A phase II study of obinutuzumab monotherapy in rituximab-refractory follicular lymphoma

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

Summary

ID

NL-OMON41828

Source
ToetsingOnline

Brief title
ZON

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
follicular 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,Hoffmann-La Roche,KWF arts-assistentenbeurs en mede financiering door bedrijf;zie G2

Intervention

Keyword: Follicular, Lymphoma, obinutuzumab, Positron-Emission Tomography, Zirconium-89

Outcome measures

Primary outcome

The primary endpoint is:

* Overall response rate using the 'Lugano Classification 2014' for disease

assessment.

Secondary outcome

The secondary endpoints are:

* Progression-free survival

* Overall survival

* Duration of response, in responders

* Duration of stable disease

* Time to next treatment

* The detection of tumour lesions employing contrast enhanced CT-scan

* The detection of tumour lesions employing 18F-FDG-PET

* The detection of tumour lesions employing 89Zr -obinutuzumab-PET

* The detection of 89Zr -obinutuzumab in normal tissue

* The description of safety data: all adverse and serious adverse events

according to the NCICTCAE v.4.

Study description

Background summary

Given the preclinical data demonstrating superior antibody-dependent cellular cytotoxicity (ADCC) and direct cell death induction with obinutuzumab when compared with rituximab, it is hypothesized that obinutuzumab can provide clinical benefit in rituximab-refractory patients. This will be the first study to assess the response rate of obinutuzumab monotherapy in patients with rituximab-refractory follicular lymphoma.
In addition we will investigate immuno-PET with 89Zr -obinutuzumab as a potential predictive imaging biomarker to select patients who will benefit from obinutuzumab, in an early stage. This study will provide insight in the feasibility of 89Zr-obinutuzumab PET and provide information for future studies with 89Zr-obinutuzumab.

Study objective

The primary objective is:
* To determine the overall response rate (ORR) of 4 weekly infusions of obinutuzumab monotherapy (Induction I) in patients with rituximab-refractory follicular lymphoma.
The secondary objectives are:
* To determine the efficacy (defined as progression free survival, overall survival, duration of response, duration of stable disease, time to next treatment) of obinutuzumab monotherapy given as 4 weekly infusions to rituximab-refractory follicular lymphoma patients
* To determine the efficacy (defined as ORR, progression free survival, overall survival, duration of response, duration of stable disease, time to next treatment) of obinutuzumab monotherapy given as 4 monthly infusions (Induction II) to rituximab-refractory follicular lymphoma patients responding to 4 weekly infusions of obinutuzumab monotherapy
* To determine the efficacy (defined as progression free survival, overall survival, duration of response, duration of stable disease, time to next treatment) of obinutuzumab maintenance given as bimonthly infusions (up to a maximum of 2 years) to rituximab-refractory follicular lymphoma patients responding to 4 weekly infusions of obinutuzumab monotherapy (Induction I), followed by 4 monthly infusions of obinutuzumab monotherapy (Induction II).
* To investigate the relationship between tumour uptake on immuno-PET and tumour response to obinutuzumab
* To compare tumour uptake using immuno-PET as a novel imaging biomarker to *standard imaging technique* (18F-FDG-PET/CT)
* To determine the value of 18F-FDG-PET-CT scanning in response assessment of follicular lymphoma patients
* To investigate the biodistribution and dosimetry in normal tissue of 89Zr-obinutuzumab
* To assess safety data by monitoring all adverse and serious adverse events (AEs/SAEs) according to the NCI CTCAE v.4.

Study design

Phase II, single-cohort, non-blinded, single-agent, interventional single center study. The Simon two-stage design will be used: 12 to 25 eligible patients will be included in the study, according to the number of responses observed. The total study duration is approximately 37 months.

Intervention

Induction I: treatment with obinutuzumab:
- week 1day 0 (100mg)
- week 1 day 1 (900 mg) + 10mg 89Zr-obinutuzumab
- week 2 day 1(1000mg)
- week 3 day 1 (1000mg)
- week 4 day 1 (1000mg)

For patients with clinical benefit of study treatment (defined as complete remission, partial remission or stable disease on PET-CT in week 10-12):
Induction II: treatment with obinutuzumab
- month 3 (1000mg)
- month 4 (1000mg)
- month 5 (1000mg)
- month 6 (1000mg)

For patients with ongoing clinical benefit of study treatment (defined as complete remission, partial remission or stable disease on PET-CT in month 6, CT in month 9 and 12)
Maintenance treatment with 1000mg obinutuzumab bimonthly, for a maximum of 2 years.

Study burden and risks

Upon enrollment of this study a baseline FDG-PET-CT scan will be obtained. Patients are scheduled for 5 treatment visits, where obinutuzumab will be administered intravenously. Patients with clinical benefit of study treatment are eligible for continuation of study treatment. During therapy and follow-up, patients are scheduled for standard laboratory analysis and PET/CT scans on visits to the outpatient clinic. The exposure to ionizing radiation is non-neglible, but patients may have clinical benefit by study treatment.

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

- biopsy -proven rituximab refractory follicular lymphoma
- no transformation to high grade or diffuse large B cell lymphoma
- radiographicaly documented measurable disease (2 or more clearly demarcated lesions with a largest diameter of at least 1.5 cm, or 1 clearly demarcated lesion with a largest diameter of at least 2 cm).
- adult patients, older than 18 years
-ECOG performance score 0,1 or 2
-written informed consent according to GCP

Exclusion criteria

-known central nervous system involvement
-concurrent use of other anti-cancer agents
-all other lymphoma treatment (except rituximab maintenance therapy) during the last 6 months
-other active malignancy
-pregnant and breastfeeding women, and subjects of childbearing potential without adequate and effective contraception

- life expectancy less than 6 months
- active infectious disease (see protocol for definition)
- clinical significant cardiovascular disease
- abnormal laboratory values at screening (see protocol for definition)

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-08-2015
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Gazyva
Generic name:	obinutuzumab
Product type:	Medicine
Brand name:	obinutuzumab-N-succinyl-desferal-zirconium-89
Generic name:	obinutuzumab-N-succinyl-desferal-zirconium-89

Ethics review

Approved WMO

Date:	26-03-2014

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-12-2015
Application type:	Amendment
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

ID: 24035
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-004635-69-NL
CCMO	NL48577.029.14
OMON	NL-OMON24035
OMON	NL-OMON26469

Study results

Date completed:	25-10-2019
Actual enrolment:	6

Summary results
Trial ended prematurely