A phase 1 Study to Evaluate the Safety and Feasibility of Intraoperative Detection of Clear Cell Renal Cell Carcinoma Using Indium-111-DOTA-girentuximab-IRDye800CW

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To assess the feasibility and safety of intraoperative dual-modality imaging in patients with renal cell carcinoma with Indium-111-DOTA-girentuximab-IRDye800CW. Secondary objectives are to assess how intraoperative fluorescence imaging results...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON43587

Source
ToetsingOnline

Brief title
Intraoperative dual-modality imaging in renal cell carcinoma

Condition

- Renal and urinary tract neoplasms malignant and unspecified
- Renal disorders (excl nephropathies)
- Renal and urinary tract therapeutic procedures

Synonym
clear cell renal cell carcinoma, Kidney cancer

Research involving

Human

Sponsors and support

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

Intervention

Keyword: CAIX, Fluorescence-guided surgery, Girentuximab, Radiolabeled antibodies

Outcome measures

Primary outcome

- Fluorescence intensity and radioactive signal scored by two different

surgeons.

- Safety measures of dual-labeled antibody injection

- Feasibility of dual-modality imaging.

- Dual-labeled tracer measurements:

* - Tumor to normal ratio

* - Tracer accumulation in tumor and normal tissue: percentage of the injected

dose per gram tissue, %ID/g.

* - Correlation of tracer uptake to histology, CAIX expression and tumor

viability.

- Optimal dose of the dual-labeled antibody preparation

- Pharmacokinetics of dual-labeled girentuximab: clearance.

Secondary outcome

Not applicable.

Study description

Background summary

Accurate tumor delineation is essential in cancer management. For many types of cancer, surgical resection is the best if not only chance for cure. Incomplete excision of tumor tissue however negatively affects the prognosis of the patient. Intraoperative tumor localization and resection can be enhanced using intraoperative imaging techniques (e.g. targeted radioguided or fluorescence guided surgery). A limitation of radioguided surgery is that it cannot provide a precise delineation of the tumor. Fluorescence guided surgery could allow accurate tumor delineation intraoperatively, but the penetration depth of emitted light in tissue is limited. A powerful synergy can be achieved by conjugating a radionuclide (e.g. Indium-111) and a fluorescent dye (e.g. IRDye 800CW) to an antibody against a tumor-associated antigen. Girentuximab (specifically recognizes carbonic anhydrase IX) is an excellent antibody for dual-modality image guided surgery in renal cancer in the form of Indium-111-DOTA-girentuximab-IRDye800CW. Results of preclinical studies have convincingly shown the potential of this targeted dual-modality approach, but translation to the clinic has never been performed yet. Therefore, in this study we aim to translate dual-modality image-guided surgery clinically in order to improve tumor detection and resection.

Study objective

To assess the feasibility and safety of intraoperative dual-modality imaging in patients with renal cell carcinoma with Indium-111-DOTA-girentuximab-IRDye800CW. Secondary objectives are to assess how intraoperative fluorescence imaging results compare to immunohistochemical results, to assess the pharmacokinetics of Indium-111-DOTA-girentuximab-IRDye800CW in patients and to assess the optimal dose of the dual-labeled antibody preparation.

Study design

This is a single center, single arm and open label study. The dual-label tracer will be administered to twenty-two patients presenting with a primary renal tumor or a recurrent or metastatic clear cell renal cell carcinoma lesion scheduled for surgery. Patients receive a single intravenous dose of Indium-111-DOTA-girentuximab-IRDye800CW. Four days after injection a SPECT/CT scan will be acquired, and 7 days after injection the resection will be carried out. This will be expanded with the use of dual-modality imaging intra-operatively. During surgery the fluorescent and radioactive signal of the primary tumor and lymph nodes will be visualized. Also, the kidney will be examined for remnant disease. After surgery, the surgical specimens will be

investigated to determine the accumulation of Indium-111-girentuximab-IRdye800CW in tumor tissue, surrounding normal tissue and lymph nodes. A dose escalation study will be performed (5, 10, 30, 50 mg). Three patients will be included per dose level. Ten additional patients will be included in the optimal dose level.

Intervention

- Day 0: Patients receive a single intravenous dose of Indium-111-DOTA-girentuximab-IRDye800CW (100 MBq).
- Day 4 or 5 SPECT/CT images will be acquired.
- Day 7: At day 7 surgery will be planned. This will be expanded with the use of dual-modality imaging intra-operatively. During surgery the fluorescent and radioactive signal of the primary tumor will be visualized. Also, the kidney will be examined for remnant disease.

Study burden and risks

The risks associated with the antibody injection are low. Indium-111-DTPA-girentuximab has been administered to more than 100 patients and adverse reactions have not been observed until now. Toxicity tests have been performed with IRDye800CW in rats and no adverse reactions were seen. The radiation dose due to the tracer injection is acceptable, because it is a single administration of 100 MBq Indium-111 and it gives the surgeon valuable extra information about tumor location. Patients need to undergo a SPECT/CT and blood samples will be taken for pharmacokinetic studies. On the day of surgery dual-modality imaging will be used intra-operatively. This will not be an extra risk or burden to the patient as surgery will be performed conform standard of care. Both the fluorescent camera as the gamma detector have a CE-mark and are safe. Study participation will not give direct benefit to the single patient. However, image-guided surgery using tumor-targeting dual-labeled antibodies shows the potential to significantly improve oncological surgery. Therefore this study is justified.

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

- Clinical diagnosis of primary clear cell renal cell carcinoma or a recurrent or metastatic clear cell renal cell carcinoma lesion planned for surgery;- Age over 18 years;- Signed informed consent

Exclusion criteria

- A known subtype other than clear cell RCC;- Administration of a radioisotope within 10 physical half lives prior to study enrollment

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-06-2015
Enrollment:	22
Type:	Actual

Medical products/devices used

Generic name:	1. Storz laparoscopic setup extended with fluorescence light source and filter 2. Gamma detector
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Dual-labeled girentuximab
Generic name:	Indium-111-DOTA-Girentuximab-IRdye800CW

Ethics review

Approved WMO Date:	12-01-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-03-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-06-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-01-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	13-09-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-02-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-09-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-10-2019
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
EudraCT	EUCTR2014-005403-25-NL
CCMO	NL51678.091.14