Advanced PET and MRI techniques for improved therapy response assessment in diffuse large B-cell lymphoma / follicular lymphoma grade 3B

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

Summary

ID

NL-OMON40554

Source
ToetsingOnline

Brief title
MITRAL; molecular imaging techniques for response assessment in lymphoma

Condition

- Lymphomas non-Hodgkin's B-cell
- Lymphomas non-Hodgkin's B-cell

Synonym
Diffuse large B-cell lymphoma / follicular lymphoma grade 3B; lymph node cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: KWF - Stichting Alpe d'Huzes (Bas Mulder award)

Intervention

Keyword: Diffuse large B-cell lymphoma, Follicular lymphoma grade 3B, Malignant lymphoma, MRI, PET

Outcome measures

Primary outcome

The first outcome parameter will be the diagnostic performance of interim conventional 18F-FDG PET, dual time-point 18F-FDG PET, and DWI in detecting residual tumor after two cycles of R-CHOP in conventional interim 18 F-FDG PET positive patients, using biopsy results as reference standard. The second outcome parameter will be the diagnostic performance of 89Zr-rituximab PET in determining status of CD20 expression, using biopsy results as reference standard. The third outcome parameter will be the diagnostic performance of interim conventional 18F-FDG PET, dual time-point 18F-FDG PET, DWI, and 89Zr-rituximab PET in predicting end-of-treatment 18F-FDG PET result and disease relapse within two years.

Secondary outcome

n.v.t.

Study description

Background summary

Malignant lymphomas are a heterogeneous group of neoplasms with highly variable

biology and prognosis. Improved understanding of the tumor biology enables selecting the most likely effective therapy, and will allow personalized monitoring of treatment response in each patient and provide the opportunity to switch from treatment strategy in case of a non-response. Early selection of effective treatment strategy increases survival rate, and early stop of an ineffective therapy will prevent unnecessary side-effects. Despite its relatively high negative predictive value, early interim conventional (i.e. single time-point) 18F-FDG PET lacks sufficient positive predictive value in diffuse large B-cell lymphoma / follicular lymphoma grade 3B patients undergoing R-CHOP chemotherapy. Consequently, biopsy confirmation of a positive interim 18F-FDG PET scan is required before a change in therapy can be justified. New non-invasive functional imaging techniques (obviating the need for biopsies and so improving quality of life) are required to improve the discrimination between residual tumor and inflammatory/necrotic changes, and to detect failure of front-line R-CHOP at an early stage. In this project, the value of dual time-point 18F-FDG PET, DWI, and 89Zr-rituximab PET for these purposes will be investigated.

Study objective

This project will first address the hypothesis that dual time-point 18F-FDG PET and DWI improve the discrimination between residual active tumor and inflammatory/necrotic changes after two cycles of R-CHOP in DLBCL / follicular lymphoma grade 3B , and, secondly, aims to demonstrate the proof-of-concept that interim 89Zr-rituximab PET after two cycles of R-CHOP can identify patients in whom front-line R-CHOP is likely going to fail by detecting loss of CD20 expression.

Study design

Patients eligible for enrollment in this multicenter, prospective, diagnostic cohort study are adults aged *18 years with a newly diagnosed, histologically proven, and previously untreated diffuse large B-cell lymphoma / follicular lymphoma grade 3B, who are scheduled to undergo standard front-line R-CHOP-21 therapy. All patients will undergo dual time-point 18F-FDG PET and DWI both before therapy and between 10 and 21 days after the second cycle of R-CHOP chemotherapy. All patients with a site that is positive for residual tumor at interim conventional (i.e. single time-point, 60 minutes after 18F-FDG administration) 18F-FDG PET will also undergo subsequent interim 89Zr-rituximab PET. Interim conventional 18F-FDG PET positive sites will be biopsied, if safely accessible, and histologically examined for the presence of residual tumor or inflammation, and degree of CD20 expression. In ten patients with a negative interim conventional 18F-FDG PET scan but with a residual abnormality on the corresponding low-dose CT-scan, a biopsy will be performed of the residual abnormality on the CT scan to compare its histological characteristics to that of interim conventional 18F-FDG PET positive sites. All patients will

routinely undergo an end-of-treatment 18F-FDG PET scan as part of standard clinical care, and all patients will also be followed-up for two years for relapsing disease. Therapy will not be changed on the basis of (interim) dual time-point 18F-FDG PET, DWI, 89Zr-rituximab PET, and biopsy results.

Study burden and risks

-Patients will receive an infusion for the PET scans, and this may give some discomfort/pain for a short time. -For the PET scans, radioactive tracers (18F-FDG and 89Zr-rituximab) will be applied. Although this gives a certain radiation dose, from previous research it is known that the health risks of the total effective dose effecieve in adult patients with diffuse large B-cell lymphoma / follicular lymphoma grade 3B are negligible / very low. Furthermore, the radioactive tracers (18F-FDG and 89Zr-rituximab) have been used safely without any side-effects so far. -Another possible disadvantage is that lying still in the PET and MRI scanners and the duration of the scans can give some discomfort. However, we will do everything we can to make it as comfortable as possible for the patients. -A selection of the patients will get a biopsy; the locale anaesthesia may give some discomfort/pain for a short time, but otherwise the patient will not experience any pain during the remainder of the procedure. Furthermore, serious complications will be avoided by aiming to biopsy superficial residual abnormalities as much as possible; risky biopsies that are anticipated to cause important complications will be avoided. There is no personal benefit for participants in this study. This study may provide new non-invasive diagnostic methods that allow for the early detection of treatment response and drug resistance and this can lead to improved, individualized treatment planning for patients with diffuse large B-cell lymphoma / follicular lymphoma grade 3B in the future. We hope this will contribute to the overall survival of patients and prevent unnecessary side-effects associated with ineffective therapies. Society will benefit from these new diagnostic methods because patients will then receive more cost-effective therapy.

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

- Male or female patients
- Age: 18 years and older
- Histologically proven diffuse large B-cell lymphoma / Follicular lymphoma grade 3B
- Patients scheduled to undergo front-line R-CHOP 21 therapy
- Patients must be capable of giving written informed consent and the consent must have been obtained before the study-related procedures

Exclusion criteria

- General contraindications for MRI (including cardiac pacemakers and claustrophobia). - Previous malignancy. However, subjects who have been free of malignancy for at least 5 years, or have a history of completely resected non-melanoma skin cancer, or successfully treated in situ carcinoma are eligible. - Diffuse large B-cell lymphoma / follicular lymphoma grade 3B central nervous system involvement. - Diffuse large B-cell lymphoma / follicular lymphoma grade 3B stage I disease. - HIV positivity (de novo or active) - Pregnant or lactating women. - Therapy has already started before pretreatment dual-time point 18F-FDG PET and DWI scans could be performed.

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):	13-11-2013
Enrollment:	110
Type:	Actual

Ethics review

Approved WMO Date:	25-07-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-12-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL45376.041.13