include: False negative SLNs, true negative SLNs,

sensitivity, specificity, upstaged patients, aberrant lymph node status,

accuracy, negative predictive value and number of SLNs identified.

Study description

Background summary

The gold standard for the treatment of colon carcinoma consists of the surgical en-bloc segmental resection, including the adjacent mesocolon containing the draining lymph nodes. Analysis of these lymph nodes is important, since lymph node status is one of the most important factors determining the use of adjuvant chemotherapy. Although patients with tumour stage I and II do not have lymph node metastasis, 15-20% develop recurrent disease. Several studies suggest that ultrastaging techniques such as immunohistochemistry (IHC) or reverse transcriptase polymerase chain reaction (RT-PCR) using multilevel

slicing result in upstaging of 14-18% of patients, due to newly found (micro) metastasis. Furthermore, several studies indicate that these micrometastasis are correlated with a significantly poorer prognosis, subsequently suggesting that this subgroup of patients might benefit of adjuvant chemotherapy.

However, ultrastaging techniques are labour- and cost intensive, and are therefore not suitable for analyses of all lymph nodes that have been collected during segmental colectomy. Sentinel lymph node (SLN) identification in colon carcinoma might overcome this problem by detecting the draining lymph node of the tumour, with the highest chance of containing metastatic tumour cells. Several studies aimed at SLN identification in colon carcinoma have been published, however, early studies using radio-guided or blue-dye guided SLN identification, showed relatively high rates of false negatives with consequent low sensitivity rates. Since mesocolon is rather fatty tissue, visualization of conventional dyes is difficult. Indocyanine green (ICG), which can be visualized using near infrared (NIR), has been put forward since I is known to penetrate relatively deep into living tissue.

Nevertheless, results of SLN identification using ICG remain unsatisfying with high false negative rates and low sensitivity. Most likely this is due to the fact that these studies included large tumours, patients with massive lymph node involvement, which are factors known to interfere with lymph drainage patterns. Furthermore, subserosal injections were frequently used, while it is suggested that submucosal injections might result in better sensitivity of the procedure. And finally, all studies in colon carcinoma use ICG alone, while ICG-nanocolloid is suggested to improve the visibility of ICG, by increasing the size of the particle complex. Therefore this prospective study aims to assess the safety and feasibility of lymph node identification using ICG-nanocolloid in patients with T1-T2 tumours, without gross lymph node involvement, using peritumoral submucosal injections.

Study objective

Primary objective:
The primary aim of this pilot study is to assess safety and feasibility of SLN identification using submucosal peritumoral ICG-nanocolloid injections.

Secondary objectives:
Secondary objectives are assessing detection rate and sensitivity of SLN identification, assessing the incidence of micrometastases after ultrastaging and studying adverse reactions towards ICG-nanocolloid.

In case safety and feasibility are adequate during this pilot study, this might result in setting up a larger multi-centre prospective cohort aimed at identifying the effectivity of the SLN identification procedure.

Study design

This is a single-centre, open-label, non-randomized cohort safety and feasibility study.

Intervention

1. Patients are identified at the outpatient clinic and asked for participation in the study.
2. Patients will be planned for robot-assisted surgical colectomy according to standard of care (SOC).
3. Mechanical bowel preparation (MBP) will take place one day prior to surgery
4. During segmental colectomy, a colonoscopy will be performed. Subsequently the gastroenterologist will inject ICG-nanocolloid peritumoral and submucosal.
5. The NIR system of DaVinci Xi (Firefly) is used to visualize the SLN, which will be marked using a stitch. If an aberrant lymph node is visualized, this node will be harvested.
6. Segmental colectomy with procurement of the adhering mesocolon will be performed according SOC.
7. After extraction of the specimen, ex-vivo examination of the specimen using the Firefly will be performed.
8. Pathological examination will be done using H&E. All tumour negative lymph nodes will be examined using serial slicing and subsequent IHC and RT-PCR.
9. Postoperative management will be according SOC.

Study burden and risks

The potential benefits or harms of the patients are based on the difference in staging that could potentially be an effect of the ultrastaging techniques. If macrometastases are detected during ultrastaging techniques, patients will be given adjuvant chemotherapy, however if micrometastases are detected during ultrastaging techniques, adjuvant chemotherapy is not given. This is according to the Dutch guideline for colorectal cancer. A potential benefit of this study could be that patients receive adjuvant chemotherapy, while this was not seen with regular staging techniques.

Since patients will receive an additional colonoscopy, preceded by an additional MBP, patient have an additional risk of complications associated with MBP and colonoscopy, even though the risk is rather small.

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

- Oral and written informed consent (IC)
- Aged 18 years and older
- Pathologically confirmed and/or suspected colon carcinoma

Exclusion criteria

- Distant metastases
- Suspicion of T3-T4 disease based on pre-operative assessment.
- Metastatic or T4 disease discovered during intraoperative staging
- A tumour too large to pass endoscopically
- Pregnant patients
- Known allergy to any of the compound used for SLN identification (ICG, Iodine)
- Suspected or proven lymph node metastasis
- Previous colon surgery
- Contra-indication for robotic surgery
- Ink marking close to the tumour

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-09-2020
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	10-02-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	23-03-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2019-003179-20-NL
CCMO	NL71065.100.19

Study results

Date completed: 01-12-2021

Results posted: 10-01-2022

Actual enrolment: 10

First publication
01-01-1900