Response assessment of post-transplant lymphoproliferative disorder with 18F-FDG-PET/CT and minimal residual disease monitoring, a multicenter multinational feasibility study

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1 - To determine the feasibility of MRD detection using next generation sequencing (NGS) on circulating tumor DNA (ctDNA) from PTLD patients using a gene panel previously used in diffuse large B-cell lymphoma (DLBCL) 2 - To explore the mutational...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas non-Hodgkin's B-cell
Study type	Observational non invasive

Summary

ID

NL-OMON48552

Source
ToetsingOnline

Brief title
Minimal residual disease monitoring in PTLD

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
post-transplant lymphoma, PTLD

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 18F-FDG-PET/CT, Minimal residual disease, Post-transplant lymphoproliferative disorder

Outcome measures

Primary outcome

1 - Detection of ctDNA at diagnosis and response evaluation

Secondary outcome

2 - Sensitivity and specificity of plasma ctDNA genotyping in comparison with

tumor sample DNA (gDNA) as gold standard

3 - Changes in ctDNA abundance throughout therapy

4 - Clinical end-points: progression free survival (PFS), overall survival

(OS), event free survival (EFS), disease specific survival (DSS)

Study description

Background summary

Post-transplant lymphoproliferative disorder (PTLD) is a serious complication after solid organ (SOT) and hematopoietic stem cell transplantation (HSCT), associated with significant morbidity and mortality. Initial treatment consists of tapering immune suppression and rituximab monotherapy. 18F-flurodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/CT) has become the main tool to assess remission status, drive decisions on treatment alteration and identify relapse in patients with PTLD. In case of positive 18F-FDG-PET/CT following rituximab, treatment is escalated with R-CHOP. However 18F-FDG-PET/CT false positives results are commonly reported and it has limited prognostic value (positive predictive value of 38% negative predictive value of 92%). Minimal residual disease (MRD) from circulating tumor DNA (ctDNA) fragments occurs under the detection threshold of 18F-FDG-PET/CT. With a blood

sample one may be able to monitor MRD, thought to be responsible for disease progression and relapse. MRD may become an early response indicator used to guide treatment. We will investigate the feasibility of MRD monitoring in PTLD patients and perform an exploratory study to evaluate if MRD monitoring may be used to trace disease status during treatment and identify early responders from (non-) responders.

Study objective

1 - To determine the feasibility of MRD detection using next generation sequencing (NGS) on circulating tumor DNA (ctDNA) from PTLD patients using a gene panel previously used in diffuse large B-cell lymphoma (DLBCL)
2 - To explore the mutational landscape of PTLD by whole exome sequencing and validate the study*s gene panel
3 - To investigate the dynamics of ctDNA at diagnosis, interim and at end-of-treatment in relation to rituximab and R-CHOP treatment
4 - To compare ctDNA abundance with 18F-FDG-PET/CT results in patients responding to therapy vs refractory or relapsing patients.

Study design

An exploratory prospective multicenter, multinational cohort study.

Tissue biopsies are performed at diagnosis as part of routine diagnostics. 18F-FDG-PET/CT scans and blood sampling for EBV measurements at diagnosis, after 4 or 8 courses with rituximab and after R-CHOP therapy are performed as standard of care. MRD measurements will be performed on blood samples obtained at diagnosis and after the 4 cycle of rituximab. In case of responsive disease MRD will be determined after the 8th cycle of rituximab. In case of unresponsive disease, MRD will be determined after cycle 2 and 4 of R-CHOP

Study burden and risks

No serious adverse events are expected from a routine venipuncture performed by specialized personnel.

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

- Patients having undergone a solid organ transplantation or hematopoietic stem cell transplantation.
- Histologically proven CD20+ monomorphic PTLD (with or without EBV association)
- Age > 18 years
- Intent to treat patient according to standard protocol (rituximab / R-CHOP). Clinicians are allowed to adapt protocol in the best interest of the patient
- Measurable disease on 18F-FDG-PET/CT at diagnosis
-Patient*s written informed consent and written consent for data collection.

Exclusion criteria

-A complete surgical resection of tumor.
-Upfront treatment with external beam radiation therapy.
-Known to be HIV positive.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-04-2019
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	22-10-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-06-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-09-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-01-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL66412.042.18
Other	NTR: Waiting number