Intratumoral holmium microspheres brachytherapy for patients with pancreatic cancer; a single center, non-randomized, feasibility study in an open surgical setting- the SLOTH1 study

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To test the first feasibility and safety of intratumoral 166-holmium microspheres implantation in pancreatic cancer in a controlled, open-surgery setting.

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

Summary

ID

NL-OMON49772

Source
ToetsingOnline

Brief title
SLOTH-1

Condition

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

Synonym
Pancreatic cancer, Pancreatic carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Holmium microspheres, Intratumoral injection, Micro brachytherapy, Pancreatic cancer

Outcome measures

Primary outcome

The main endpoint is to establish the feasibility of intratumoral implantation of 166Ho-PLLA-MS by evaluating the average tumour absorbed dose in Gy calculated on SPECT. Microsphere distribution, absorbed dose and non-target absorbed dose are also analysed using MRI and CT. Additionally, safety, expressed in Common Terminology Criteria for Adverse Events (CTCAE v4.0) events grade >= 3 deemed possibly, probably or definitely related to the implantation procedure or medical device implanted, is monitored. Tumor response is evaluated according to the RECIST 1.1 guidelines at 3 months.

Secondary outcome

• Safety, expressed in Common Terminology Criteria for Adverse Events (CTCAE v4.0) events grade >= 3 deemed possibly, probably or definitely related to the implantation procedure or medical device implanted.

• To evaluate the average tumour absorbed dose in Gy calculated on MR images.

• To evaluate the average tumour absorbed dose in Gy quantified using CT images

• To evaluate the distribution of absorbed dose throughout the 3D target area (dose coverage).

• To evaluate non-target dose deposition (within the pancreas and outside the

pancreas).

• To evaluate the implant efficiency.

• To evaluate tumour response according to RECIST 1.1 at 3 months.

• The implant experience using a questionnaire for the performing physician(s).

• To evaluate radiation safety aspects for operators.

Study description

Background summary

Pancreatic cancer holds one of the worst prognoses of all known malignancies. When curative resection of the tumor is no longer possible due to local advancement, only intensive palliative chemotherapy or best-supportive care remains, and survival decreases drastically to just 3% after 5 years. Minimal invasive intratumoral injection of beta-minus (β-) emitting 166-holmium microspheres (micro brachytherapy) may be feasible for patients with pancreatic cancer who are no longer eligible for surgical resection.

Study objective

To test the first feasibility and safety of intratumoral 166-holmium microspheres implantation in pancreatic cancer in a controlled, open-surgery setting.

Study design

This is a single centre, non-randomized, open label, feasibility study with a medical device in 2 to 6 patients.

Intervention

Intratumoral injection of beta-minus (β-) emitting holmium-166 poly(L-lactic acid) microspheres (166Ho-PLLA-MS, QuiremSpheres©) in a suspension of 0.9% NaCl and 0.1% Pluronic (phosphate buffer).

Study burden and risks

Patients who are eligible for inclusion will need to undergo one additional screening when compared to conventional work-up for surgical resection.

Patients need to undergo one additional CT scan which increases radiation dose; however, this is negligible when compared with the absorbed dose of the 166-holmium microspheres. Patients have an increased risk of pancreatitis, bleeding, fistula*s, or local infection. However, the mortality rate of 166Ho microsphere implantation is expected to remain the same as that of a pancreas resection, at 1%. Clear benefits are the fulfilment of a treatment wish when resection is no longer possible and the contribution to development of new therapies for pancreatic cancer in future patients. Although benefit cannot be assured, depending on stage, adjuvant/palliative care, and patient characteristics, benefits may include pain reduction, local tumor control, tumor shrinkage, and down-staging.

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

1. Female or male aged 18 years and over.
2. Diagnosis of primary borderline resectable pancreatic cancer by Dutch Pancreatic Cancer Group (DPCG) guidelines:
3. Patient is deemed eligible for surgical resection of the pancreatic cancer, however, during open surgery a more advanced disease than initially anticipated is found and resection is no longer feasible.
4. Life expectancy of 12 weeks or longer.
5. World Health Organisation (WHO) Performance status 0-1.
6. One or more measurable lesions of at least 10 mm in the longest diameter by spiral CT or MRI according to the Response Evaluation Criteria in Solid Tumours (RECIST) 1.1 criteria.
7. Negative pregnancy test for women of childbearing potential.

Exclusion criteria

1. Radiation therapy within the last 4 weeks before the start of study therapy.
2. Calcifications in the pancreas or tumour that are highly expected to obstruct the needle tract
3. Any unresolved toxicity greater than National Cancer Institute (NCI), Common Terminology Criteria for Adverse Events (CTCAE version 4.0) grade 2 from previous anti-cancer therapy.
4. Serum bilirubin > 250 µmol/l
5. Leukocytes < 4.0 10^9/l and/or platelet count < 100 10^9/l.
6. Significant cardiac event (e.g. myocardial infarction, superior vena cava (SVC) syndrome, New York Heart Association (NYHA) classification of heart disease >=2 within 3 months before entry, or presence of cardiac disease that in the opinion of the Investigator increases the risk of ventricular arrhythmia.
7. Patient is deemed ineligible for implantation of 166Ho by an expert panel (surgeon, nuclear medicine physician and researcher) due to tumour anatomy or nearby structures.
8. Pregnancy or breast feeding (women of child-bearing potential).
9. Patients suffering from psychic disorders that make a comprehensive judgement impossible, such as psychosis, hallucinations and/or depression.
10. Patients who are declared incompetent.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	13-12-2021
Enrollment:	6
Type:	Actual

Medical products/devices used

Generic name:	Intratumoral Holmium-166 microspheres
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	29-03-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-08-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-08-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL76311.091.20

Study results

Date completed: 18-02-2024

Summary results
Trial ended prematurely