# Visualizing VEGF producing lesions in Von Hippel-Lindau disease

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Endocrine disorders congenital |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON37198

**Source**
ToetsingOnline

**Brief title**
VHL image

### Condition

- Endocrine disorders congenital
- Miscellaneous and site unspecified neoplasms benign

**Synonym**
angiogenesis, hemagioblastoma

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Groningen
**Source(s) of monetary or material Support:** subsidie van Von Hippel Lindau alliance

## Intervention

**Keyword:** biomarker, imaging, Vascular Endothelial Growth Factor, Von Hippel-Lindau disease

## Outcome measures

### Primary outcome

The primary endpoint is the detection rate of VHL associated lesions with

89Zr-bevacizumab PET scans in patients with VHLD.

### Secondary outcome

The secondary endpoint is progressive lesions after 6 months, defined as new

lesions or lesions that show an increase in size of at least 5% of the longest

diameter on MRI, or lesions that become symptomatic.

# Study description

### Background summary

Von Hippel Lindau disease (VHLD) is an inherited autosomal dominant syndrome. The commonest manifestations are cerebral and retinal hemangioblastomas, clear cell renal cell carcinomas (RCC*s), pheochromocytomas and neuroendocrine tumors of the pancreas. Patients with VHLD are characterized by a germline mutation of 1 allele of the VHL-gene, disease manifestations occur when the function of the wild type allele is also lost. Absence of a functional VHL protein results in transcription of pro-angiogenic growth factors, the most important being vascular endothelial growth factor (VEGF). Patients with VHLD are routinely screened for disease manifestations. Hemangioblastomas can remain dormant for unpredictable periods of time or present with accelerated growth. Currently there are no clinical, radiographic or molecular markers that can predict the natural history of a given lesion.
Bevacizumab is a humanized monoclonal antibody against VEGF. At the University Medical Centre Groningen, non-invasive in vivo VEGF imaging with radiolabeled bevacizumab for application in patients has been developed. We hypothesize that VEGF producing lesions in patients with VHLD can be visualized with 89Zr-bevacizumab PET imaging. When additional lesions are detectable with 89Zr-bevacizumab PET imaging, this modality can be a complementary diagnostic tool to routine investigations. Quantifying VEGF might give prognostic

information on the behaviour of individual lesions and might assist in decision making on which lesions should be excised and which lesions might respond to angiogenesis inhibitors.

### Study objective

The primary objective is to determine if disease associated lesions in patients with VHLD can be visualized with 89Zr-bevacizumab PET scans. Secondary objectives are to explore if 89Zr-bevacizumab PET imaging can differentiate progressive from non-progressive lesions in patients with VHLD and to explore relationships between angiogenesis related biomarkers and endothelial activation markers and 89Zr-bevacizumab PET uptake.

### Study design

This is a feasibility study to evaluate 89Zr-bevacizumab PET scanning as a diagnostic tool for imaging disease associated lesions in patients with VHLD. Patients must have had routine MRI scans of CNS and upper abdomen within 4 weeks of inclusion. Patients will be injected intravenously with 37 MBq, protein dose 5 mg 89Zr-bevacizumab at day 0. A PET scan will be done at day 4. Standardized uptake values (SUVs) and Relative Tissue Uptake (RTU) in disease associated lesions will be determined. After 6 months MRI scans will be repeated.

### Study burden and risks

Patients will be intravenously injected at 1 time point with 37MBq. Together with the PET-CT this results in a radiation dose of 19,5 mSv. According to ICRP 62 this radiation dose falls in category III (moderate risk).
The risk of development of a secondary malignancy is small and clinically likely not relevant.
Patients have to pay 2 extra visits to the hospital. Blood samples for biomarkers will be drawn at 2 time points, one of these time points corresponds with routine blood investigations and the other time point means an extra vena puncture.
There is no direct benefit for the patients in this study. If 89Zr-bevacizumab PET imaging however is a predictive biomarker for progressive lesions, future patients can be spared serious morbidity because treatment can be offered before lesion become symptomatic.

## 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

•clinically or genetically proven VHLD
•at least 1 measurable, VHL associated lesion on MRI
•routine MRI of the CNS and upper abdomen <= 4 weeks before inclusion
•age >= 18 years
•written informed consent must be given according to good clinical practice (GCP), and local regulations

## Exclusion criteria

•pregnancy
•any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol, those conditions should be discussed with the patient before registration in the trial

# Study design

## Design

**Study type:** Observational invasive

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

## Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 15-09-2009 |
| Enrollment: | 30 |
| Type: | Actual |

## Medical products/devices used

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

# Ethics review

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| Approved WMO Date: | 16-07-2009 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 24-07-2009 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 02-05-2011 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |

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| Approved WMO Date: | 06-09-2011 |
| Application type: | Amendment |
| 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 | EUCTR2009-011479-62-NL |
| ClinicalTrials.gov | NCT00970970 |
| CCMO | NL27519.042.09 |