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

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25431

Source
NTR

Brief title
LUMINA trial

Health condition

Intracranial meningioma

Sponsors and support

Primary sponsor: Department of Neurosurgery, University Medical Center Groningen, Hanzeplein 1, 9713 GZ, Groningen
Source(s) of monetary or material Support: University Medical Center Groningen (MD/PhD bench fee)
UMCG Kanker Researchfonds

Intervention

Outcome measures

Primary outcome

- Optimal dose of Bevacizumab-IRDye800CW in meningioma surgery
One of the primary objectives of this pilot study is to determine the optimal dose of Bevacizumab-IRDye800CW for an adequate TBR in intracranial meningioma surgery. The ex vivo TBR will be used as primary endpoint. For that purpose, explorative statistics will be applied. The differences between paired and unpaired data will be tested using a Wilcoxon test and Mann-Whitney test respectively. Data will be presented as median values with interquartile ranges. For statistical analysis and graph design, GraphPad Prism will be used.

- Safety aspects of administration Bevacizumab-IRDye800CW
Number of participants with adverse events (AE), serious adverse events (SAE) and suspected unexpected serious adverse reaction (SUSAR) related to the use of Bevacizumab-IRDye800CW.

Secondary outcome

- Correlation of ex vivo fluorescent signal in meningioma and normal tissue with histopathology and immunohistochemistry.
- Quantification of fluorescent signal by spectroscopy.
- Ability to detect the in vivo (intra-operative) fluorescent signal in meningioma and normal tissue using the Zeiss Pentero with IR800 fluorescence module (operative microscope/optic device), and the Yoda (fluorescence camera system).
- Macroscopic quantification of the fluorescent signal of pathological confirmed meningioma.

Study description

Background summary

Rationale and objective: Meningiomas are the most frequently diagnosed intracranial tumor, and therapy is only successful (curative) with complete surgical resection. Recurrence rates increase with incomplete resection and thus, methods to improve surgical resection are needed. One of those methods is Molecular Fluorescence Guided Surgery (MFGS), by which a biomarker upregulated in tumor tissue is specifically targeted using a biomarker-specific dye, which can increase demarcation of the tumor border and/or provide better detection of residual tissue. In meningiomas, Vascular Endothelial Growth Factor A (VEGF-A) can be targeted with Bevacizumab-IRDye800CW, which is Bevacizumab labelled with a fluorophore. In this study, we aim to determine the feasibility and safety of intraoperative qualitative and quantitative imaging using Bevacizumab-IRDye800CW.

Study design: This trial is a non-randomized, non-blinded, prospective single-center phase I/II feasibility study.

Study population: Mentally competent patients with suspicion of convexity or sphenoid wing meningioma undergoing resection at the UMCG will be included in this trial. Participants must be 18 years or older.

Intervention: Patients will be given a fixed dose of Bevacizumab-IRDye800CW (4.5, 10, or 25 mg) two to four days prior to surgery. Intra-operatively, fluorescence signal will be assessed both qualitatively and qualitatively. Quantitative imaging will be performed using a standard of care neurosurgical camera system (Zeiss Pentero with IR800 module) and a newly developed fluorescence imaging system (Yoda). Qualitative assessment will be performed using spectroscopy. These measurements will be performed prior, during and after resection. Operation time will be extended with a maximum of 30 minutes. Patients will receive standard of care resection and no additional tissue will be resected based on fluorescence findings.

Main study parameters/endpoints: The primary endpoints will be 1) Discrimination between tumorous and non-tumorous tissue based on ex vivo Bevacizumab-IRDye800CW qualitative fluorescence measurements; and 2) Number of participants with adverse events (AEs), serious adverse events (SAEs) and suspected unexpected serious adverse reaction (SUSARs) related to the use of Bevacizumab-IRDye800CW.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: This study is a non-therapeutic, diagnostic feasibility study. For the participating patients, there is no diagnostic or treatment benefit related to the study. Participation may possibly produce useful scientific data for the future. The tracer Bevacizumab-IRDye800CW is an IMP, and is developed for fluorescence imaging to visualize tumors in the operative and endoscopic setting. With this imaging technique, it is possible to visualize tumors with a targeted fluorescence tumor agent, without the use of radioactive compounds. Extensive clinical experience has been obtained within the UMCG with Bevacizumab-IRDye800CW. The tracer has been administered intravenously to more than 200 patients in several clinical trials at the UMCG, in doses ranging from 4.5 mg to 50 mg. No toxicity of the tracer Bevacizumab-IRDye800CW was observed in any of these patients.

Study objective

Bevacizumab-IRDye800CW is safe for application in meningioma patients and can distinguish meningioma tissue from normal/healthy background tissue; differentiation of dural tail.

Study design

- Bevacizumab-IRDye800CW administration 2-4 days prior to surgery.
- Qualitatively and quantitatively measuring intra-operative fluorescence multiple times.
- Ex vivo analysis in the days/weeks following surgery.

Intervention

Intravenous administration of a fixed dose (4.5, 10 or 25 mg) of Bevacizumab-IRDye800CW, two to four days prior to craniotomy;

During surgery:
1. Craniotomy will be performed by one of the neurosurgeons [standard care]
2. Fluorescence will be determined qualitatively and quantitatively in vivo. This will be

performed prior to dural opening, at least once during resection, after removal of tumor bulk, and prior to closing of the dural defect.
3. The dural defect, bone flap and skin incision will be closed [standard care].
Expected prolonged operation time caused by (study-related) imaging will be around 30 minutes.

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following 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

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Has been injected with another Investigational Medicinal Product (IMP) within the past month;
- Concomitant malignancies, including metastasized colon-, rectal-, breast carcinoma, non-

small cellular lung carcinoma (NSCLC); primary epithelial ovarian-, falopian tube-, primary peritoneal- or cervical carcinoma. 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). These patients will also undergo a pregnancy test prior to tracer administration.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-08-2021
Enrollment:	19
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Plan description
Deidentified data available upon reasonable request from corresponding author.

Ethics review

Positive opinion

Date:	09-09-2021
Application type:	First submission

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
NTR-new	NL9721
Other	METC UMCG : METC 2021/044

Study results