A double-blind, randomized, two-dose-arm, parallel group, international, multi-center trial of HuMax-CD20, a fully human monoclonal anti-CD20 antibody, in patients with Follicular Lymphoma who are refractory to rituximab in combination with chemotherapy

Published: 25-07-2006
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To determine the efficacy of two dose regimens of HuMax-CD20 in patients with Follicular Lymphoma who are refractory to rituximab in combination with chemotherapy or to rituximab given as maintenance treatment.

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

Summary

ID

NL-OMON29878

Source
ToetsingOnline

Brief title
HuMax-CD20 in FL patients refractory to rituximab

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
Folliculair Lymphoma, Lymphnode Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Genmab
Source(s) of monetary or material Support: vierde geldstrom;derde geldstroom is nvt

Intervention

Keyword: Follicular Lymphoma, HuMax CD20, Rituximab refractory

Outcome measures

Primary outcome

Objective response as measured over a 6 month period from start of treatment

assessed by an Independent endpoints Review Committee (IRC) according to

the standardized response criteria for Non-Hodgkin*s Lymphomas.

Secondary outcome

1. Duration of response

2. Progression Free Survival (PFS)

3. Time to next FL therapy

4. Overall survival

5. Reduction in tumor size

6. CD19+ and CD20+ cells in peripheral blood

7. Conversion from BCL2 positive to BCL2 negative in peripheral blood (by PCR)

8. Prognostic value of Fc *receptor polymorphism, FLIPI (Follicular

Lymphoma International Prognostic Index) and C1qA-276 mutation

9. Adverse Events

10. Human Anti Human Antibodies (HAHA)

11. Complement: CH50

12. Pharmacokinetic (PK) profile: AUC, Cl, Cmax, Cmin, Tmax, T*, Vz

Study description

Background summary

The standard of care for patients with stage III or IV FL has changed considerably during the recent years. Today, most centers use rituximab in combination with chemotherapy in first line. Obviously, less toxic treatments, e.g. novel monoclonal antibodies, might be of value for patients that relapse on or shortly after rituximab-containing chemotherapy regimens, i.e. rituximab refractory patients.

Study objective

To determine the efficacy of two dose regimens of HuMax-CD20 in patients with Follicular Lymphoma who are refractory to rituximab in combination with chemotherapy or to rituximab given as maintenance treatment.

Study design

double-blind, randomized, two-dose-arm, parallel group, international, multi-center trial

Intervention

Administration of HuMax-CD20

Study burden and risks

This is a double-blind, randomized, two-dose-arm, parallel group, phase III trial.

At screening, a physical examination, CT scans, a bone marrow biopsy, if necessary an excisional lymph node biopsy and a full blood analysis are done to evaluate the patient for eligibility in the trial. If the patient gives a separate consent, a fine needle aspirate from an involved lymph node will be performed as well.

The patient will be randomized to one of the two Humax-CD20 dose arms (500 or 1000 mg), as soon as the patient is evaluated to be eligible for the trial and has given informed consent.

During the treatment period, each patient will receive eight weekly infusions of Humax-CD20. The first infusion in both dose arms will be 300 mg, followed by 7 weekly infusions of 500 or 1000 mg.

If the patient has given a separate consent, a fine needle aspirate from an involved lymph node will be repeated at Week 8.

Disease status will be assessed at Month 3, 6, 9, 12, 18 and 24, including physical examination, CT scans and a full blood analysis. Evaluation of response will be done at Month 3, 6, 9, 12, 18 and 24.

Burden and risks for the patient in this trial are comparable to the ones the patient would have with other treatment such as for example with Rituximab.

A second bone marrow biopsy will be performed immediately after onset of CR or CRu (as judged
by the investigator) and only in case the screening biopsy was positive for CD20+ lymphoma as assessed by the central pathologist.

After Month 24, the patients will be monitored for CD19+ and CD20+ cells until normal range or until a value * the baseline value or until initiation of alternative FL treatment or Month 60. Patients will be followed until initiation of alternative FL treatment at 6-months intervals until Month 60.

The evaluation of response will be done centrally and blinded by an IRC.

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

diagnosis of Follicular Lymphoma grade 1* 2 refractory to rituximab in combination with chemotherapy or to rituximab given as maintenance treatment

Exclusion criteria

The most important exclusion criteria consist of allogenic stem cell transplantation at any time, autologous stem cell transplantation within 6 months prior to Visit 1, more than 1 previous cycle of radio immunotherapy, anticancer therapy or corticosteroid therapy within 4 weeks prior to Visit 1 or known or suspected transformation of the follicular lymphoma to aggressive lymphoma unless new biopsy confirms FL.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2008
Enrollment:	9
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	HuMax-CD20
Generic name:	ofatumumab

Ethics review

Approved WMO Date:	25-07-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2006
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-05-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-07-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-02-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	22-04-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-05-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-04-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-10-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2010
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-001433-17-NL
CCMO	NL12422.018.06