A phase III, open label, randomized, multicenter trial of ofatumumab maintenance treatment versus no further treatment in subjects with relapsed chronic lymphocytic leukemia (CLL) who have responded to induction therapy

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON34951

Source
ToetsingOnline

Brief title
HOVON101 CLL/OMB112517

Condition

- Leukaemias

Synonym
Chronic Lymphocytic Leukemia; CLL

Research involving

Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline

Intervention

Keyword: CLL, maintenance treatment, ofatumumab, relaps

Outcome measures

Primary outcome

Progression free survival (PFS), defined as the interval from randomization

until disease progression or death

Secondary outcome

Improvement in response

Time to next treatment

Overall survival

Quality of Life

Effectivity and safety of Ofatumumab

prognostic markers in respons to clinical outcome

Pharmacokinetics of Ofatumumab

Study description

Background summary

Despite progress in therapy, chronic lymphocytic leukemia (CLL) remains incurable. Response rates are promising but remain transient and all subjects eventually relapse. There is currently no approved maintenance therapy. The objective of this study is to evaluate if maintenance therapy with ofatumumab will prolong remission duration.

The purpose of this study is to assess the benefit of ofatumumab maintenance treatment in subjects in remission from relapsed CLL based upon:
1) the similarities in biological behavior between CLL and FL;
2) in relapsed FL, maintenance treatment with anti-CD20 MAb, rituximab is the standard of care;
3) results in a phase II study with rituximab induction and maintenance resulted in prolongation of PFS in MRD positive CLL in first remission after fludarabine;
4) ofatumumab has higher in vitro activity against CLL cells; and
5) ofatumumab has also demonstrated efficacy in relapsed CLL as monotherapy (Study Hx-CD20-406).

Study objective

The primary objective is to evaluate progression free survival (PFS) of ofatumumab maintenance treatment versus no further treatment after remission induction in subjects with relapsed CLL.
Secondary objectives are to evaluate clinical benefit, safety, tolerability and health-related quality of life of subjects treated with ofatumumab versus no further treatment. An additional secondary objective is to evaluate the pharmacokinetics in CLL subjects on maintenance ofatumumab.

Study design

This is an open-label, two-arm, randomized, Phase III study of ofatumumab or no further treatment in subjects in CR or PR after remission induction treatment for relapsed CLL.
Eligible subjects will be stratified at randomization based on:
1) CR or PR at study entry
2) Number of previous induction treatments (2 vs 3)
3) Type of prior treatment : chemoimmunotherapy, only alkylating monotherapy, or other treatment
During the treatment phase, subjects will be randomized 1:1 to receive either:
Arm A: ofatumumab as infusions every 8 weeks (The first dose will be 300mg followed 1 week later by 1000 mg and 1000 mg every 8 weeks thereafter for up to 2 years) or
Arm B: No treatment (i.e. observation only)

Intervention

n.a.

Study burden and risks

n.a.

Contacts

Public
GlaxoSmithKline

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Scientific
GlaxoSmithKline

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Adults with documented diagnosis of CLL based on the modified IWCLL updated NCI-WG guidelines [Hallek, 2008]
- CR or PR according to the revised 2008 NCI-WG CLL criteria, confirmed by CT scan, after 2nd/3rd line treatment
- The anti-leukemic treatment before study entry should have been at least 4 months of monotherapy with alkylating agents and/or at least 4 consecutive cycles of polychemotherapy (e.g. CVP), fludarabine-containing chemotherapy or immunochemotherapy
- ECOG Performance Status of 0-2
- Signed written informed consent

Exclusion criteria

- Primary or secondary fludarabine-refractory subjects, defined as treatment failure (failure to achieve a CR or PR) or disease progression within 6 months of last anti-leukemic therapy [Hallek, 2008]
- Prior maintenance therapy
- Known transformation of CLL (e.g. Richter*s transformation)
- Known prolymphocytic leukemia (PLL)
- Known CNS involvement of CLL
- Active Autoimmune Hemolytic Anemia (AIHA) requiring treatment except if in the opinion of the investigator and medical monitor it is thought not to affect the subject*s safety, the conduct of the study or the interpretation of the data
- Previous autologous or allogeneic stem cell transplantation
- Chronic or current active infectious disease
- Other past or current malignancy
- Clinically significant cardiac disease
- History of significant cerebrovascular disease or event with symptoms or sequelae
- Glucocorticoid unless given in doses <= 100 mg/day hydrocortisone (or equivalent dose of other glucocorticoid) if for exacerbations other than CLL (e.g. asthma)
- Known HIV positive
- Known or suspected hypersensitivity to ofatumumab
- Subjects who have received treatment with any non-marketed drug substance or experimental therapy within 5-terminal half-lives or 4 weeks whichever is longer prior to first dose of study medication or currently participating in any other interventional clinical study
- Subjects known or suspected of not being able to comply with a study protocol (e.g. due to alcoholism, drug dependency or psychological disorder)
- Lactating women, women with a positive pregnancy test at Visit 1 or women (of childbearing potential) as well as men with partners of childbearing potential, who are not willing to use adequate contraception from study start through one year following last ofatumumab dose.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-09-2010
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ofatumumab
Generic name:	Ofatumumab

Ethics review

Approved WMO Date:	12-02-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-08-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-08-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-09-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-09-2012
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-08-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2018
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
Other	clinicaltrials.gov
EudraCT	EUCTR2009-012518-39-NL
CCMO	NL30218.018.10