89Zr-RO5323441 PET imaging in patients with recurrent glioblastoma treated with bevacizumab

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON37750

Source
ToetsingOnline

Brief title
89Zr-RO5323441 PET imaging in glioblastoma

Condition

- Nervous system neoplasms malignant and unspecified NEC
- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain tumor, recurrent glioblastoma multiforme

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Roche,Roche levert bevacizumab voor de

behandeling;RO5323441 en vergoeding van PET scans

Intervention

Keyword: bevacizumab, PET imaging, recurrent glioblastoma, RO5323441

Outcome measures

Primary outcome

89Zr-RO5323441 tumor uptake and organ distribution will be scored visually and quantitatively. Standardized uptake value (SUV) and relative uptake value (RUV) will be determined and compared in the recurrent GBM lesions and in relevant tissues at baseline and day 15.

Secondary outcome

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Study description

Background summary

Glioblastomas (GBM) account for 70% of all gliomas (80% of all malignant brain and CNS tumors) and remain the most aggressive sub-type of glioma, with a particularly poor prognosis (5 y OS 10%). Surgery aimed to complete resection is the first therapeutic modality, however, the infiltrative nature of the disease makes a complete resection nearly impossible. Currently, concomitant temozolomide and radiotherapy followed by 6 cycles of temozolomide remains the standard of care for newly diagnosed GBM. Almost all GBM patients experience relapse and there is no one generally agreed standard of care in recurrent GBM. Vascular endothelial growth factor-A (VEGF-A), a central regulator of physiological and pathological angiogenesis, is considered to play a major angiogenic role in GBM. Bevacizumab, a humanized monoclonal antibody against VEGF-A, has shown RR 28%, 6-month PFS 43% and provided a consistent clinical benefit both in terms of delayed progression and increased median overall survival over historical controls. This benefit is limited however, with the tumor eventually evading treatment by for example compensatory upregulation of angiogenic factors like placental growth factor (PlGF). Therefore, targeting PlGF could be a new strategy of tumor angiogenesis inhibition, complementary to VEGF(R) inhibition. In preclinical setting, inhibiting PlGF has shown to

inhibit growth and metastasis of various tumors. Humanized monoclonal PlGF antibody RO5323441 was evaluated in phase I trials in healthy volunteers and in cancer patients; no Dose Limiting Toxicity (DLT) was found, thus no Maximum Tolerated Dose (MTD) defined. Stable disease was observed in 6/23 patients on different dose levels. A phase I/II study of bevacizumab in combination with RO5323441 is currently ongoing in patients with recurrent GBM (NCT01308684). However, the amount of RO5323441 to reach the recurrent GBM, and how this is affected by bevacizumab treatment, are yet unknown. This can be determined by repetitive measurement of RO5323441 tumor uptake with 89Zr-RO5323441 PET.

Study objective

The objectives of this study are to assess the penetration of RO532441 into recurrent GBM by 89Zr-RO5323441 PET imaging and to quantify its uptake, to visualize and quantify 89Zr-RO5323441 organ distribution, and to measure effect of bevacizumab treatment on 89Zr-RO5323441 uptake in recurrent GBM.

Study design

This is a single center, 89Zr-RO5323441 PET imaging and bio- distribution study in patients with recurrent GBM treated with bevacizumab.

Intervention

Bevacizumab at a dose of 10 mg/kg body weight i.v. in 90 min on day 1 is given every 2 weeks in cycles of 6 weeks. 89Zr-RO5323441 will be administered i.v. at a tracer dose of 5 mg (37 MBq) on day -3 and on day 11 of cycle 1 of bevacizumab treatment. Four PET scans will be performed (2 brain only PET scans and 2 whole body PET scans). Brain only PET scans will be performed 2 hours after each 89Zr-RO5323441 administration on day -3 and day 11. Whole body PET scans will be performed 4 days after each 89Zr-RO5323441 administration (before dosing with bevacizumab on day 1 and day 15).

Study burden and risks

Bevacizumab is registered in the Netherlands for use in metastasized colon and breast cancer, in lung cancer and in advanced renal cell carcinoma and has already been tested in GBM clinical trials. Bevacizumab is expected to have clinical benefit for patients enrolled in this study and similar safety profile compared to the other indications. RO5323441 monotherapy was well tolerated in patients with advanced malignant diseases. In our study, a patient will receive a low total protein dose of 10 mg RO5323441 (2X5mg) in the tracer and it is expected that RO5323441 will not enhance bevacizumab related side effects. The total radiation dose of 89Zr-RO5323441 for a patient participating in this study would be 36 mSv for women and 30 mSv for men. According to the investigators this radiation burden is justifiable in this patient group by the

information that can be obtained in this study.

-Outpatient clinic visit with physical examination, ECG, blood and urine sample prior to start the study
- Injection with 89Zr-RO5323441 intravenously on day-3 and day 11 of cycle 1 of bevacizumab treatment, with 2 hrs observation afterwards
- 89Zr-RO5323441 PET scans on the day of tracer injection and 4 days after
- Bevacizumab infusion every 2 wks till progression, unacceptable toxicity or patients best interest
- Clinical visit, physical examination, blood and urine samples at 2-6 wks during bevacizumab treatment
- MRI scans every 6 weeks in the first 6 months of treatment (4 cycles) and every 3 months thereafter during bevacizumab treatment

Number of extra visits: 5 in the first 2 weeks + therafter 1 at every 2 wks for bevacizumab treatment

Number of extra blood samples: in the first 2 weeks 6 bloodsamples, and then at every 2 wks 1 bloodsample, not more than 25 ml/sample

Risk: radiation of 89Zr-RO5323441 PET scan, possibility of allergic recation to protein in the tracer, possible side-effect of bevacizumab tretament.

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;• WHO Performance status 0 - 2;• Histologically or biopsy proven glioblastoma at recurrence;• Patients treated with one line of systemic chemotherapy (combined treatment with temozolomide/ RT followed by 6 cycles of temozolomide is considered as one line of systemic chemotherapy).;• Adequate hematological functions: Neutrophils >= 1.5 x 109 cells/L, platelets >= 100 x 109 cells/L, Hb >= 6.2 mmol/L;• Adequate liver function: Bilirubin < 1.5 x upper limit of the normal range (ULN), alkaline phosphatase and transaminases (ASAT/ALAT) < 2.5 x ULN, INR < 1.5;• Adequate renal function:;- Serum creatinine increased * 3x ULN or/and Calculated (Cockcroft-Gault) or measured creatinine clearance > 30 mL/min;- Urine dipstick for proteinuria < 2+. Patients with >= 2+ proteinuria on dipstick urinalysis at baseline should undergo 24 hrs urine collection and must demonstrate <= 1 g of protein/24 hr;• Women of reproductive potential, female patients within one year of entering the menopause as well as males must agree to use an effective non-hormonal method of contraception during the treatment period and for at least 6 months after the last dose of bevacizumab;• Patients must be able to give written informed consent to participate.

Exclusion criteria

• Last surgical procedure (including biopsy, surgical resection, wound revision, or any other major surgery involving entry into a body cavity) < 28 days prior to start study treatment;• Current or recent (within 4 weeks of enrolment) treatment with another investigational drug or participation in another investigational study;• No radiotherapy within the 1 months prior to the diagnosis of progression;• No chemotherapy in the past 4 weeks;• Arterial or venous thrombosis <= 6 months prior to registration;• History of myocardial infarction (<= 6 months prior to inclusion), unstable angina, New York Heart Association (NYHA) Grade II or greater congestive heart failure, or serious cardiac arrhythmia requiring digoxin treatment;• Uncontrolled hypertension defined by a systolic blood pressure (BP) > 140 mm Hg and/or diastolic pressure > 100 mm Hg, with or without anti-hypertensive medication. Patients with initial blood pressure elevation are eligible if initiation or adjustment of anti-hypertensive medication lowers pressure to meet the entry criteria;• Current or recent (within 10 days of first dose of bevacizumab) use of aspirin (> 325 mg/day) or other NSAID with anti-platelet

activity or treatment with dipyramidole, ticlopidine, clopidogrel and cilostaz;• Use of therapeutic-dose oral or parenteral anticoagulants or thrombolytic agent for therapeutic (as opposed to prophylactic) purposes;• Clinically serious (as judged by the investigator) non-healing wounds, active skin ulcers or incompletely healed bone fracture;• Evidence of any active infection requiring hospitalization or antibiotics, within 2 weeks prior to day 1 of cycle 1;• Known hypersensitivity to any part of the bevacizumab formulation;• No geographical, psychological or other non-medical conditions interfering with follow-up;• Pregnant or lactating females. Serum pregnancy test to be assessed before entry in the trial

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	7
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin
Generic name:	Bevacizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	25-11-2011

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-03-2012
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	EUCTR2011-004974-27-NL
Other	het onderzoek wordt op clinicaltrials.gov gezet, NCT nummer is nog niet bekend.
CCMO	NL38507.042.11