ISRCTN11642464 https://doi.org/10.1186/ISRCTN11642464

Intestinal cancer and the risk for other cancer in the same person

Submission date	Recruitment status	[_] Prospectively registered
11/06/2023	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
16/06/2023	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
15/06/2023	Cancer	

Plain English summary of protocol

Background and study aims
Disparities between tumors arising via different carcinogenetic pathways have not been studied systematically. This study evaluated the differences in the risk for non-intestinal cancer between patients with intestinal cancer originating from different carcinogenetic statuses.

Who can participate?
Adult patients with histologically confirmed colorectal cancer

What does this study involve?
This is a retrospective cohort study describing the association between intestinal and not intestinal cancer among patients with different carcinogenetic backgrounds. This retrospective European multicenter cohort study included 1706 CRC patients treated between 1986 and 2019, in three different countries.

What are the possible benefits and risks of participating?
The possible benefit is to understand the relationship between different types of cancer in the same patient. There are no risks for participants.

Where is the study run from?
Umeå University (Sweden)

When is the study starting and how long is it expected to run for?
January 2013 to March 2021

Who is funding the study?
1. Faculty of Medicine at Umeå University
2. Cancer Foundation Finland
3. Cancer Research Foundation in Northern Sweden
4. Nordic Cancer Union
5. The Northern Healthcare Regional Association

Who is the main contact?
Ioannis Gkekas (Senior Consultant Surgeon), ioannis.gkekas@umu.se (Sweden)

Contact information

Type(s)
Principal Investigator

Contact name
Dr Ioannis Gkekas

ORCID ID
http://orcid.org/0000-0002-7382-3636

Contact details
Hoppets Gränd 8
Umeå
Sweden
90334
+46703660249
gkekasioannis@windowslive.com

Type(s)
Scientific

Contact name
Prof Ulf Gunnarsson

ORCID ID
http://orcid.org/0000-0002-3806-2114

Contact details
Umeå University
Faculty of medicine
Department of Surgical and Perioperative Science, Surgery,
Kungsgatan 81
Umeå
Sweden
903 30
+46706320353
ulf.gunnarsson@umu.se

Type(s)
Public

Contact name
Prof Karin Strigård

ORCID ID

http://orcid.org/0000-0001-5838-9133

Contact details
Umeå University
Faculty of medicine
Department of Surgical and Perioperative Science, Surgery,
Kungsgatan 81
Umeå
Sweden
903 30
0046733820772
karin.strigard@umu.se

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Sporadic deficient mismatch repair in colorectal cancer increases the risk for non-colorectal malignancy

Acronym
registerMMR

Study objectives
A higher association between sporadic deficient mismatch repair (dMMR) status and the risk of non-colorectal malignancy in patients with known colorectal cancer (CRC)

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 02/12/2014, Regional Medical Review Board in Umeå, Department of Medical Strengthening (Regional etikprövningsnämnden i Umeå Avdelningen fur Medicinsk Forstkning) (Samverkanshuset, C/o Umeå Universitet, Umeå, 90187, Sweden; +46 (0)104750800; registrator@etikprovning.se), ref: 2014-371-31M

Study design
Multicenter retrospective cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Laboratory, Medical and other records

Study type(s)
Screening

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Association between sporadic dMMR status and the risk of non-colorectal malignancy in patients with known colorectal cancer

Interventions
This study is a retrospective cohort describing the association between intestinal and not intestinal cancer among patients with different carcinogenetic backgrounds. This retrospective European multicenter cohort study included 1706 CRC patients treated between 1986 and 2019, in three different countries. The proficiency (pMMR) or deficiency (dMMR) of mismatch repair was determined by immunohistochemistry. Cases were analyzed for BRAFV600E mutation, and BRAF mutation cases were further analyzed for hypermethylation status in the promotor region of MLH1 in order to distinguish between sporadic and hereditary cases. Scandinavian patients were matched against their respective National Cancer Registries. Thorough scrutiny of medical files was performed for the Czech cohort to identify any non-colorectal malignancy within 20 years prior to or after the diagnosis of CRC. Poisson regression analysis was performed to identify the incidence rate of non-colorectal malignancy. For validation purposes, standardized incidence ratios (SIR) were calculated for each cancer reported, adjusted for age, year, and sex.

Intervention Type
Other

Primary outcome measure
The risk for non-colorectal malignancy before and after this diagnosis, compared to patients with different MMR tumors is measured using Incidence Rate Ratio (IRR) in both the univariable and multivariable analyses at one timepoint

Secondary outcome measures
Standardized incidence ratios (SIR) are calculated for each of the cancer forms reported (patients with pMMR and dMMR separately) and adjusted for sex, year (in one-year classes), and age (in five-year classes) at one timepoint

Overall study start date
01/01/2013

Completion date

02/03/2021

Eligibility

Key inclusion criteria
1. Histologically confirmed CRC
2. Stage confirmed and transformed to the American Joint Committee on Cancer (AJCC) TNM classification
3. Available clinical and pathological data regarding the course of the disease and demographic data

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
Both

Target number of participants
2107

Total final enrolment
1706

Key exclusion criteria
1. Patients younger than 18 years
2. Inconclusive immunohistochemical analysis (IHC) or missing data

Date of first enrolment
29/10/2015

Date of final enrolment
12/01/2021

Locations

Countries of recruitment
Czech Republic

Finland

Sweden

Study participating centre
Umeå University hospital
Daniel Naezéns väg
Umeå
Sweden
907 37

Study participating centre
Helskinki University Hospital Department of Surgery
Haartmaninkatu 8
P.O. Box 63
Helsinki
Finland
00014

Study participating centre
Masaryk Memorial Cancer Institute
Žlutý kopec 543/7
Brno
Czech Republic
60200

Sponsor information

Organisation
Cancer Research Foundation in Northern Sweden (Cancerforskningsfonden i Norrland)

Sponsor details
Oncology, Norrland University Hospital (Onkologi, Norrlands Universitetssjukhus)
Umeå
Sweden
901 85
+46 (0)90-785 28 54
pia@cancerforskningsfonden.se

Sponsor type
University/education

Website
https://cancerforskningsfonden.se/

Funder(s)

Funder type
University/education

Funder Name
Medicinska fakulteten, Umeå Universitet

Alternative Name(s)
Faculty of Medicine at Umeå University, Faculty of Medicine, Umeå University, Faculty of Medicine, Medicinska fakulteten

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Funder Name
Syöpäsäätiö

Alternative Name(s)
Cancer Foundation Finland, Cancerstiftelsen

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Finland

Funder Name
Cancer Research Foundation in Northern Sweden

Alternative Name(s)
Northern Sweden Cancer Foundation

Funding Body Type

Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Sweden

Funder Name
Nordic Cancer Union

Funder Name
Northern Healthcare Regional Association

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
30/06/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Ioannis Gkekas, ioannis.gkekas@umu.se. The type of data that will be shared is completely anonymization for every variable and includes sex, age, cancer stage, and type of cancer. These data will be available immediately. Consent from participants was not required or obtained. Ethical and legal restrictions are in concordance with the ethical approval obtained.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Thesis results	Doctoral thesis; study V	21/05/2021	15/06/2023	No	No