Unraveling the Genetic Background of Colorectal Cancer in Adolescents and Young Adults.

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To unravel the genetic makeup of colorectal cancer (CRC) in adolescents and young adults (AYAs) in order to improve genetic counseling, surveillance and, ultimately, treatment and disease outcome.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and hereditary disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON40790

Source
ToetsingOnline

Brief title
CRC predisposition in AYA's

Condition

- Congenital and hereditary disorders NEC
- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
colon cancer, large bowel cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboudumc

Source(s) of monetary or material Support: Maag-lever-darm stichting

Intervention

Keyword: AYA, Colorectal cancer, exome sequencing, Genetic predisposition

Outcome measures

Primary outcome

Understanding the molecular etiology and pathogenesis of CRC in AYAs is expected to yield novel genetic risk factors. that will facilitate clinical decision making, including early tumor detection, in AYAs with CRC and their siblings at risk.

Secondary outcome

Identification of novel genetic risk factors voor CRC will facilitate clinical decision making, including early tumor detection in AYAs with CRC and their siblings at risk.

Study description

Background summary

AYAs with CRC represent a clinical entity distinct from elderly CRC patients, with many mucinous and poorly differentiated adenocarcinomas and advanced-stage tumors, resulting in a worse prognosis. Based on these clinical characteristics, the genetic aberrations underlying tumor initiation and progression are also expected to be different between these two patient groups. A young age of onset is a hallmark of hereditary CRC. Indeed, occasionally CRCs in AYAs can be explained by known CRC predisposing syndromes. In most cases, however, a positive family history for cancer is absent. Considering the poor prognosis within this subgroup, we hypothesize that strong genetic factors are not inherited in a dominant fashion, but rather have occurred de novo or follow a recessive or digenic pattern of inheritance.

Study objective

To unravel the genetic makeup of colorectal cancer (CRC) in adolescents and young adults (AYAs) in order to improve genetic counseling, surveillance and, ultimately, treatment and disease outcome.

Study design

We will perform whole-exome sequencing on germline DNA of 15 patients diagnosed with CRC <=25 years of age and their healthy parents. This strategy will enable the identification of high-penetrant variants that follow de novo, recessive or digenic patterns of inheritance. In addition, we will perform genome-wide copy number analysis and high-throughput targeted sequencing of tumor DNA of these 15 and 40 additional patients with CRC <=25 years of age, to uncover the overlapping, and thus clinically most relevant, somatic mutation spectra of these CRCs. This integrated germline-somatic approach on a stringently selected CRC patient cohort is expected to entail enough power to draw firm conclusions.

Study burden and risks

The risk of this study is considered to be negligible. The only physical burden is a venepuncture. There is a small risk of unsolicited findings when exome or genome sequencing is performed. Patients and/or their caretakers will be thoroughly counselled about these risks and possible psychosocial consequences. Furthermore the protocol that is used for unsolicited findings has already been established in the department of Clinical Genetics and is approved by the Commissie Mensgebonden Onderzoek Regio Arnhem-Nijmegen (ref CD/CMO 0507).

Contacts

Public
Radboudumc

Geert Grooteplein 10
Nijmegen 6500HB
NL
Scientific
Radboudumc

Geert Grooteplein 10
Nijmegen 6500HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

15 individuals diagnosed with CRC <=25 years of age and
• a mismatch repair-proficient tumor
• polyposis syndromes excluded if polyps are present;and their parents. ;In addition we will anonymously include tumor DNA of 40 patients with CRC diagnosed <=25 years of age.

Exclusion criteria

A known genetic defect in the family for a cancer unrelated condition, of which the child might be a carrier but about which the child/parents do not want to be informed.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-01-2015
Enrollment:	85
Type:	Actual

Ethics review

Approved WMO Date:	08-12-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-02-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-02-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-05-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL49317.091.14