[68Ga]Ga-PSMA-11 PET/MR-imaging of malignant intra-axial brain tumors; primary assessment of PSMA expression, optimization of compound delivery and determination of theranostic potential.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON49568

Source
ToetsingOnline

Brief title
[68Ga]Ga-PSMA-11 PET/MR-imaging of malignant intra-axial brain tumors.

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
malignant intra-axial primary brain tumors; brain metastases

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Stichting Semmy

Intervention

Keyword: Brain tumors, PET/MRI, PSMA expression

Outcome measures

Primary outcome

The main study endpoints are the tumor SUV (upon intravenous and local intra-arterial injection), the SUV tumor-to-background ratio, [68Ga]Ga-PSMA-11 biodistribution, the correlation between the SUV and the degree of immunohistochemical PSMA expression of the tumor.

Secondary outcome

Semi-quantitative comparison of tracer uptake in the tumor upon intravenous versus local intra-arterial injection of [68Ga]Ga-PSMA-11.

Study description

Background summary

PSMA is a transmembrane protein specifically expressed in the vascular endothelium of malignant brain tumors, most notably glioblastoma (GBM) and not in healthy brain parenchyma. It has been shown to be involved in (neo)angiogenesis and endothelial cell invasion. Since the development of 68Ga-labeled PSMA ligands, investigators are not only equipped to non-invasively visualize PSMA expression on GBM (neo)vasculature in vivo by means of PET, but also to use it as a therapeutic target. Therapeutic targeting of malignant brain tumor (neo)vasculature is attractive as it may be exposed to a therapeutic agent much more readily than the tumor parenchyma itself, which is protected by the blood-brain barrier. The primary aim of this study is to confirm PSMA as suitable diagnostic and theranostic target in patients with intra-axial brain tumors by means of [68Ga]Ga-PSMA-HBEC-CC ([68Ga]Ga-PSMA-11) PET. The secondary aim is to assess whether uptake is increased with

intra-arterial injection in those tumors that show uptake after intravenous injection of [68Ga]Ga-PSMA-11.

Study objective

The primary objective is to evaluate the uptake, including the distribution, of [68Ga]Ga-PSMA-11 in enhancing glioma and brain metastases eligible for (re-)resection by performing [68Ga]Ga-PSMA-11 PET/MRI scans, in order to study the potential of PSMA as a diagnostic and therapeutic target. In case of a positive [68Ga]Ga-PSMA-11 PET signal at the tumor site, the secondary objective is to perform semi-quantitative (i.e., SUVmean and SUVmax) comparison of tracer uptake in the primary tumor upon intravenous versus local intra-arterial injection of [68Ga]Ga-PSMA-11, in order to determine the optimal route of administration. Tertiary objectives are (i) to calculate SUV tumor-to-background ratio*s in order to determine PSMA specificity, (ii) to evaluate [68Ga]Ga-PSMA-11 biodistribution in order to determine sites potentially at risk for toxicity, (iii) to assess the number of lesions visualized by [68Ga]Ga-PMSA-11 PET and by MRI in order to establish whether new metastatic lesions may be found, (iv) to perform semi-quantitative lesion by lesion comparison of tracer uptake (in case of metastases), (v) to correlate the SUV of the tumor to the degree of immunohistochemical PSMA expression, (vi) to perform diagnostic interpretation of lesions (i.e., differentiation between recurrent/residual tumor and radiation necrosis).

Study design

Non-randomized, single center, prospective imaging study.

Study burden and risks

Risks associated with venous and arterial puncture (i.e., infection, rebleeding). Risks associated with catheterization of the intracranial vessels (i.e., thromboembolic events and vessel spasm, shown to be <1%). Risks associated with [68Ga]Ga-PSMA-11 injection (i.e., allergic reactions, radiation). Burden associated with the procedures mentioned above (i.e., fear of and pain from puncture). Burden associated with undergoing a PET/MRI (i.e., laying still for a certain time, noise, possible claustrophobia). Time burden (i.e., one or two hospital day visits). This study offers no benefit for patients. The study will not involve minors or incapacitated 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

- Radiologically presumed/histologically confirmed: glioma (grade II-IV) showing enhancement on post-contrast MRI; brain metastases
- Planned for (re-)resection
- Age >= 18 years old
- Good clinical condition (Karnofsky performance status score >= 70
- Ability and willingness to provide written informed consent

Exclusion criteria

- Impaired renal function: eGFR (MDRD) <30 ml/min/1,73 m2
- Impaired liver function: AST and ALT >= 2.5 x ULN
- Karnofsky Performance score of less than 70
- Previous other malignancies, except for any previous malignancy which was treated with curative intent more than 3 years prior to enrollment, and except for adequately controlled limited basal cell carcinoma of the skin, squamous carcinoma of the skin or carcinoma in situ of the cervix
- Known history of cerebrovascular disease (e.g. ischemic stroke, cerebral

hemorrhage)
- Severe claustrophobia prohibiting PET/MRI scanning
- A neurologic or psychiatric condition impairing judgement, making adequate informed consent impossible
- Any psychological, familial, sociological or geographical condition hampering participation
- Contra-indications for PET imaging (pregnancy or lactation; known allergic reaction to therapeutic radiopharmaceuticals)
- Contra-indications for MR imaging
- Contra-indications for arterial catheterization

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-03-2021
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	10-07-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-09-2020
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL73457.078.20