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Randomised phase III study on the effect of early intensification of rituximab in combination with two-weekly cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) chemotherapy followed by rituximab maintenance in elderly patients (66 to 80 years) with diffuse large B-cell lymphoma

Submission date
23/08/2007

Registration date
23/08/2007

Last Edited
07/10/2021

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.hovon.nl

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HO84

Study information

Scientific Title
Randomised phase III study on the effect of early intensification of rituximab in combination with two-weekly cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) chemotherapy followed by rituximab maintenance in elderly patients (66 to 80 years) with diffuse large B-cell lymphoma

Acronym
HOVON 84 NHL

Study objectives
First randomisation:
The hypothesis to be tested is that the outcome in arm B (early intensification of rituximab combined with two weekly CHOP) is better than in arm A (no intensification of rituximab).

Second randomisation:
The hypothesis to be tested is that the outcome in arm 2 (maintenance treatment with Rituximab) is better than in arm 1 (no further treatment).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/05/2007, the METC of the Erasmus Medical Center in Rotterdam (Netherlands), ref: 2007-055

Study design
Multicentre randomised active-controlled parallel-group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Diffuse large B-cell lymphoma

Interventions
Arm A: eight cycles of rituximab and cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP14) plus Granulocyte Colony-Stimulating Factor (G-CSF) pegfilgrastim (Neulasta)
Arm B: eight cycles of R-CHOP14 plus G-CSF pegfilgrastim (Neulasta) with intensification of rituximab (MabThera) during the first four cycles

Arm 1: no further treatment
Arm 2: maintenance treatment with rituximab (MabThera) once every eight weeks until relapse (for a maximum period of 24 months)

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Rituximab and cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP)

Primary outcome measure
First randomisation:
Response rate (complete remission and 18-fluoro-2-deoxy-glucose-positron emission tomography [FDG-PET] negative partial remission or unconfirmed complete remission)

Second randomisation:
Failure free survival (measured from the date of second randomisation)

The protocol prescribes response evaluation during treatment after 4 and 8 cycles of R-CHOP and every 8 weeks during maintenance/observation. Thereafter follow up will be done every 6 months during the next 3 years and annually thereafter till 10 years after entry of the last patient. The total number of patients is expected to be recruited within 5 years. The analysis will be done approx 1 year after entry of the last patient.

Secondary outcome measures
First randomisation:
1. Failure free survival measured from the date of registration. Patients still alive or lost to follow up are censored at the last day they were known to be alive

2. Overall survival measured from the time of registration
3. Time to reach response
4. Toxicity

Second randomisation:
1. Overall survival
2. Toxicity

The protocol prescribes response evaluation during treatment after 4 and 8 cycles of R-CHOP and every 8 weeks during maintenance/observation. Thereafter follow up will be done every 6 months during the next 3 years and annually thereafter till 10 years after entry of the last patient. The total number of patients is expected to be recruited within 5 years. The analysis will be done approx 1 year after entry of the last patient.

Overall study start date
01/08/2007

Completion date
31/03/2012

Eligibility

Key inclusion criteria
1. Patients with a confirmed histological diagnosis of Diffuse Large B-Cell Lymphoma (DLBCL) based upon a representative histology specimen according to the World Health Organisation (WHO) classification
2. DLBCL must be CD20 positive
3. Ann Arbor stages II - IV
4. Greater than or equal to 66 and less than or equal to 80 years
5. Age WHO performance status 0 to 2
6. Written informed consent

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
550

Total final enrolment
600

Key exclusion criteria
1. Intolerance of exogenous protein administration
2. Severe cardiac dysfunction (New York Heart Association [NYHA] classification III - IV or Left

Ventricular Ejection Fraction [LVEF] less than 45%). Congestive heart failure or symptomatic coronary artery disease or cardiac arrhythmias not well controlled with medication. Myocardial infarction during the last six months
3. Severe pulmonary dysfunction (vital capacity or diffusion capacity less than 50% of predicted value) unless clearly related to Non-Hodgkin lymphoma (NHL) involvement
4. Patients with uncontrolled asthma or allergy, requiring systemic steroid treatment
5. Significant hepatic dysfunction (total bilirubin greater than or equal to 30mmol/l or transaminases greater than or equal to 2.5 x upper normal limit), unless related to NHL
6. Significant renal dysfunction (serum creatinine greater than or equal to 150 umol/l or clearance less than or equal to 60 ml/min), unless related to NHL
7. Clinical signs of severe cerebral dysfunction
8. Suspected or documented central nervous system involvement by NHL
9. Patients with a history of uncontrolled seizures, central nervous system disorders or psychiatric disability judged by the investigator to be clinically significant and adversely affecting compliance to study drugs
10. Testicular DLBCL
11. Primary mediastinal B cell lymphoma
12. Transformed indolent lymphoma
13. Epstein Barr Virus (EBV) lymphoproliferative disorder
14. Secondary lymphoma after previous chemotherapy or radiotherapy
15. Major surgery, other than diagnostic surgery, within the last four weeks
16. Patients with active uncontrolled infections
17. Patients known to be Human Immunodeficiency Virus (HIV)-positive
18. Active chronic hepatitis B or C infection
19. Serious underlying medical conditions, which could impair the ability of the patient to participate in the trial (e.g. ongoing infection, uncontrolled diabetes mellitus, gastric ulcers, active autoimmune disease)
20. Life expectancy less than six months
21. Prior treatment with chemotherapy, radiotherapy or immunotherapy for this lymphoma, except a short course of prednisone (less than one week) and/or cyclophosphamide (less than one week and not in excess of 900 mg/m^2 cumulative) or local radiotherapy in order to control life threatening tumour related symptoms
22. History of active cancer during the past five years, except basal carcinoma of the skin or stage 0 cervical carcinoma

Date of first enrolment
01/08/2007

Date of final enrolment
31/03/2012

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus Medical Centre
Rotterdam

Netherlands
3000 CA

Sponsor information

Organisation
Dutch Haemato-Oncology Association (Stichting Hemato-Oncologie Volwassenen Nederland) (HOVON) (The Netherlands) - Data Centre

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Sponsor type
Research organisation

Website
http://www.hovon.nl

ROR
https://ror.org/056kpdx27

Funder(s)

Funder type
Industry

Funder Name
HOVON receives unrestricted grants and/or financial support from Amgen, Johnson & Johnson-Orthobiotech, Roche and Novartis for the execution of investigator sponsored trials. In addition HOVON is supported by the Dutch Cancer Society.

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		30/07/2020	07/10/2021	Yes	No