Image guided surgery in sinonasal inverted papilloma by targeting vascular endothelial growth factor

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON45848

Source
ToetsingOnline

Brief title
SNIPER

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
benign sinonasal tumor, inverted papilloma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Benign head and neck tumors, Fluorescence, Near-infrared tracer, VEGF

Outcome measures

Primary outcome

- Macroscopic fluorescent signal levels (TBR) and tracer distribution observed by NIR fluorescence imaging using the intraoperative multispectral F2 camera system as well as the ex vivo back-table imaging;

- Macroscopic and real-time quantification of the fluorescent signal observed by means of the MDSFR/SFF spectroscopy probe (M/m3);

- Standard histopathological assessment (i.e. hematoxylin and eosin staining) to correlate fluorescent and non-fluorescent areas detected in vivo with histology using in vivo obtained biopsies and surgical specimen;

- VEGF expression by means of VEGF immunohistochemistry;

Secondary outcome

- Patient characteristics (age, sex, BMI, history and morbidity, localization and extent of SNIP, treatment outcome, blood pressure, pulse and temperature before and after tracer administration, baseline blood count/liver and kidney function, signs and symptoms before and after tracer administration);

- Surgical specimen histopathologic characteristics;

- Histopathologic examinations related to ex vivo VEGF expression and bevacizumab-IRDye800CW distribution.

Study description

Background summary

During surgical resection, it is very challenging to discriminate between sinonasal inverted papilloma (SNIP) and surrounding tissue, as SNIP is associated with inducement of granulomatous inflammation of the environment. As a result, the surgeon has to perform a thorough resection in order to remove all tumor tissue, which is associated with substantial morbidity. Clearly, there is need for an instrument that is able to guide the surgeon to discriminate between SNIP and surrounding tissue. Molecular imaging techniques using targeted optical contrast agents is a promising technique to accommodate this need. Vascular Endothelial Growth Factor (VEGF) is overexpressed in SNIP compared to normal epithelium of the sinonasal area and has been used effectively in molecular imaging.

Study objective

The main objective is to study if the conjugate bevacizumab-IRDye800CW accumulates more in sinonasal inverted papilloma than in normal sinonasal mucosa, with a TBR of *2 as cutoff value.

Study design

The current study is a non-randomized, non-blinded, prospective, single center, pilot dose-escalation study. A minimum of five and a maximum of eight patients with SNIP will be included. Five patients will be administered with 10 mg bevacizumab-IRDye800CW. An interim analysis is performed after inclusion of the first three patients to determine if a tumor-to-background ratio (TBR) of *2 is obtained by either intraoperative fluorescence in vivo measurements or by ex vivo back-table fluorescence imaging. If a TBR of *2 is found, inclusion is continued to five patients. If not, the dose is adjusted to 25 mg. Again, a similar interim analysis is performed after inclusion of the first three patients to determine the TBR.

Intervention

Patients will - after written informed consent - receive an intravenous injection of the fluorescent tracer. Two to four days later, the fluorescence guided surgery will be performed using a combination of the SurgVision F2 multispectral imaging system (SurgVision BV, *t Harde, the Netherlands) and a nasopharyngeal endoscope.

Study burden and risks

Burden:
Time investment: Patients need to visit the UMCG two to four days before their planned surgery which will take approximately two hours. Extra procedures:

1) Intravenous administration of bevacizumab-IRDye800CW.
2) The estimated time for taking fluorescence images and MDSFR-spectroscopy measurements is approximately 15 minutes. Therefore the time under general anesthesia will be prolonged.
3) Prior to surgical resection, biopsies are taken of fluorescent and non-fluorescent areas, or areas of inverted papilloma and normal mucosal lining of sinonasal cavities involved as identified by the surgeon when intraoperative fluorescent signal is not detected.
4) Immediately after resection of the inverted papilloma, biopsies will be taken from areas in the wound bed showing high fluorescent signal.

Risks:
Risks to study participants are mainly related to the, already present, risks of the surgical procedure and to the administration of the tracer in increasing dosages. A data safety monitoring board (DSMB) will not be installed as in more than two hundred patients receiving bevacizumab-IRDye800CW, no (serious) adverse events were observed.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Biopsy confirmed diagnosis of SNIP and scheduled to undergo surgical resection as decided by the Multi-Disciplinary Head and Neck Tumor Board of the UMCG;
- Age * 18 years;
- Written informed consent;
- Mentally competent person that is able and willing to comply with study procedures;
- Acceptable hematologic status, kidney function and liver function, as standard surgery protocol requires.

Exclusion criteria

- Medical or psychiatric conditions that compromise the patient*s ability to give informed consent;
- Concurrent uncontrolled medical conditions;
- Received an investigational drug within 30 days prior to the dose of the fluorescent tracer;
- Tumors at sites of which the surgeon would assess that in vivo imaging would not be feasible;
- History of myocardial infarction, cerebrovascular accident, uncontrolled cardiac heart failure, significant liver disease or unstable angina within 6 months prior to enrollment;
- Inadequately controlled hypertension with or without current antihypertensive medications;
- History of infusion reactions to bevacizumab or other monoclonal antibody therapies;
- Pregnant or lactating women. Documentation of a negative pregnancy test must be available for women of childbearing potential. Woman of childbearing potential are premenopausal women with intact reproductive organs and women less than two years after menopause;
- Lab values that in the opinion of the primary surgeon would prevent surgical resection;
- Life expectancy < 12 weeks;

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-05-2019
Enrollment:	8
Type:	Actual

Medical products/devices used

Generic name:	intraoperative fluorescence camera system
Registration:	No
Product type:	Medicine
Brand name:	bevacizumab-IRDye800CW
Generic name:	bevacizumab-IRDye800CW

Ethics review

Approved WMO Date:	09-10-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-01-2019
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	EUCTR2018-002519-93-NL
CCMO	NL66494.042.18