# 89Zr-Bevacizumab PET/CT imaging of vestibular schwannomas for the prediction of bevacizumab treatment effect in patients with symptomatic neurofibromatosis type 2.

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This study has been transitioned to CTIS with ID 2024-512860-75-00 check the CTIS register for the current data. The aim of this feasibility study is to validate pre-treatment [89Zr]-bevacizumab PET/CT as an imaging biomarker for prediction of...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Inner ear and VIIIth cranial nerve disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON52411

**Source**
ToetsingOnline

**Brief title**
89Zr-Bevacizumab PET/CT imaging in NF2 patients

### Condition

- Inner ear and VIIIth cranial nerve disorders
- Nervous system neoplasms benign
- Nervous system neoplasms benign

**Synonym**
hereditary tumor syndrome, NF

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Patiëntenvereniging "Stichting Kitty"

## Intervention

**Keyword:** - [89Zr]-bevacizumab, - Neurofibromatosis type 2 (NF2), - PET/CT imaging

## Outcome measures

### Primary outcome

The primary endpoint for treatment efficacy will be the correlation of the results of the pre-treatment 89Zr-Bevacizumab with the proportion of patients with confirmed hearing response (HR) and radiographic response (RR) to bevacizumab therapy. Secondary end points are correlations with patient-reported outcome measures (PROM), cranial nerve (dys)function, renal function and nontarget schwannoma response. Vestibulair function.

### Secondary outcome

NA

# Study description

### Background summary

Neurofibromatosis type 2 (NF2) is an autosomal dominant tumor predisposition syndrome caused by mutations in the NF2 gene. The pathognomonic hallmark of NF2 is development of bilateral vestibular schwannomas (VS) and many NF2 patients also develop schwannomas of other nerves, multiple meningiomas and spinal ependymomas. Nearly all VSs in NF2-patients express vascular endothelial growth factor (VEGF), which can be selectively targeted by the monoclonal antibody bevacizumab. Bevacizumab has been shown to improve hearing function and quality of life of NF2 patients. However, not all VSs respond to bevacizumab and bevacizumab may add substantial toxicity to the patient. To avoid unnecessary

toxicity and costs for non-responding individuals, a predictive biomarker marker for treatment efficacy, such as 89Zr-Bevacizumab, could be very useful.

### Study objective

This study has been transitioned to CTIS with ID 2024-512860-75-00 check the CTIS register for the current data.

The aim of this feasibility study is to validate pre-treatment [89Zr]-bevacizumab PET/CT as an imaging biomarker for prediction of treatment response to bevacizumab treatment in patients with NF2 related (vestibular) schwannomas.

### Study design

This pilot study is a phase II, prospective study. All patients will undergo standard-of-care treatment with the sole addition of a pre-treatment [89Zr]-bevacizumab PET/CT-scan. Patients will receive 5 mg / 37 MBq [89Zr]-bevacizumab 4 days before PET/CT scan.

### Intervention

All patients will undergo intravenous infusion of 89Zr-Bevacizumab 4 days prior to baseline PET/CT.

### Study burden and risks

All patients undergo one 89Zr-Bevacizumab-PET/CT scan of head/abdomen (effective dose: <20 mSv). The procedures of PET-imaging involve patient preparation, placement of intravenous catheter, intravenous injection of the radiopharmaceutical and patient monitoring (total duration 90 min), followed by PET-acquisition after 4 days (duration ~25 min). Occurrence of infusion-related reaction (e.g. allergy) is unlikely. The radiation burden attached to each of the procedure is 19,5 mSv. All other procedures are part of clinical protocol. The proposed study does not include minors or incapacitated individuals. There will be no individual benefit for enrolled subjects.

## 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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Patients aged 18 years or older
- Confirmed diagnosis of NF2 by revised Manchester criteria (appendix C)
- Provided written informed consent
- Patients must have measurable disease, defined as at least one VS > 0.4 ml (on volumetric analysis) that can be accurately measured by contrast-enhanced T1-weighted cranial MRI scan.
- Eligible and planned for bevacizumab treatment

## Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Patients with a contra-indication for PET and MRI, such as pregnancy and metal elements.
- Patients with a known allergy to substances used in this study
- Concurrend treatment with Everolimus

# Study design

## Design

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| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 20-10-2022 |
| Enrollment: | 24 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | 89Zr-bevacizumab |
| Generic name: | 89Zr-bevacizumab |

# Ethics review

Approved WMO

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| Date: | 03-03-2020 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

Approved WMO

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|---|---|
| Date: | 18-03-2021 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |

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|---|---|
| | metc-ldd@lumc.nl |
| Approved WMO Date: | 01-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |
| Approved WMO Date: | 28-12-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |
| Approved WMO Date: | 16-01-2023 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |
| Approved WMO Date: | 10-11-2023 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |
| Approved WMO Date: | 02-04-2024 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
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## 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 |
|---|---|
| EU-CTR | CTIS2024-512860-75-00 |
| EudraCT | EUCTR2020-000156-35-NL |
| CCMO | NL72743.058.20 |