Glioma Longitudinal AnalySiS in the Netherlands (GLASS-NL): Molecular and imaging markers for malignant evolution of IDH-mutant astrocytoma.

Published: 19-11-2019
Last updated: 09-04-2024

Primary Objective: The present study aims to generate detailed molecular characterization of paired tumor samples (i.e. obtained at first operation and at the time of tumor recurrence) of patients with glioma, with specific interest for at least 100...

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

Summary

ID

NL-OMON48720

Source
ToetsingOnline

Brief title
GLASS-NL

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
Brain tumor

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Koningin Wilhelmina Fonds;projectnummer 11026

Intervention

Keyword: Astrocytoma, Glioma, IDH, Molecular Evolution

Outcome measures

Primary outcome

The present study aims to generate detailed molecular characterization of paired tumor samples (i.e. obtained at first operation and at the time of tumor recurrence) of patients with glioma, with specific interest for at least 100 well-annotated patients with IDH-mutant (1p/19q non-codeleted) astrocytomas.

Molecular data will be correlated to clinical and imaging data of these patients to identify molecular and/or imaging markers indicative for early malignant progression.

Secondary outcome

To identify molecular alterations in the recurrent tumors that occur under pressure of different therapeutic modalities.

To identify new targets for further therapeutic interference.

Study description

Background summary

Each year, over 1000 new patients in the Netherlands are diagnosed with a glioma. The vast majority of these are so-called diffuse gliomas. Primary brain tumors account for approximately 3% of human cancers. The tumors are characterized by diffuse infiltrative growth in the brain parenchyma. Diffuse gliomas are amongst the most frequent and devastating brain tumors. Up till

now, curation of these tumors is impossible, and standard treatment (surgery, irradiation and/or chemotherapy with generally a single cytotoxic agent) has generally limited efficacy. Without exception these neoplasms thus represent a fatal disease with high disease burden. Overall survival (OS) of patients with the most malignant form of glioma, i.e. glioblastoma, is generally less than 1-1.5 years after diagnosis. Patients with a lower grade diffuse glioma have a variably longer survival, but due to the fact that these tumors are generally diagnosed in younger patients the average number of years of life lost in these patients is even higher than for patients with glioblastoma. Especially for the initially often less aggressive, IDH-mutant astrocytoma the disease course is notoriously unpredictable. In other words, it is unclear which of these tumors will rapidly progress to high grade malignancy and which patients thus need more intense treatment right away. Gliomas that recur after a first round of treatment are increasingly therapy resistant.
To improve the prognosis of patients with diffuse glioma we need a better onderstanding of tumor evalutiona and appropriate timing of treatment. In addition, we need new molecular markers of glioma that may lead to developement of better treatments for this patient group. In only a limited group of patients, a second surgical treatment can be considered. Thusfar it is clear that the progressive tumors do not always mirror the primary tumor molecularly. In addition, changes in molecular make-up of the tumor may result in different tumor responses to the treatment.
As patients that have underwent two operations to treat their tumors are scarce, large-scale collaborations are needed to help us understand the impact of treatment on evolutionary dynamics and thereby develop novel treatments to prevent and overcome resistance to treatment. GLASS-NL is part of the international GLASS consortium, that aims to perform comprehensive molecular profiling of matched primary and recurrent glioma specimens from 1,500 patients, 500 in each of the three major glioma molecular subtypes.
GLASS-NL, the first nationwide glioma consortium in the Netherlands, is driven by the extremely urgent clinical need to improve the outcome for patients suffering from a diffuse glioma. While cure of these tumors is currently impossible, there is a lot to gain by improved timing of standard treatment and by finding leads for new therapeutic strategies. Hopefully, these efforts will ultimately contribute to transform diffuse gliomas into a 'chronic disease' with not only improved survival but also increased quality of life.

Study objective

Primary Objective:

The present study aims to generate detailed molecular characterization of paired tumor samples (i.e. obtained at first operation and at the time of tumor recurrence) of patients with glioma, with specific interest for at least 100 well-annotated patients with IDH-mutant (1p/19q non-codeleted) astrocytomas.

Molecular data will be correlated to clinical and imaging data of these

patients to identify molecular and/or imaging markers indicative for early malignant progression.

Secondary Objective(s):
To identify molecular alterations in the recurrent tumors that occur under pressure of different therapeutic modalities.
To identify new targets for further therapeutic interference.

Study design

GLASS-NL (Glioma Longitudinal AnalySiS in the Netherlands) is an unprecedented collaboration of all major centers in the Netherlands treating patients with glioma. This consortium will be using the national translation research infrastructure as available and being extended by Health-RI, to collect, manage and share a critically important reference data set of patients that underwent surgery for a glioma at least twice (interval between operations is at least 6 months). At least 100 patients with IDH-mutant lower grade astrocytoma at first diagnosis will be collected as specific group of interest of the GLASS-NL consortium (see KWF proposal). Also patients with glioma that have not the IDH-mutant non-1p19q co-deleted genotype and that fulfill the general inclusion criteria of the GLASS International consortium will be collected. MR imaging results obtained in the course of the disease process will be critically reviewed in search for parameters that can be used as early indicators of malignant progression. Furthermore, the paired samples of these patients will be analyzed using whole exome sequencing, RNA sequencing and methylation profiling. Integrated data analysis will be performed in order to approach the full scope of molecular alterations in the course of time, and in relation to clinical, imaging and pathological characteristics.

Study burden and risks

Patients won*t benefit personally of being enrolled in this study. There are no significant risks for patients included in this study. The burden for patients consists of withdrawing 20 ml of blood that is preferably taken during routine laboratory investigation during routine follow-up. There are no direct risks for participating subjects because of the observational nature of the study.

Contacts

Public
Vrije Universiteit Medisch Centrum

de Boelenlaan 1117
Amsterdam 1081HV

NL
Scientific
Vrije Universiteit Medisch Centrum

de Boelenlaan 1117
Amsterdam 1081HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients are 18 years or older at first diagnosis
Patients are willing and able to give written informed consent
Diagnosis of glioma is confirmed by histological examination
Patients underwent surgery at least twice with minimal 6 months in between
Patients are willing to contribute tumor tissue of both operations to the study
Presence of normal non-neoplastic DNA or is available at time of inclusion
If no normal DNA is available, patients are willing to donate 20 ml of blood to isolate normal DNA

Exclusion criteria

Patients who do not meet the inclusion criteria will be excluded of this study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-03-2020
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO

Date:	19-11-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	21-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL66612.029.19