

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 \leq 4 weeks before inclusion
- age \geq 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

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 15-09-2009

Enrollment: 30

Type: Actual

Medical products/devices used

Product type: Medicine

Brand name: 89Zr-bevacizumab

Generic name: 89Zr-bevacizumab

Ethics review

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)

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