Fluorescence guided surgery for intra-operative detection of meningioma using Bevacizumab-IRDye800CW

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Ethical review	Approved WMO
Status	Completed
Health condition type	Nervous system neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON50918

Source
ToetsingOnline

Brief title
Fluorescence guided surgery of meningioma using Bevacizumab-800CW (LUMINA)

Condition

- Nervous system neoplasms benign
- Nervous system neoplasms benign

Synonym
meningioma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: MD/PhD bench fee B.M. Dijkstra;UMCG

Kanker Research Fonds

Intervention

Keyword: Bevacizumab-IRDye800CW, Meningioma, Molecular Fluorescence Guided Surgery

Outcome measures

Primary outcome

- Determine the optimal dose of Bevacizumab-IRDye800CW for an adequate tumor-to-background ratio (TBR) ex vivo in intracranial meningioma.

- Determine the safety profile of up to 25mg Bevacizumab-IRDye800CW in meningioma patients.

Secondary outcome

- Correlate and validate ex vivo fluorescence signals with histopathology and immunohistochemistry.

- Determine the suitability of currently available intraoperative systems (Zeiss Pentero and the Yoda).

- Quantify sensitivity and specificity of Bevacizumab-IRDye800CW for meningioma in order to make a power size calculation for a possible subsequent diagnostic accuracy study.

Study description

Background summary

Meningiomas are the most frequently occurring brain tumors in adults, accounting for one third of all cases. In the last decades, treatment of meningiomas has mainly remained unchanged. Surgical treatment of newly diagnosed meningiomas has a curative intent and aims for both complete tumor resection and preservation of neurological function. Neurosurgeons depend on visual inspection to distinguish tumor tissue from healthy surrounding brain

tissue. Unfortunately, the human eye is not competent enough to detect molecular changes in intracranial lesions that have the same color and structure, or to distinguish tumor lesions from benign scare tissue originating from a previous surgery. This is the major cause of tumor recurrence/regrowth. Currently, differentiation between meningioma tumor invasion in the dura mater or adjacent bone and reactive tissue is limited.

MFGS, a promising imaging technique for real-time intraoperative tumor detection by using a tumor-targeted fluorescence tracer, could serve as a *red-flag* imaging technique to assist in optimal tumor identification. In the UMCG, we have extensive experience with fluorescence imaging, using Bevacizumab-IRDye800CW in both preclinical and clinical setting.

Study objective

In the present study, we aim to perform a feasibility study with Bevacizumab-IRDye800CW in patients with meningioma who are scheduled for elective surgical resection. The ability of fluorescence imaging to identify residual meningioma tissue that is missed by visual inspection may have the potential to obtain the goal of complete, safe resection in the future.
Patients with complete resection (Simpson grade I) have decreased morbidity and mortality, and lower recurrence rates, compared with incompletely resected meningioma patients.

Data from this trial may be used to design further studies regarding intraoperative fluorescence detection of residual tissue in meningioma in a sufficiently powered final multicenter diagnostic accuracy study.

Study design

This trial is a non-randomized, non-blinded, prospective single-center phase I/II feasibility study to be carried out at the UMCG. A maximum number of 19 patients will be included.

The first part of the study will consist of a dose escalation scheme with three cohorts (4.5 mg, 10 mg and 25 mg Bevacizumab-IRDye800CW) of three patients each. We will start with a dosage group of 4.5 mg (n=3), followed by dosages of 10 mg (n=3) and 25 mg (n=3). After all three dosage groups have been completed (total n=9), we will evaluate the safety profile and whether the tumor can be distinguished from background tissue based on qualitative fluorescence imaging ex vivo. Background tissue will be defined as the tissue next to the tumor. The TBR will be calculated by dividing tumor fluorescence by surrounding tissue fluorescence.

For the dosing cohort, we will select either the best group, or the two best groups of the dose escalation scheme, depending on the differences between the

three cohorts at the moment of interim analysis. When a single group is selected, that cohort will be extended to 10 patients (thus including 16 patients in total in this study). When the two best groups are selected, these will first be expanded to six patients each, after which four patients will be additionally included in the best group (thus including 19 patients in total). The data from the group with a total of 10 patients will be used to perform a power size calculation for future diagnostic accuracy studies. An overview of the dose escalation scheme is displayed in figure 3.

The study will be terminated if, after the interim analysis of the first nine evaluable patients, no uptake of Bevacizumab-IRdye800CW in tumor tissue can be shown by fluorescence imaging or an inadequate TBR is determined.

Intervention

Patients will receive an intravenous dose of the fluorescent tracer (max 25 mg Bevacizumab-IRDye800CW) two to four days prior to the surgical resection at the UMCG. After an observation period of one hour directly after tracer injection, the patient can go home. The surgeries will be performed as standard of care by a neurosurgeon. Additionally, fluorescence will be detected intra-operatively using two fluorescence camera systems (Yoda and Zeiss Pentero) and it will be quantified using spectroscopy. This will add 30 minutes to the operation time.

Study burden and risks

Time investment
To decrease the burden of study procedures, we will aim to plan the surgical resection on a Monday or Tuesday. Thereby, the tracer administration and admission to hospital will coincide on Friday.

Risks
The administration risks of Bevacizumab-IRDye800CW are reported in the IMPD. No adverse events have been reported from previous administrations with the tracer in more than 200 patients. Patients will be observed for one hour after tracer administration. A crash-car with adrenalin, tavegil and prednison will be available. The intravenous injection and the use of a cannula are known to carry a small risk of infection and hematoma. Due to fluorescence imaging, operation time will be extended with 30 minutes. Risks of imaging are comparable to standard of care with the Zeiss Pentero.

Benefit
There is no direct diagnostic or treatment benefit for the patients, as all procedures are processed following standard clinical guidance. No decisions according to clinical care will be based on study results.

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

- Age >= 18 years;
- Patients with convexity or sphenoid wing meningioma determined by preoperative imaging, e.g. MRI and/or CT;
- Scheduled to undergo elective resection at the UMCG as part of the standard preoperative work- up;
- Mentally competent person who is able and willing to comply with study procedures;
- Signed written informed consent.

Exclusion criteria

- Has been injected with another Investigational Medicinal Product (IMP) within the past month;
- Concomitant malignancies, except for adequately treated basocellular carcinoma of the skin or in situ carcinoma of the cervix uteri. Subjects with prior malignancies must be disease-free for at least five years;
- Previous allergic reaction to Bevacizumab;
- Medical or psychiatric conditions that compromise the patient*s ability to give informed consent;
- Pregnant or lactating women. During standard of care, pregnancy is a contraindication for elective (neuro)surgical procedures. Therefore, the possibility of pregnancy will be discussed with women of childbearing potential (defined as premenopausal women with intact reproductive organs and women less than two years after menopause).

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-08-2021
Enrollment:	19
Type:	Actual

Medical products/devices used

Generic name:	1) SFR/SFF spectroscopy probe; 2) UMCG fluorescence imaging system "Yoda; 3) Zeiss Pentero neurosurg
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	18-05-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-05-2021
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	EUCTR2020-006141-19-NL
CCMO	NL76467.042.21