Tumor uptake of ofatumumab and rituximab, labeled with 89Zirconium, in patients with malignant lymphoma.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON20421

Source
NTR

Health condition

Diffuse large B cell lymphoma
Diffuus grootcellig B cel lymfoom

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: VU University Medical Center
GlaxoSmithKline

Intervention

Outcome measures

Primary outcome

The detection of 89Zr-ofatumumab and 89Zr-rituximab in DLBCL tumor lesions:

1. Visual (present/absent);

2. Quantitative (measured in peak Standardized Uptake Value (SUVpeak)).

Secondary outcome

1. The detection of 18F-FDG in DLBCL tumor lesions:

A. Visual (present/absent);

B. Quantitative (in SUVpreak).

2. The detection of 89Zr-ofatumumab and 89Zr-rituximab in normal tissue:

A. Visual: Description of biodistribution;

B. Quantitative (% uptake (of total injected) 89Zr-ofatumumab and 89Zr-rituximab, calculated residence times and calculated organ absorbed doses for 89Zr-ofatumumab and 89Zr-rituximab).

3. Clinical outcome:

A. In categories: complete remission, partial remission, stable disease or relapsed/progressive disease, using the Revised Response Criteria for Malignant Lymphoma (RRMCML) for disease assessment, assessed by CT after the second cycle of therapy / by PET performed after the third cycle of therapy, conform OMB110928 study protocol.

Study description

Background summary

Rationale:

For patients with a diffuse large B cell lymphoma (DLBCL) the efficacy of the anti-CD20 monoclonal antibody rituximab combined with salvage chemotherapy in the second-line setting has decreased due to more effective first-line treatment with rituximab containing chemo-immunotherapy. We hypothesize that ofatumumab, a second generation anti-CD20 monoclonal antibody with a different binding site, has a better efficiency of tumor targeting and can overcome relative or complete rituximab resistance, improving response rates.

Objectives:

The primary objective is:

1. To compare the biodistribution and uptake in DLBCL of 89Zirconium (89Zr)-ofatumumab and 89Zr-rituximab (visual and quantitative).

The secondary objectives are:

1. To compare the biodistribution and uptake in DLBCL of 89Zr-ofatumumab and 89Zr-rituximab with 18F-fluoro-2-deoxy-D-glucose (18F-FDG) (visual and quantitative);

2. To quantify biodistribution and dosimetry in normal tissue of 89Zr-ofatumumab and 89Zr-rituximab;

3. To investigate whether increased uptake in DLBCL on immuno-positron emission tomography (immuno-PET) is associated with clinical efficacy.

Study design:

Pilot study.

Study population:

45 patients with DLBCL, treated in or conform the OMB110928 study (15 in the ofatumumab arm, 30 in the rituximab arm). OMB 110928 study is a phase III, parallel group, randomised, registration trial of ofatumumab versus rituximab in addition to salvage chemotherapy.

Intervention:

Patients will be injected with 10 mg 89Zr-ofatumumab (74 MBq) or 10 mg 89Zr-rituximab (74 MBq) intravenously, on the first day of the second-line treatment with respectively ofatumumab or rituximab plus chemotherapy. Immuno-PET scans will be obtained at 1, 72 and 144 hours post injection. A 18F-FDG PET scan, conform the OMB 110928 protocol, will be performed within a maximum interval of 2 weeks before the first immuno-PET scan. Patients will undergo blood sampling for pharmocokinetic purposes.

Main study parameters/endpoints:

The primary endpoint is:

1. The detection of 89Zr-ofatumumab and 89Zr-rituximab in DLBCL tumor lesions:

A. Visual (present/absent);

B. Quantitative (measured in peak Standardized Uptake Value (SUVpeak)).

The secondary endpoints are:

1. The detection of FDG in DLBCL tumor lesions:

A. Visual (present/absent);

B. Quantitative (in SUVpreak).

2. The detection of 89Zr-ofatumumab and 89Zr-rituximab in normal tissue:

A. Visual: description of biodistribution;

B. Quantitative (% uptake (of total injected) 89Zr-ofatumumab and 89Zr-rituximab, calculated residence times and calculated organ absorbed doses for 89Zr-ofatumumab and 89Zr-rituximab).

3. Clinical outcome:

A. In categories: complete remission, partial remission, stable disease or relapsed/progressive disease, using the Revised Response Criteria for Malignant Lymphoma (RRMCML) for disease assessment, assessed by CT after the second cycle of therapy / by PET performed after the third cycle of therapy, conform OMB110928 study protocol.

Other study parameters:

1. Pharmacokinetics of 89Zr-ofatumumab and 89Zr-rituximab;

2. Assessment of (89Zr-ofatumumab SUVpeak / 18F-FDG SUVpeak) and (89Zr-rituximab SUVpeak / 18F-FDG SUVpeak) for the five tumor lesions with the highest antibody uptake.

Nature and extent of the burden and risks associated with participation, and benefit:

Patients will be asked for 2 extra visits to obtain PET-scans and blood samples. The risk level according to the ICRP-62 model is stated as Category III “moderate”(effective doses greater than 10mSv (adults), while the social benefit is regarded as “substantial”. Patients do not require shielding after injection of 89Zr-labeled ofatumumab or rituximab.

Study objective

For patients with a diffuse large B cell lymphoma (DLBCL) the efficacy of the anti-CD20 monoclonal antibody rituximab combined with salvage chemotherapy in the second-line

setting has decreased due to more effective first-line treatment with rituximab containing chemo-immunotherapy. We hypothesize that ofatumumab, a second generation anti-CD20 monoclonal antibody with a different binding site, has a better efficiency of tumor targeting and can overcome relative or complete rituximab resistance, improving response rates.

Study design

Immuno-PET scans obtained 1 hour, 72 hours and 144 hours post injection of 89Zirconium-ofatumumab or 89Zirconium-rituximab.

CT after the second cycle of therapy / by PET performed after the third cycle of therapy, conform OMB110928 study protocol.

Intervention

Patients will be injected with 10 mg 89Zr-ofatumumab (74 MBq) or 10 mg 89Zr-rituximab (74 MBq) intravenously, on the first day of the second-line treatment with respectively ofatumumab or rituximab plus chemotherapy. Immuno-PET scans will be obtained at 1, 72 and 144 hours post injection. A 18F-FDG PET scan, conform the OMB 110928 protocol, will be performed within a maximum interval of 2 weeks before the first immuno-PET scan. Patients will undergo blood sampling for pharmocokinetic purposes.

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Eligibility criteria

Inclusion criteria

Patients to be included must be before initiation of second-line treatment in or conform OMB 110928 study, meeting the following criteria (conform the inclusion criteria of OMB 110928 study protocol):

1. Patients have refractory or relapsed (see protocol for definition) CD20 positive DLBCL during or after first line treatment with rituximab combined with anthracycline-based chemotherapy, confirmed by biopsy after first line treatment;

2. Age 18 years or older;

3. Baseline 18F-FDG PET scan with positive lesions, compatible with CT defined anatomical tumor sites;

4. CT-scan showing at least one or more clearly demarcated lesions with a largest diameter larger or equal to 1.5 cm, or 1 clearly demarcated lesion with a largest diameter larger or equal to 2.0 cm (not previously irradiated);

5. ECOG performance status 0,1 or 2

6. Patients must be eligible for high dose chemotherapy and autologous stem cell transplantation;

7. Resolution of toxicities from first-line therapy to grade 1 or below;

8. Patients must be able to adhere to the study appointments and other protocol requirements;

9. Patients must be capable of giving written informed consent and the consent must have been obtained prior to the study related procedures.

Exclusion criteria

Patients are excluded if they meet the following criteria (conform the exclusion criteria of OMB 110928 study protocol):

1. Any previous therapy for DLBCL, with the exception of first-line treatment with rituximab in combination with anthracycline-based chemotherapy, or radiotherapy as part of the first-line treatment plan or to a limited field at a maximum dose equal to or less than 10Gy to control life-threatening symptoms;

2. Received any of the following treatments within 4 weeks prior to start of trial therapy (unless otherwise stated): Anti-cancer therapy, radiotherapy (unless limited field at a maximum dose equal to or less than 10Gy to control life-threatening symptoms), treatment with any known non-marketed drug substance or experimental therapy within 5 terminal half lives or 4 weeks prior to enrolment (whichever is longer) or currently participating in any other interventional clinical study, glucocorticoid use, unless given in doses equal to or less than 100 mg/day hydrocortisone (or equivalent dose of other glucocorticoids) for < 7 days for exacerbations other than lymphoma (e.g. asthma);

3. Significant cerebrovascular disease;

4. Chronic or active infections with systemic treatment with antibiotics, antifungal or antiviral medication;

5. Other malignancy;

6. Prior treatment with monoclonal antibodies, with the exception of rituximab, within 3 months prior to start of the study;

7. Pregnancy or lactation;

8. Women of childbearing potential or male subjects, unable or unwilling to adhere to the adequate contraception conform study protocol.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-06-2012
Enrollment:	45
Type:	Anticipated

Ethics review

Positive opinion

Date:	12-04-2012
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	NL3240
NTR-old	NTR3392
Other	ABR / EudraCT : 40422 / 2012-001597-29;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A