ISRCTN36459506 https://doi.org/10.1186/ISRCTN36459506

Determining colorectal cancer features using a Rwandan population to lay a foundation and inform precise colorectal cancer clinical management

Submission date
06/12/2021

Recruitment status
No longer recruiting

Registration date
24/12/2021

Overall study status
Completed

Last Edited
21/12/2021

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Genetics aspects of colorectal cancer throughout the world are gaining considerable scientific attention due to their impact on surveillance and management, including targeted therapy. Microsatellites are short tandem repeat DNA sequences distributed throughout the human genome. Secondary to their repeated structure, microsatellites are disposed to errors that are ordinarily fixed by the mismatch repair system (MMR), which when faulty, leads to a strong mutator phenotype known as microsatellite instability (MSI). MSI is one of the major pathways causing colorectal cancer, as it accounts for 15% of all colorectal cancer cases in Caucasian populations.

Several clinical trials have demonstrated that MSI-high colorectal cancer is significantly responsive to immunotherapy using immune checkpoint inhibitors. In Africa, there is a dearth of data on the subject, and in Rwanda specifically, there is presently no reported data on this subject. To our knowledge, this is the largest MSI status study on CRC in an African population.

There are mismatch repair (MMR) genes that are responsible for correcting errors that arise during DNA replication. Proteins within the MMR system are MLH1, PMS2, MSH2, MSH6, MLH3, MSH3, PMS1, and Exo1. When the repair system is ineffective, it results in a strong mutator phenotype called microsatellite instability (MSI). MSI is one of the major carcinogenic (cancer-causing) pathways of colorectal cancer, and there are usually two mechanisms:
1. Hereditary nonpolyposis colorectal cancer, commonly known as Lynch Syndrome, where a mutation in one of the MMR genes is inherited from a parent
2. Sporadic mutation (a mutation that occurs throughout the course of a person's lifetime and is not inherited), which accounts for 15% of colorectal cancers, mostly occurring in the MLH1 gene

Who can participate?
Colorectal cancer patients who have been diagnosed either at King Faisal Hospital (KFH) or at Rwanda Military Hospital (RMH) between 01/01/2019 and 31/12/2021.

What does the study involve?
This study will look at the medical records of all colorectal cancer patients meeting the selection criteria during the study period. Data will be entered directly into a Microsoft Excel data collection tool and stored on a password-protected laptop. Colorectal cancer tissue or blood collected as part of routine medical care will be used for DNA analysis to identify microsatellite instability (MSI). A commercial kit from Promega (MSI Analysis System, Version 1.2) will be used to categorise MSI in one of three categories: MSI-H, MSI-L, or MSS.

What are the possible benefits and risks of participating?
There is no anticipated patient risk in this study. Findings from this study will inform better CRC management in Rwanda.

Where is the study run from?
The study will be run at the King Faisal Hospital (Rwanda) and at the Rwanda Military Hospital (Rwanda)

When is the study starting and how long is it expected to run for?
From January 2020 to July 2022

Who is funding the study?
VLIR-UOS (Netherlands)

Who is the main contact?
1. Dr. Yvan Butera, yvan.butera@moh.gov.rw
2. Nadia Hitimana, hitnada@gmail.com

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Molecular and genetic profile of colorectal cancer in Rwanda

Study objectives
Data from this study will contribute to the knowledge on molecular and genetic characteristics of colorectal cancer patients in Rwanda and have a significant role both as prognostic and predictive factors.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/11/2021, The University of Rwanda - the College of Medicine and Health Sciences (CMHS) Institutional Review Board (IRB) (P.O.Box 3286 Kigali, Rwanda; +250784575900; researchcenter@ur.ac.rw), ref: No 328/CMHSIRB/2021

Study design
Mixed (retrospective and prospective) cross-sectional descriptive laboratory study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Colorectal cancer

Interventions
This is a mixed (retrospective and prospective) descriptive laboratory study of colorectal cancer patients who have undergone diagnosis either at King Faisal Hospital (KFH) or at Rwanda Military Hospital (RMH) from 01/01/2019 to 29/02/2021, and prospectively from 21/03/2021 to 31/05/2021.

Retrospective data will be collected from the surgery logbooks and electronic medical records (EMR) of all colorectal cancer patients diagnosed at KFH meeting the selection criteria during the study period. Data will be entered directly into a Microsoft Excel data collection tool and stored on a password-protected laptop. A de-identified database will be established from the data collection tool and EMR data query results. All datasets will be password-protected and saved on a backup drive.

A commercial kit from Promega (MSI Analysis System, Version 1.2) will be used for MSI typing. Three categories of MSI status are observed by using Promega kit, MSI-H, MSI-L, and MSS. Laboratory studies will be done in the following steps:
1. DNA extraction from paraffin-embedded CRC tissues and blood
2. Amplification of microsatellites by PCR
3. Capillary electrophoresis on an automated sequencer
4. Data analysis using GeneMapper® software
After completion of the run, DNA fragments will be analyzed using AlleleLink software provided by the manufacturer.

Intervention Type
Genetic

Primary outcome measure
MSI status, categorised as MSI-H, MSI-L, or MSS, measured using Promega (MSI Analysis System, Version 1.2) kit at a single time point

Secondary outcome measures
1. Demographics measured from electronic medical records (EMR) at a single time point
2. Family history measured from electronic medical records (EMR) at a single time point
3. Clinical history, including treatment measured from electronic medical records (EMR) at a single time point
4. Diagnostic method (colonoscopy + biopsy) measured from electronic medical records (EMR) at a single time point
5. Location of tumor in the bowel measured from electronic medical records (EMR) and surgery logbooks at a single time point
6. Gross appearance measured from electronic medical records (EMR) at a single time point
7. Histopathological type and grade measured from electronic medical records (EMR) at a single time point
8. Lymphocytic infiltration measured from electronic medical records (EMR) at a single time point
9. Signet-ring cell measured from electronic medical records (EMR) at a single time point
10. Tumor stage measured from electronic medical records (EMR) at a single time point

Overall study start date
01/01/2020

Completion date
29/07/2022

Eligibility

Key inclusion criteria
1. Histologically confirmed colorectal cancer
2. Diagnosis made or reviewed at King Faisal Hospital (KFH) between 01/01/2019 and 29/02

/2021, or prospectively from 21/03/2021 to 31/05/2021
3. Adult

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
300

Key exclusion criteria
Patients with colorectal masses that are not histologically confirmed

Date of first enrolment
01/01/2019

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
Rwanda

Study participating centre
King Faisal Hospital
KG 544 Street
Kigali
Rwanda
-

Study participating centre
Rwanda Military Hospital
KK739 Street
Kigali
Rwanda
-

Sponsor information

Organisation
KU Leuven

Sponsor details
Krakenstraat 3 box 5508
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Sponsor type
Industry

Website
https://www.kuleuven.be

ROR
https://ror.org/05f950310

Funder(s)

Funder type
University/education

Funder Name
Not applicable

Results and Publications

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

Intention to publish date
01/02/2023

Individual participant data (IPD) sharing plan
Written consent will be obtained from all participants. All data (demographic and lab data) will be stored on a passworded study computer, only accessible to the research team. Biopsy and blood samples will be stored in both hospitals involved in this research (RMH and KFH) according to their storage policies.

IPD sharing plan summary
Stored in non-publicly available repository