Fluorescence visualisation during lymph node procedure in pediatric patients

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The standard-of-care sentinel lymph node (SLN) procedure in paediatric cancer patients consists of a preoperative intradermal injection with 99mTechnetium-nanocolloid as radiotracer in combination with an intraoperative injection of blue dye for...

Ethical review	Not applicable
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON28104

Source
Nationaal Trial Register

Brief title
TBA

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Health condition

Melanoma or sarcoma of extremity or head/neck/trunk

Research involving
Human

Sponsors and support

Primary sponsor: Prinses Maxima Centrum
Source(s) of monetary or material Support: Prinses Maxima Centrum

Intervention

- Surigical procedure

Explanation

Outcome measures

Primary outcome

The intraoperative detection of SLNs in paediatric patients who received a pre-operative injection of ICG-99mTc-nanocolloid without blue dye.

Secondary outcome

1. Evaluation of NIR fluorescence for the SLN procedure by the surgeon by means of a short questionnaire; 2. Correlation between NIR fluorescent and radioactive SLNs; 3. Number of failures to find the preoperatively detected SLN; 4. Tumor to background ratio; 5. The safety of using a pre-operative injection of ICG-99mTc-nanocolloid for the SLN procedure in paediatric patients.

Study description

Background summary

The standard-of-care sentinel lymph node (SLN) procedure in paediatric cancer patients consists of a preoperative intradermal injection with 99mTechnetium-nanocolloid as radiotracer in combination with an intraoperative injection of blue dye for optical guidance. This method has been proven to accurately detect the SLN in paediatric melanoma and sarcoma patients with a detection rate of around 95% nowadays. To localize a SLN a radiotracer such as 99mTc-nanocolloid is essential, because successful SLN identification depends on the radioactive signal detected by a handheld gamma probe. However, disadvantages of using a radiotracer are the disturbance of the radioactive signal originating from the injection site, a low spatial resolution and the fact that the surgery has to be interrupted in order to use the gamma probe. Consequently, it is sometimes difficult to find the true SLN. These limitations of the radiotracer can be abolished by using at the same time an agent that could aid optical guidance and does not interrupt the surgery. Therefore, if deemed necessary, blue dye is currently used to optically support the surgeon during the SLN procedure. However, the use of blue dye has evident disadvantages such as risk of severe allergic reactions and long lasting tattooing, in addition to the limited penetration depth and alteration of the surgical field. Furthermore, the efficacy is low with only 60% of SLNs staining blue.

In adult melanoma patients, near-infrared (NIR) fluorescence imaging using indocyanine

green (ICG) has been shown to be a safe, efficient and accurate method for intra-operative visual identification of SLNs, with a higher sensitivity (up to 97%) compared to blue dye. Furthermore, good safety profiles are also established for the paediatric population, although for other indications. Due to the high performance of ICG in adults and the good safety and favourable side-effects profile of ICG compared to blue dye, we expect that a combined intradermal injection of ICG noncovalently bound to 99mTc-nanocolloid (ICG-99mTc-nanocolloid) is able to retain or even improve the optical guidance during surgery, while preventing the considerable risk of side-effects when using blue dye.

Study objective

The standard-of-care sentinel lymph node (SLN) procedure in paediatric cancer patients consists of a preoperative intradermal injection with 99mTechnetium-nanocolloid as radiotracer in combination with an intraoperative injection of blue dye for optical guidance. This method has been proven to accurately detect the SLN in paediatric melanoma and sarcoma patients with a detection rate of around 95% nowadays. To localize a SLN a radiotracer such as 99mTc-nanocolloid is essential, because successful SLN identification depends on the radioactive signal detected by a handheld gamma probe. However, disadvantages of using a radiotracer are the disturbance of the radioactive signal originating from the injection site, a low spatial resolution and the fact that the surgery has to be interrupted in order to use the gamma probe. Consequently, it is sometimes difficult to find the

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In adult melanoma patients, near-infrared (NIR) fluorescence imaging using indocyanine green (ICG) has been shown to be a safe, efficient and accurate method for intra-operative visual identification of SLNs, with a higher sensitivity (up to 97%) compared to blue dye. Furthermore, good safety profiles are also established for the paediatric population, although for other indications. Due to the high performance of ICG in adults and the good safety and favourable side-effects profile of ICG compared to blue dye, we expect that a combined intradermal injection of ICG noncovalently bound to 99mTc-nanocolloid (ICG- 99mTc-nanocolloid) is able to retain or even improve the optical guidance during surgery, while preventing the considerable risk of side-effects when using blue dye.

Study design

A feasibility single-institution trial to assess the use of ICG combined with 99mTc-nanocolloid

for the SLN procedure of paediatric patients with melanoma or sarcoma of the extremity, paratesticular, head, neck or trunk. Standard-of-care SLN procedure will be performed (99mTc-nanocolloid). ICG will be premixed with 99mTc-nanocolloid prior to injection (two separate agents). In accordance with the standard-of-care SLN procedure, blue dye will be used in addition if deemed necessary by the surgeon.

Intervention

Indocyanine Green

Study burden and risks

Using ICG in adjunct to the already used 99mTc-nanocolloid does not give any extra burden for the patients, since no extra visits, physical examinations or other tests, questionnaires or diaries, injections or blood samples are needed. In addition, no significant risks were identified by our institutional prospective risk analysis other than a very small risk (<1:10.000) of an allergic reaction to ICG. In order to minimize this risk, patients with an allergy for iodine and those with a renal insufficiency are excluded from this study. Because of the favourable side-effect profile in addition to the increased SLN identification of ICG compared to blue dye, ICG is currently used as standard-of-care in many hospitals treating adult patients, showing the evident potential benefit for paediatric patients. Furthermore, although the use of the Quest NIR camera for this indication is outside its intended use, we do not expect any additional risk, because the visualization method is similar to tissue perfusion: its intended use.

Contacts

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Eligibility criteria

Age
Newborns
Newborns
Babies and toddlers (28 days-23 months)
Babies and toddlers (28 days-23 months)
Children (2-11 years)
Children (2-11 years)
Adolescents (12-15 years)
Adolescents (12-15 years)
Adolescents (16-17 years)
Adolescents (16-17 years)

Inclusion criteria

Patients <18 years with melanoma, or sarcoma of extremity or head/neck/trunk and an indication for a sentinel node procedure

Exclusion criteria

1. Allergy to iodine (since ICG is resolved in a solution containing 5% sodium iodine) 2. Hypersensitivity to ICG (not expected to be known) 3. Since in patients with severe kidney insufficiency the risk of anaphylactic reactions is increased, these patients will be excluded (eGFR<55) 4. Patients with clinical manifest hyperthyroidism/ autonomous thyroid adenoma (since iodine can influence the thyroid function and tests)

Study design

Design

Study phase:	N/A
Study type:	Interventional
Intervention model:	Single
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-07-2020
Enrollment:	22
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO

Date:	14-05-2020
Application type:	First submission
Review commission:	METC NedMec

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
NTR-new	NL7935
Other	NL71166.041.20
EudraCT	2020-000509-96

Study results

Results posted:	05-12-2023
Actual enrolment:	15

First publication
15-01-2023