Role of genomic factors on late adverse events after lymphoma

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lymphomas Hodgkin's disease
Study type	Observational invasive

Summary

ID

NL-OMON52606

Source
ToetsingOnline

Brief title
BETER-REFLECTIE study

Condition

- Lymphomas Hodgkin's disease
- Cardiac disorders, signs and symptoms NEC
- Miscellaneous and site unspecified neoplasms benign

Synonym
Non-Hodgkin lymphoma; Hodgkin lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut
Source(s) of monetary or material Support: KWF kankerbestrijding;grantnummer 8237

Intervention

Keyword: Genetics, Hodgkin lymphoma, Late effects, Non-Hodgkin lymphoma

Outcome measures

Primary outcome

The main study endpoints are the occurrence of clinically diagnosed second malignant neoplasms (SMNs) and cardiovascular disease CVD) at least 5 years after treatment for lymphoma. We will the association of genomic markers with the risk of SMNs and/or CVD in 5-year survivors of HL or DLBCL.

Secondary outcome

As secondary study endpoints we will assess the occurrence of other late adverse events and (intermediate) parameters of treatment-associated toxicity. These include the metabolic syndrome and health-related quality of life measures. We will also assess the functional impact of identified genomic markers on relevant gene and protein expression levels. In an optional part of the study, we will assess the molecular profile of treatment-associated second malignancies.

Study description

Background summary

Despite the increased cure rates of Hodgkin lymphoma (HL) and diffuse large B* cell lymphoma (DLBCL), life expectancy remains compromised due to the occurrence of late treatment-related complications, such as cardiovascular disease and second malignant neoplasms. The risk of late adverse events can only be partially explained by treatment-related factors and lifestyle, suggesting a substantial genomic component. However, the genomic determinants of late adverse events have not been comprehensively studied. We hypothesize that genomic markers contribute to the risk of late adverse events and can be

used for risk stratification.

Study objective

Our main objective is to dissect the genomic determinants of treatment-related adverse events after lymphoma, specifically cardiovascular disease and second malignant neoplasms. As such, we will assess the association of genetic and epigenetic markers with the risk of late adverse events in 5-year survivors of lymphoma. We will evaluate whether genomic signatures and polygenic risk scores based on these markers can modulate and predict the risk of late adverse events. In addition, we will evaluate to what extent genomic determinants are shared across different types of late adverse events and assess the role of genomic markers identified in the general population. In an optional part of the study, we will also assess the molecular profile of therapy-induced second malignancies.

Study design

This observational study will be performed in a well-defined cohort of 5-year survivors of HL and DLBCL identified through the BETER consortium.

5-year survivors of HL or DLBCL who were identified through the BETER consortium will be invited to participate in this study. Living survivors will be approached and invited by their treating physician at the BETER survivorship clinic, or, when they do not visit a BETER survivorship clinic, by their former treating physician at the participating BETER clinic. Biospecimens of deceased survivors will be collected through the national pathology registry (PALGA). In total, we plan to include 8,000 survivors in our study.

Study burden and risks

With the results of our study, we will advance the knowledge about the susceptibility to late adverse events after lymphoma and the underlying pathophysiology. In addition, identified genomic risk factors can inform personalized treatment of future lymphoma patients and benefit personalized screening of current lymphoma survivors for adverse events. The burden is considered low: it is an observational study with a single blood draw (and a health questionnaire for survivors who do not undergo screening).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- 5-years survivors of Hodgkin lymphoma (HL) or diffuse large B-cell non-Hodgkin lymphoma (DLBCL)
- Age at HL/DLBCL diagnosis between 15 and 60 years
- Treated at one of the participating BETER centers
- Living survivors: written informed consent

Exclusion criteria

we will exclude survivors who have previously indicated at the BETER clinic that they do not want to be approached for (further) research (less than 2% of the BETER population).

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-03-2021
Enrollment:	5000
Type:	Actual

Ethics review

Approved WMO Date:	21-08-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	15-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-05-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-06-2021
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-02-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-06-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL69049.031.19