Tumor uptake of 89Zirconium-ofatumumab and 89Zirconium-rituximab in diffuse large B cell lymphoma patients

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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-...

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

Summary

ID

NL-OMON37544

Source
ToetsingOnline

Brief title
Tumor uptake of 89Zr-ofatumumab and 89Zr-rituximab

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
diffuse large B cell lymphoma, lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,GlaxoSmithKline

Intervention

Keyword: Antibodies, Diffuse, Immuno-PET, Large B-Cell, Lymphoma, Monoclonal, Zirconium-89

Outcome measures

Primary outcome

The primary endpoint is:

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

* visual (present/absent).

* quantitative (measured in peak Standardized Uptake Value (SUVpeak)).

Secondary outcome

The secondary endpoints are:

1.The detection of FDG in DLBCL tumor lesions:

* visual (present/absent)

* quantitative (in SUVpreak).

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

* visual: description of biodistribution

* 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:

* 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:

* Pharmacokinetics of 89Zr-ofatumumab and 89Zr-rituximab.

* 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.

Study description

Background summary

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 objective

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

This is a single-center pilot study. 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.

Study burden and risks

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.

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 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):;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.;Age 18 years or older. Baseline 18F-FDG PET scan with positive lesions, compatible with CT defined anatomical tumor sites. CT-scan showing at least one or more clearly demarcated lesions with a largest diameter * 1.5 cm or 1 clearly demarcated lesion with a largest diameter * 2.0 cm (not previously irradiated). ECOG performance status 0,1 or 2. Patients must be eligible for high dose chemotherapy and autologous stem cell transplantation. Resolution of toxicities from first-line therapy to grade * 1. Patients must be able to adhere to the study appointments and other protocol requirements. 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):;- 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 aximum dose of *10Gy to control life-threatening symptoms.;- 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 of * 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 *100 mg/day hydrocortisone (or equivalent dose of other glucocorticoids) for < 7 days for exacerbations other than lymphoma (e.g. asthma). ;- Significant cerebrovascular disease. ;- Chronic or active infections with systemic treatment with antibiotics, antifungal or antiviral medication. ;- Other malignancy. ;- Prior treatment with monoclonal antibodies, with the exception of rituximab, within 3 months prior to start of the study.;- Pregnancy or lactation;- Women of childbearing potential or male subjects, unable or unwilling to adhere to the adequate contraception conform study protocol.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-09-2012
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	89Zirconium-ofatumumab
Generic name:	ofatumumab-N-succinyldesferal-zirconium-89
Product type:	Medicine
Brand name:	89Zirconium-rituximab
Generic name:	rituximab-N-succinyldesferal-zirconium-89

Ethics review

Approved WMO

Date:	15-05-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	10-07-2012
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
EudraCT	EUCTR2012-001597-29-NL
CCMO	NL40422.029.12

Study results

Date completed: 22-03-2017

Actual enrolment: 7

Summary results
Trial ended prematurely