Fluorescent Guided Surgery in Penile Carcinoma using Cetuximab-800CW

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The purpose of the current study is to determine the feasibility of using MFGS using Cetuximab-800CW as an intraoperative margin assessment tool for penile carcinoma.

Ethical review	Approved WMO
Status	Pending
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON49605

Source
ToetsingOnline

Brief title
GLANS

Condition

- Skin neoplasms malignant and unspecified

Synonym
penile cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: EGFR, near infrared fluorescence, penile cancer

Outcome measures

Primary outcome

The main objective of this feasibility study is to investigate whether

cetuximab-800CW could be used for margin assessment during surgery in patients

with PSCC.

Secondary outcome

Not applicable

Study description

Background summary

The main treatment modality for Penile Squamous Cell Carcinoma (PSCC) is surgery with curative intent. There is no difference in mortality between organ sparing surgery and radical surgery, and for optimal cosmetic and functional results small resection (3-5mm) margins are used. In organ sparing surgery a tumor-positive margin of up to 36% exist. Tumor-positive surgical margins are an independent risk factor for local recurrence, which has been reported to be up to 18%. These local remaining tumor depositions can be continuous or discontinuous from the main tumor, which makes it hard for the treating surgeon to recognize them clinically. Tumor-positive margins always lead to extra, penile sparing surgery, which leads to longer hospitalization, higher exposure to anesthetic interventions and a worse psychological outcome.
Currently, no intraoperative imaging technique that provides real time feedback for resection margins exists in PSCC. Molecular fluorescence-guided Surgery (MFGS) using targeted near-infrared (NIR) optical contrast agents like for example Cetuximab-800CW is a promising technique to accommodate this need. Epidermal Growth Factor Receptor (EGFR) is overexpressed in PSCC and has safely and successfully been used as target for molecular imaging, particularly for assessment for tumor margins in head and neck squamous cell carcinoma.

Study objective

The purpose of the current study is to determine the feasibility of using MFGS using Cetuximab-800CW as an intraoperative margin assessment tool for penile carcinoma.

Study design

The study is a single-center prospective, phase1 feasibility study. In total, fifteen patients with biopsy proven PSCC will be included. 2 days before surgery, a predose of 75mg *cold* cetuximab will be administered intravenously, followed by 15mg of cetuximab-800CW intravenously, with 1 hour between start of the cold dose and the cetuximab-800CW. After 3 patients are included, an interim analysis will be performed. If a tumor to background of >2 is obtained by ex-vivo analysis, the next 12 patients will be included. If a TBR of <2 is reached, the dose of cetuximab-800CW will be increased to 25mg with the same predosing scheme, 75mg of cold cetuximab. When 3 patients are included second dose, a second interim analysis will be performed. If a tumor to background of >2 is obtained by ex-vivo analysis, 12 patients more will be included. If not, another dose of cetuximab-800CW will be used and another interim analysis will be performed after 3 patients.

Intervention

After written informed consent is obtained, patients will receive an intravenous administration of 75mg *cold* cetuximab followed by 15mg of cetuximab-800CW 1 hour after the administration of the predose. Two days after the injection of the imaging agent, fluorescence imaging is performed intraoperatively, both in vivo and ex vivo. 1 day after surgery, fluorescence imaging will again be performed during pathological processing on the excised tissue. Both intraoperatively and during the pathology process, fluorescence will be quantified by MDSFR/SFF spectroscopy.

Study burden and risks

Burden:
The extra burden the patients associated with the study procedure is an extra visit to the hospital 2 days before surgery for the administration of cetuximab-800CW. This will take approximately 2 hours. Also, the surgical procedure will be prolonged 15-20 minutes due to fluorescence imaging and spectroscopy measurements.
Risks:
Risks to study participants are mainly related to the risks of the administration of the imaging agent. No preclinical or clinical study reported higher than grade 2 adverse events using cetuximab-800CW, moreover, these studies used significant higher doses of the investigational product. Previous studies with cetuximab-800CW reported no imaging agent related serious events. Currently, a phase 2 trial is performed at the UMCG with Cetuximab-800CW (NCT03134846), no grade 2 or higher imaging agent related serious advents were reported so far.
Benefit:
Patients will have no benefit from this study directly. Surgery will be planned

as usual. During surgery, no decisions will be made based on the fluorescence imaging.

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. Biopsy confirmed diagnosis of primary or recurrent PSCC and scheduled to undergo surgical resection of primary or recurrent tumor with or without (sentinel) lymph node procedure as decided by the Urology Department of the UMCG.
2. Age >= 18 years
3. Written informed consent
4. Adequate potential for follow-up

Exclusion criteria

1. Medical or psychiatric conditions that compromise the patient*s ability to give informed consent
2. Concurrent uncontrolled medical conditions
3. Received an investigational drug within 30 days prior to the dose of cetuximab-800CW
4. Tumors at sites of which the surgeon would assess that in vivo imaging would not be feasible
5. Had within 6 months prior to enrollment: myocardial infarction, cerebrovascular accident, uncontrolled cardiac heart failure, significant liver disease, unstable angina
6. Inadequately controlled hypertension with or without current antihypertensive medications
7. History of infusion reactions to cetuximab or other monoclonal antibody therapies
8. Evidence of QT prolongation on pretreatment ECG (greater than 440 ms in males or greater than 450 ms in females)
9. Lab values that in the opinion of the primary surgeon would prevent surgical resection
10. Patients receiving Class Ia (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalol) antiarrhythmic agents
11. Magnesium, potassium and calcium deviations that might lead to cardiac rhythm (grade II or higher deviations by CTCAE)
12. Life expectancy < 12 weeks
13. Karnofsky performance status < 70%

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2020

Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Cetuximab
Generic name:	Cetuximab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Cetuximab-800CW
Generic name:	Cetuximab-800CW

Ethics review

Approved WMO Date:	25-11-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-01-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2020-002624-37-NL
CCMO	NL74185.042.20