Phase II study on the feasibility and efficacy of consolidation with 90Y-ibritumomab tiuxetan in patients with relapsed or refractory aggressive B-cell non-Hodgkin*s lymphoma having achieved partial or complete remission after induction with R-PECC chemotherapy.

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To assess the feasibility and efficacy of 90Y-ibritumomab tiuxetan consolidation treatment after R-PECC chemotherapy as second or third line treatment in patients with refractory or relapsed aggressive B-cell NHL, after or not eligible for...

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

Summary

ID

NL-OMON36830

Source
ToetsingOnline

Brief title
HOVON 85 NHL

Condition

- Lymphomas non-Hodgkin's B-cell
- Lymphomas non-Hodgkin's B-cell

Synonym
Aggressive B-cell NHL; lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: KWF.,Spectrum pharmaceuticals

Intervention

Keyword: Aggressive B-cell NHL, Consolidation 90Y-ibritumomab tiuxetan, induction Rituximab-PECC, Relapsed or Refractory

Outcome measures

Primary outcome

Feasibility and safety

Primary endpoint

- The incidence of grade >2 adverse events after treatment with 90Y-ibritumomab

tiuxetan.

Efficacy

Primary endpoint

- Failure free survival measured from the start of 90Y-ibritumomab tiuxetan

Secondary outcome

Feasibility and safety

Secondary endpoints

- Incidence and duration of hypoplasia after treatment with 90Y-ibritumomab

tiuxetan

- Incidence of adverse events (any grade) after treatment with 90Y-ibritumomab

tiuxetan

- Percentage of patients treated with R-PECC who proceed to 90Y-ibritumomab

tiuxetan treatment

- Incidence of adverse events (any grade) after treatment with R-PECC

Efficacy

Secondary endpoints

- Conversion to PET negative CR after 90Y-ibritumomab tiuxetan treatment of

patients who are PET positive before start of 90Y-ibritumomab tiuxetan

- Overall survival measured from the start of 90Y-ibritumomab tiuxetan

- Response rates to R-PECC and response duration

- Failure free survival and overall survival measured from the start of R-PECC

Study description

Background summary

Aggressive B-cell non-Hodgkin lymphoma (NHL) is the most common NHL and mainly occurs in elderly patients.
The current treatment with immuno-chemotherapy results in a long-term disease free survival of 51-70%. In a considerable part of the patients, the disease is refractory or relapses. Elderly patients are not eligible for treatment with high-dose chemotherapy followed by autologous stem cell transplantation because of the toxicity of such treatment. The results of current second line chemotherapy are disappointing. Most patients NHL will die within 2 years of the recurrence of the disease.
Treatment with radio-immunotherapy is usually well tolerated and has a relatively mild toxicity profile. In this trial a new treatment approach will therefore be evaluated. The relapsed or refractory NHL will be treated with oral chemotherapy courses (PECC) combined with rituximab. Patients with a partial or complete remission subsequently receive a consolidation treatment with radio-immunotherapy consisting of one administration of 90Y-ibritumomab tiuxetan.

If this treatment approach is safe and leads to promising results, then it will be compared to the current second line treatment regimens in a following trial.

Study objective

To assess the feasibility and efficacy of 90Y-ibritumomab tiuxetan consolidation treatment after R-PECC chemotherapy as second or third line treatment in patients with refractory or relapsed aggressive B-cell NHL, after or not eligible for autologous stem cell transplantation.

Study design

This is a phase II prospective, multicenter, non-randomized clinical trial in patients with relapsed or refractory aggressive B-cell NHL. Patients will be treated with R-PECC chemotherapy.
After 2 and after 4 cycles of R-PECC patients will be evaluated for response. All patients who have not at least attained a stable disease after 2 cycles of R-PECC and a PR after 4 cycles of R-PECC will go off study. Patients in PR or CR after 4 cycles of R-PECC will receive consolidation treatment with a single dose of 90Y-ibritumomab tiuxetan.

Intervention

90Y-ibritumomab tiuxetan consolidation.

Study burden and risks

The new treatment consists of oral chemotherapy courses in combination with rituximab. Patients who respond will subsequently be treated with radio-immunotherapy consisting of one administration of 90Y-ibritumomab tiuxetan. The aim is to prolong the disease free period. It is expected that the total treatment will be acceptable for patients and that is has a relatively mild toxicity.

Investigations and assessments are standard policy for these patients. No extra investigations or assessments are required.
The risks for patients who participate in this trial are related to the treatment and are standard.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Histologically confirmed aggressive B-cell NHL according to the World Health Organization (WHO) classification (see appendix A):
Follicular lymphoma grade 3b or Diffuse large B-cell lymphoma
-Refractory disease or histologically confirmed first or second relapse
(Refractory is defined as no response or partial remission according to CT. Patients in partial response (PR) can only be included in case of positive PET scan or positive biopsy)
-CD20 positive (assessed at 1st diagnosis or from fresh histology at confirmation of relapse or immunophenotyping of circulating CD20-positive NHL cells from peripheral blood)
-Current measurable disease, i.e. measurable in two perpendicular dimensions on physical examination or computerized tomography (CT) scan using standardized response criteria for NHL (Cheson et al19, 1999) (see appendix B)
-Age 18 years or older
-WHO performance status 0, 1 or 2 (see appendix E)
-Life expectancy of at least 3 months
-Absolute neutrophil count >1.5 x10^9/l and platelet count >100 x10^9/l (unless caused by NHL infiltration in the bone marrow)
-Written informed consent

Exclusion criteria

-Prior allogeneic stem cell transplantation
-Prior radioimmunotherapy
-Patients who have received chemotherapy or radiotherapy within 6 weeks prior to study entry or who have not recovered from toxicities related to prior therapies
-Eligibility for ASCT
-ASCT within 12 months of study entry
-Investigational drugs within 4 weeks prior to entry on this study or persistent toxic side effects of such therapy
-Treatment with external-beam radiation therapy to more than 25% of active bone marrow (see appendix F)
-A history of intolerance to rituximab
-Severe cardiac, pulmonary, neurological, psychiatric or metabolic disease which could compromise participation in the study, or serious underlying medical conditions which could impair the ability of the patient to participate in the trial
-Hepatic dysfunction, bilirubin or transaminases 2.5x upper normal limit or higher (unless caused by the NHL)
-Renal dysfunction, serum creatinine 180 umol/l or more or clearance 40 ml/min or less (unless caused by the NHL)
-Active uncontrolled infections
-Patients known to be HIV-positive
-Current or chronic hepatitis B or hepatitis C infection
-Symptomatic NHL localization in the central nervous system (CNS). Lumbal puncture is not required unless CNS involvement with NHL is clinically suspected
-Transformed indolent lymphoma
-Post-transplant lymphoproliferative disorder
-Pregnant or breast-feeding female patients. Negative serum pregnancy test at study is mandatory for female patients of childbearing potential

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-08-2008
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cecenu, Belustine
Generic name:	lomustine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Leukeran
Generic name:	chlorambucil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MabThera
Generic name:	rituximab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prednisolone, prednisone
Generic name:	prednisolone, prednisone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vepesid
Generic name:	etoposide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Zevalin
Generic name:	90Y-ibritumomab tiuxetan (Zevalin)

Ethics review

Approved WMO Date:	21-03-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-06-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-05-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-06-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-04-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2006-007083-28-NL
CCMO	NL16852.078.07