Platelet RNA Expression Directs Identification of Clear Tumorprogression in Glioblastoma

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

Summary

ID

NL-OMON56789

Source
ToetsingOnline

Brief title
PREDICT

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
glioblastoma, malignant brain tumor

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Koningin Wilhelmina Fonds

Intervention

Keyword: Glioblastoma, Liquid biopsy, Pseudoprogression, Tumor-educated platelets

Outcome measures

Primary outcome

The difference in platelet RNA profile between blood taken at true progression and blood taken at pseudoprogression/radionecrosis.

Secondary outcome

Established clinical prognostic factors and TEP-Glioblastoma-score will be analyzed in univariate and multivariate models of progression free and overall survival. Also, the effect of temozolomide and radiotherapy on the platelet RNA profiles will be evaluated by comparing groups of samples collected at moment of these therapies, and at moments when these therapies are not provided.
In addition, the tumor size will be correlated to the TEP-Glioblastoma-score, and the levels of individual platelet RNAs.
Finally, gene ontology analyses will be performed, aiming to elucidate involved molecular pathways in the platelets as a response to the intracranial tumor status, including DAVID GO, and PANTHER GO, as described and performed by us previously.

Study description

Background summary

Glioblastoma is one of the most lethal of all cancers with a median prognosis of 16-18 months. The current standard of care consists of maximal safe resection followed by combined radiation therapy with temozolomide chemotherapy and adjuvant temozolomide courses. Due to its infiltrative growth pattern

glioblastomas virtually always recur sooner or later. Therapeutic options for patients depend largely on interval between recurrence and initial treatment. To make treatment decision even more complex in virtually all patient*s new contrast-enhancing lesions will appear on the MRI scan at some point during follow-up. Notably, not all new lesions denote tumor progression. During the course of the disease up to 66% of patients experience contrast-enhancing lesions on the MRI scan that resolve spontaneously over time without additional treatment. These lesions result from therapy-induced radionecrosis and/or oedema formation, a phenomenon also known as glioma pseudo-progression. Follow-up with MRI scans is currently the standard to discriminate both entities, but consequences of misdiagnosis may be severe, e.g. premature therapy abrogation on one hand, too early or too late start of new treatment on the other. More innovative approaches to discriminate these two very different identities are urgently needed, at which stage liquid biopsies may offer a potential solution. Blood platelets carry valuable up-to-date information on glioblastoma-status as they are replenished every 7-10 days.

Study objective

Our central hypothesis is that the RNA content of TEPs allows for the identification of glioblastoma progression, including the differentiation from pseudo-progression and radionecrosis. For this we plan to use two parallel approaches, i.e. the TEP-Glioblastoma-score and the *progressor versus non-progressor*-test. Further validation of these platelet RNA-based scores may provide an easily accessible companion diagnostics
test that could solve the most urgent need in management of glioblastoma patients, e.g. reliable establishment of tumor progression, to date.
To test our hypothesis, we will collect longitudinal blood samples from glioblastoma patients in two different countries, that is The Netherlands and the United Kingdom. Samples collected in the Netherlands will be employed for further optimization of both tests, aiming to reach >95% accuracy to correctly detect the patient*s tumor status. Samples collected in the United Kingdom will serve as an external validation series to confirm the generalizability of both tests.

Study design

Investigator-initiated, observational study

Study burden and risks

A maximum of 18 mL of blood will be collected on average five times per patient, depending on survival. Venipuncture can result in temporary pain and the formation of a hematoma. We consider these effects to be relatively mild, especially considering that on most occasions, blood will have to be drawn anyway. We do not expect that the extra volume of blood taken will cause any

noticeable discomfort.

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

Radiologic suspicion of high grade glioma on MRI
Eligible for resection
Older than 18 years of age
Dutch speaking

Exclusion criteria

Known malignancy elsewhere in the body

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2024
Enrollment:	190
Type:	Anticipated

Medical products/devices used

Generic name:	thromboSeq
Registration:	No

Ethics review

Approved WMO

Date:	31-05-2024
Application type:	First submission
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	NL84923.000.24