Pilot study on the determination of therapy resistant areas within the tumor in patients with high-grade glioma by repeated 18F-FDG-PET-CT scans.

Published: 15-11-2007
Last updated: 10-05-2024

To determine the localisation within the primary tumor of the therapy resistant cells, before and during radiotherapy to determine the accurate boost volume. To determine changes during treatment intra- and extratumoral within the irradiated area.(...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Observational invasive

Summary

ID

NL-OMON31444

Source
ToetsingOnline

Brief title
PET-CT high-grade glioma

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
high grade glioma

Research involving
Human

Sponsors and support

Primary sponsor: MAASTRO clinic

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: blood proteins, FDG-PET-CT, high grade glioma, prognosis

Outcome measures

Primary outcome

The end-point is the prediction of the localisation of the persistent tumour

cells with remaining FDG-uptake -at the end of radiotherapy compared to the

baseline PET and PET during radiotherapy,- as a function of the FDG-uptake

dynamics during radiotherapy.

Secondary outcome

not applicable

Study description

Background summary

Patients harboring a primary intracerebral high grade tumor (WHO III- IV) have a median survival of six to 12 months. Combined chemoradiotherapy with temozolomide is now the standard of care since results of the joint EORTC-NCIC phase III study randomizing between radiotherapy alone and combined radiochemotherapy with temozolomide showed a significant improvement in 2-years survival from 8% to 24% for the combined treatment arm (Stupp 2005).
A differentiation between possible responders and non-repsonders before the start of irradiation may eventual be possible by the use of 18F-FDG PET-CT.
Preliminary own results have shown that a higher metabolic activity in glioblastoma as measured on a simulation 18F-FDG PET-CT scan can be a prognosticator for shortened survival (Baumert, 2006).
Our preliminary data show that a high uptake of 18F-FDG on a PET-CT scan before radiotherapy in glioblastoma could be a marker for reduced survival.
Popperl et al showed that dual phase FDG PET imaging is superior in differentiating low-grade from high-grade recurrent astrocytomas (Popperl, 2006). Visual analysis of delineation of glioma showed that the delayed images (imaged first 0-90 min and once or twice later at 180-480 min after injection) better distinguished the high uptake in tumors relative to uptake in gray

matter. SUV comparisons also showed greater uptake in the tumors than in gray matter, brain, or white matter at the delayed times (Spence et al).
These findings support the view that by using FDG-PET scans we could image active areas within the tumor. Indeed, in vivo, a cancer is made up by different types of cells, including hypoxic cells, cells that proliferate more fast, as well as by non-malignant tissues, including inflammatory cells and vasculature.
Intra-tumor heterogeneity in malignant glioma is often oberserved and can be visualised also by current PET-CT techniques.
The dynamics of the tracer uptake in the different tumor sub-volumes may give important information about the biological characteristics as well. Indeed, the dynamics of FDG uptake per cell are dependent on the blood flow, the uptake in the cell and the phosphorylation. All these of these steps give information on the biology of the cancer in that particular area of the tumor.

Study objective

To determine the localisation within the primary tumor of the therapy resistant cells, before and during radiotherapy to determine the accurate boost volume.
To determine changes during treatment intra- and extratumoral within the irradiated area.(Intratumoral: change of up-take - decrease, increase, change of localization/ Extratumoral: effects of temporal changes in up-take - e.g. due to oedema).

Study design

Study design:
Patients treated with radical radiotherapy for a high grade glioma and post-operative visible tumour will undergo:

Standard examinations:
- A first dynamic PET-CT scan, , with standard I.V. contrast before radiotherapy (= simulation PET-CT scan acquisition). After FDG injection the acquisition time starts and continous for ca. 60 minutes.
- An MRI planning scan

Additional examinations:
- A second dynamic PET-CT scan with standard I.V. contrast in week 2 of radiotherapy.
- A third dynamic PET-CT scan with standard I.V. contrast at the end of radiotherapy (after 60 fractions, 1 fraction a day, 5 fractions a week) in week 7.
- A fourth dynamic PET-CT scan with standard I.V. contrast 3 months after radiotherapy.

- At each of these time-points, 10 ml of blood (1 EDTA tube) will be taken for

analysis of markers for hypoxia (osteopontin), inflammation (IL-6) and angiogenesis (VEGF). These markers may give more insight in the biochemical correlation of the imaging data (correlation with FDG uptake measured by SUV).

Study burden and risks

The extra burden for the patients, including the extra dual phase PET-CT scans (meaning that the patient has to lie down on the PET-CT scan from the time of FDG injection to the end of the examination which will take approximately 45 minutes, whereas in the standard situation FDG is injected, the patient in lying in a bed for 60 minutes, thereafter the scanning is done) as well as the serum samples will be mentioned by the physician. After 1-3 hours a second scan is made.

Contacts

Public
MAASTRO clinic

Postbus 5800
6202 AZ Maastricht
Nederland
Scientific
MAASTRO clinic

Postbus 5800
6202 AZ Maastricht
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

•Histologically confirmed gliomas III - IV (glioblastoma, anaplastic astrocytoma, gliosarcoma) at primary diagnosis
•WhO PFS <= 2
•Tumours which do enhance on pre-operative imaging.
•Post-operative enough visible residual tumour on PET or status after biopsy only
•Age >18 years
•Availability of deep fresh frozen tissue for molecular biologic evaluation - if possible
•Patient able to tolerate full course of conventional RT and follow serial scanning
•No previous radiotherapy to the head and neck and brain area.
•Prior neurosurgery within 6 weeks of treatment
•No previous chemotherapy before treatment of the glioma. Standard radiochemotherapy with temozolomide is not excluded
•No prior or concurrent medical condition which would make treatment difficult to complete. Medication with steroids is allowed.
•No incapacitated patients.

Exclusion criteria

No Histologically confirmed gliomas II - IV (glioblastoma, anaplastic astrocytoma, gliosarcoma) at primary diagnosis;
WHO PFS >2
Tumours which do not enhance on pre-operative imaging.
Post-operative not enough visible resiudal tumor on PET or status after biopsy only
Age < 18 years
Patient is not able to tolerate full course of conventional RT and follow serial scanning
Previous radiotherapy to the head and neck and brain area.
Prior neurosurgery not within 6 weeks of treatment
Previous chemotherapy before treatment of the glioma.
Prior or concurrent medical condition which would make treatment difficult to complete.
Incapacitated patients.

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):	30-05-2008
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	15-11-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-04-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2007-005530-36-NL
Other	is geregistreerd, nummer volgt
CCMO	NL19461.068.07