New strategies to detect cancers in carriers of mutations in RB1: blood tests based on tumor-educated platelets, or extracellular vesicles.

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- The development of blood-based tests, either platelet or EV-based, for the detection of (the type of) tumors in RB1-mutation carriers.- Determine the non-cancerous baseline in adult RB1-mutation carriers (heritable-Rb-survivors).- Contribute to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON50529

Source
ToetsingOnline

Brief title
NIRBTEST

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Ocular neoplasms

Synonym
eye cancer, retinoblastoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ERA-NET TRANSCAN (uibetaald door KWF)

Intervention

Keyword: Bloodtest, RB1 gene mutation, Retinoblastoma, Second primary malignancies (SPM)

Outcome measures

Primary outcome

- The development of a test which can detect cancers in the RB1-mutation carriers.

Secondary outcome

- The determination whether either the EV or the platelet-based technique performs superior as a test, or that both test will be complementary.

- The cell free DNA fraction will also be isolated from collected blood samples. This material will serve as part of an contingency plan when EV or platelet testing is not discriminative enough. Furthermore, if additional funding is acquired by the Curie site, cfDNA from patients with SPMs (10 patients are expected with SPMs) will be used for additional testing. Results will be compared to germline DNA isolated from leukocytes present in the buffy coat and to second tumor material if available. The samples will be whole exome sequenced, combined with targeted sequencing of specific regions. For this study, involving whole genome sequencing, an extra consent form will be signed by the patients.

Study description

Background summary

Individuals with a cancer predisposition due to a mutation in the paradigm tumor suppressor gene RB1, have a high risk to develop the childhood cancer retinoblastoma (Rb). Biopsies are not possible in Rb, before treatment selection. Heritable Rb patients have also a high risk to develop other types of second primary, either childhood or adult, malignancies (SPMs), notably sarcomas and melanomas. Remarkably, SPMs are now the leading cause of death in heritable-Rb-survivors. Unfortunately, there are no well-developed regular surveillance protocols for SPMs in Rb survivors available right now. Recently, new non-invasive cancer test have been developed, based on either RNA-sequencing data from platelets (ThromboSeq), on extracellular membrane vesicles (EVs) on cell free DNA (cfDNA) or on other blood fractions derived from tumor cells present in blood.

Study objective

- The development of blood-based tests, either platelet or EV-based, for the detection of (the type of) tumors in RB1-mutation carriers.
- Determine the non-cancerous baseline in adult RB1-mutation carriers (heritable-Rb-survivors).
- Contribute to the biobanking of blood and cancerous tissues from RB1-mutation carriers with SPMs.

Study design

Cross-sectional multicenter trial.

Study burden and risks

Two blood samples totalling 10ml blood will be collected for every participant. Additionally, a short questionnaire has to be filled in concerning their and their family*s cancer history. In addition questions will be asked about the presence of infectious diseases in the week before blood draws. Blood draws will be done, when participants are already present in the hospital for other appointments, and thus no extra visits are required. For all children, blood will be collected through an already present IV, and so no extra venepuncture is required. Children have to be included because Rb is a tumor only present in this patient group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- Adult:
Group 1: germline mutation RB1
Group 2 (control): no germline mutation RB1
- Pediatric:
Group 1: mutation RB1 and retinoblastoma
Group 2 (control): no mutation RB1

Exclusion criteria

- Adult:
Group 1: concomitant heritable (inherited) disorder other than caused by monoallelic mutation of RB1
Group 2 (control): cancer or already known cancer predisposition syndrome
- Pediatric:
Group 1: concomitant heritable (inherited) disorder other than caused by monoallelic mutation of RB1
Group 2: cancer or already known cancer predisposition syndrome

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-12-2018
Enrollment:	91
Type:	Actual

Ethics review

Approved WMO

Date:	06-09-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	18-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2020
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
CCMO	NL64672.029.18