Cardiotoxicity and other Late effects After Radiotherapy and ImmunochemoTherapy in Non-Hodgkin lYmphoma

Published: 15-02-2019
Last updated: 16-05-2025

Objective: Our main objective is to assess in detail risk factors for cardiovascular disease and cardiotoxicity and to compare heart function parameters, vascular parameters and biomarkers associated with cardiovascular function among 5- to 18-year…

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

Summary

ID

NL-OMON55490

Source
ToetsingOnline

Brief title
CLARITY

Condition

- Lymphomas non-Hodgkin's B-cell
- Heart failures
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Non-Hodgkin lymhoma; Lymphatic cancer

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut
Source(s) of monetary or material Support: Collectebusfonds KWF. Grantnummer: 10424

Intervention

Keyword: Cardiovascular disease, Late effects, Non-Hodgkin lymphoma, Therapy

Outcome measures

Primary outcome

Main study parameters/endpoints: The main study parameters will be symptoms of CVD, biomarkers, echocardiographic systolic and diastolic heart parameters and global longitudinal strain measurement, electrocardiography, arterial stiffness (by pulse wave velocity measurements), endothelial function (by peripheral arterial tonometry), advanced glycation end products will be assessed by skin autofluorescence (AGE-reader). Late effects and risk factors will be assessed through questionnaires and physical measurements. Exposure to (R-)CHOP and radiotherapy will be extracted from the medical history. Multivariable logistic and linear regression analyses will be used for analyses.

Secondary outcome

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Study description

Background summary

Rationale: Few studies have thus far addressed the burden from treatment-related cardiovascular disease in long-term survivors of non-Hodgkin*s lymphoma (NHL). The life expectancy of patients with aggressive B-cell NHL has significantly increased since treatment regimens have improved.

Although the addition of rituximab to CHOP chemotherapy does not appear to increase cardiotoxicity during treatment, little is known about the long-term cardiac safety of R-CHOP. Nonetheless, cardiotoxicity due to doxorubicin exposure appears to be a key problem in clinical practice, while radiation exposure of the heart may add to cardiac disease risk.

Study objective

Objective: Our main objective is to assess in detail risk factors for cardiovascular disease and cardiotoxicity and to compare heart function parameters, vascular parameters and biomarkers associated with cardiovascular function among 5- to 18-year survivors, treated for aggressive B-cell NHL, and sibling controls. Secondary objectives are to assess the prevalence of other late effects (quality of life, metabolic syndrome), the effects of individual immune- and chemotherapeutic agents and radiation exposure and the predictive value of newly developed markers for CVD.

Study design

Study design: We will evaluate these parameters in a cross-sectional study, nested in a well characterized cohort of DLBCL survivors.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: With the results of our study, guidelines for follow up and prevention will be developed which will benefit the participants during their own follow up in the future. The burden of participating is expected to be low since the study is observational and we combine assessments required in the context of research as much as possible with the provided standard of care for survivors during one or two hospital visits.

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

In order to be eligible to participate in this study, a subject must meet the following criteria.
Survivors:
• 350 survivors of mediastinal large B-cell non-Hodgkin lymphoma (ICD-code 9679) or diffuse large B-cell non-Hodgkin lymphoma (ICD-code 9684), treated with at least five cycles of (R-)CHOP (250 mg/m2 anthracyclines or more) or treated with a combination of mediastinal radiotherapy and anthracyclines (independent of dose).
o 200 survivors treated between five to thirteen years ago (2007-2015)
o 150 survivors treated between thirteen to eighteen years ago (2002-2007)
• The survivors were treated in one of the following centers, participating in the BETER-consortium: Amsterdam UMC (location VUmc or AMC), EMC, UMCU, UMCG, UMC Radboud or ASZ.
• Age at diagnosis 15 up to 60 years.
• Age at the time of inclusion: younger than 75 years old., Comparison group:
• 175 siblings of the above mentioned patients with their date of birth closest to the birthdate of the survivor.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Use of immunosuppressant and/or prednisolone
• HIV-infected individuals

• Pregnant women
• Mental disability or psychological condition potentially hampering compliance with the study protocol
• Insufficient understanding of the Dutch language

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-02-2020
Enrollment:	525
Type:	Actual

Ethics review

Approved WMO Date:	15-02-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2019
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	21-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-04-2021
Application type:	Amendment
Review commission:	METC NedMec

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
CCMO	NL66682.031.18
Other	The NCT number (clinicaltrials.gov) will follow