HGG-TCP High Grade Glioma Tumor Concentrations of protein kinase inhibitors

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28204

Source
NTR

Brief title
HGG-TCP

Health condition

Targeted Therapy
High-grade glioma
Kinase inhibitor
Angiogenesis

Targeted therapie
Hooggradig glioom
Kinase remmer
Angiogenese

Sponsors and support

Primary sponsor: VU University Medical Center
De Boelelaan 117, 1081 HV Amsterdam
Source(s) of monetary or material Support: fund = initiator = sponsor

Intervention

Outcome measures

Primary outcome

To determine PKI and active metabolites concentrations in tumor tissue after approximately two weeks of treatment in patients with a newly diagnosed HGG.

Secondary outcome

1) To determine the correlation of PKI and active metabolites concentrations in tumor with PKI and active metabolites concentrations in plasma- and CSF after approximately two weeks of treatment.

2) To test the feasibility of determining the (phospho)proteomic profiles and kinase activity profiles in tumor tissue and CSF after two weeks of treatment.

3) To determine whether approximately two weeks of treatment with PKIs induces significant difference of the (phospho)proteomic profiles and kinase activities of tumor tissue from study patients and from patients in a control group (without PKI treatment prior to resection).

Study description

Background summary

In clinical trials for HGG, multiple agents targeting various oncogenic signaling pathways that play an important role in the biology of HGG have been studied, but unfortunately only a small number of patients seem to benefit from these treatment strategies. Whether these disappointing results are due to a restricted drug delivery through the blood-brain barrier, or due to differential biological characteristics of these HGGs, remains unknown. To better understand these clinical observations and to find potential insight how to overcome them, we intend to measure tumor concentrations of PKIs after approximately two weeks treatment and to determine whether these tumor concentrations correlate with plasma- and CSF concentrations of PKIs. Subsequently, we intend to determine the (phospho)proteomic profiles and kinase inhibitory activity in tumor tissue from these HGG patients after approximately two weeks of treatment with a PKI.

Study objective

Our hypothesis is that changes in (phospho)proteomic and kinase activity profiles in tissue before and after treatment with PKIs should provide more insight into which differential markers can be clinically used to predict response to this type of targeted therapy. We will

investigate the feasibility of obtaining surrogate markers for response prediction provided by comparing kinase activity and (phospho)peptide levels in tumor tissues obtained from study patients (after treatment with PKIs prior to resection) and in tumor tissues obtained from patients in a control group (without treatment with PKIs prior to resection).

Study design

Patients will be treated for 2 weeks with kinase inhibitors

Intervention

Patients will be cohort-wise treated with kinase inhibitors for 2 weeks prior to surgery, which is part of standard care. During and at the end of the PKI treatment and during surgery venous bloodsamples will be taken for laboratory analysis. CSF samples will be taken for laboratory analysis during surgery.

Arm1: Drug: Sunitinib

50 mg, once daily, oral use for 14 days

Arm2: Drug: Vandetanib

300 mg, once daily, oral use for 14 days

Arm3: Drug: Erlotinib

150 mg, once daily, oral use for 14 days

Contacts

Public
De Boelelaan 1117
H.M.W. Verheul
Amsterdam 1081 HV
The Netherlands
+31 (0)20 4444321/300
Scientific
De Boelelaan 1117

H.M.W. Verheul
Amsterdam 1081 HV
The Netherlands
+31 (0)20 4444321/300

Eligibility criteria

Inclusion criteria

1. Patients without a history of brain tumor

2. Initial brain MR-scan suggesting a high grade glioma, according to the interpretation of an expert neuroradiologist

3. On initial MR-scan a tumor localisation that is deemed resectable without major neurological deficits

4. Patients must have a Karnofsky Performance Score >70%

5. Patients must have a RTOG Neurologic Function Status of 0-2

6. Patients need to have adequate hematological, renal and hepatic function as assessed by the following laboratory requirements to be conducted within seven days prior to start study treatment: - Hemoglobin > 7.0 mmol/l - Absolute neutrophil count (ANC) >1,5 x 10*9/l - Platelet count > 100 x 10*9/l - ALT and AST< 2.5 x ULN - Alkaline phosphatase < 4 x ULN - Serum creatinine eGFR > 50 ml/min

7. Patients are 18 years of older

8. Male and female patients with reproductive potential must use an approved contraceptive method during and for three months after discontinuation of study treatment

9. Patients need to give informed consent

10. Patients should be able to swallow oral medication

Exclusion criteria

1. Patients receiving prior chemotherapy, radiotherapy or anti-angiogenic therapy

2. Use of anti-coagulant therapy

3. Use of CYP3A4 enzyme-inducing drugs, other than dexamethasone (including Carbamazepine, Phenytoine, Phenobarbital)

4. Initial MR-scan of the brain showing tumor hemorrhage or intracerebral hemorrhage

5. Patients with progressive neurological symptoms despite dexamethasone

6. Inability to comply with protocol or study procedures

7. Pregnancy

8. Patients with uncontrolled arterial hypertension. Blood pressure must be <160/95 mmHg at the time of screening on a stable antihypertensive regimen.

9. Patients with a history of cardiac arrhythmias requiring anti-arrhythmic therapy (beta blockers or digoxin are permitted)

10. Patients with evidence or history of bleeding diathesis

11. Patients with a history of venous or arterial thrombo-embolic events or hemorrhagic disease during the past six months

12. Patients with a history of congestive heart failure (NYHA III, IV)

13. Patients with a history of peripheral vascular disease (Fontaine stage III and IV)

14. Patients with stroke or myocardial infarction during the past six months

15. Patients with a history of a recent peptic ulcer disease (endoscopically-proven gastric ulcer, duodenal ulcer of esophageal ulcer) during the past six months

16. Patients with uncontrolled infections (> grade 2 NCI-CTC version 4.0)

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2014
Enrollment:	15
Type:	Anticipated

Ethics review

Positive opinion

Date:	28-08-2014
Application type:	First submission

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
NTR-new	NL4609
NTR-old	NTR4760
Other	VUmc METc : 2013.465

Study results