MOlecular stool testing for Colorectal CAncer Surveillance

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1. To determine the accuracy (i.e. sensitivity, specificity, PPV and NPV) of: a. A molecular stool test, i.e. Cologuard® (Exact Sciences, Madison, WI, USA) consisting of a stool DNA test and an immunochemical assay for human hemoglobin;b. FIT: OC-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational non invasive

Summary

ID

NL-OMON50418

Source
ToetsingOnline

Brief title
MOCCAS

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
colorectal carcinoma, colorectal neoplasia

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: KWF/Alpe d'Huzes

Intervention

Keyword: colorectal cancer, Molecular stool test, surveillance

Outcome measures

Primary outcome

1. The accuracy (sensitivity, specificity, PPV and NPV) of the molecular stool test (Cologuard®) and FIT compared to colonoscopy in the detection of advanced neoplasia compared in a surveillance population.

2. Health outcomes and cost-effectivess of multiple surveillance strategies based on accuracies from endpoint 1.

Secondary outcome

- The accuracy of the molecular stool test (Cologuard®) and FIT in relation to patient characteristics ((i.e. age, gender, family history, BMI and smoking);

- The presence of the molecular markers (included in the molecular stool test) in the resected polyps;

- The correlation between the presence of the molecular markers and the result of the molecular stool test.

- The identification of low- and high risk adenomas based on previously identified progression biomarkers in all the post-polypectomy tissue samples;

- The impact of molecularly defined high-risk adenoma*s on the obtained sensitivity data of the molecular stool test (Cologuard®) and FIT;

- The impact of the integration of molecularly defined high-risk adenoma*s on the health outcomes and cost-effectiveness of the multiple surveillance strategies.

- The additional value of risk assessment through a questionnaire (addressing

gender, age, BMI20,21, family history22,23, physical activity, nutritional

habits and smoking) on the accuracy of the molecular stool test (Cologuard®)

and FIT;

Study description

Background summary

With more than 13.000 new patients and >5.000 deaths per year in the Netherlands, colorectal cancer (CRC) poses a big health problem. Screening for early stage, treatable tumours is a cost-effective approach to tackle this problem. Therefore, population-wide CRC screening was implemented in the Netherlands in 2014, using the Faecal Immunochemical Test (FIT). About 6% of screenees will test positive, yielding approximately 80.000 extra colonoscopies per year. Of these screenees >40% will have (advanced) adenomas and most of them will qualify for surveillance colonoscopies according to the current guideline.

While post-polypectomy surveillance consumes about 25% of colonoscopy capacity, experts agree that evidence for the impact of colonoscopic post-polypectomy surveillance on the ultimate endpoint, i.e. death from CRC, is limited and current surveillance strategies lead to overdiagnosis and over-treatment. The revised Dutch surveillance guideline (2013), although more risk-based than the previous guidelines and than international guidelines, will not be able to solve this. Besides the overuse, colonoscopy is an invasive procedure with a burden and also a risk for complications. Therefore there is a need for alternative, preferably non-invasive, surveillance tests.

Stool-based molecular testing may well be an alternative for colonoscopy surveillance as molecular tests are more specific than colonoscopy for relevant adenomas and less burdensome for patients. While the sensitivity of a single molecular test for the detection of cancers and advanced adenomas is lower than that of colonoscopy, an approach of repeated molecular tests (e.g. biennially) may yield similar detection rates as a colonoscopy based surveillance programme. If validated for this purpose, stool-based molecular surveillance tests has the potential to dramatically decrease the demand for colonoscopy capacity.

Study objective

1. To determine the accuracy (i.e. sensitivity, specificity, PPV and NPV) of:
a. A molecular stool test, i.e. Cologuard® (Exact Sciences, Madison, WI, USA)

consisting of a stool DNA test and an immunochemical assay for human hemoglobin;
b. FIT: OC-sensor® (Eiken Chemical Co., Tokyo, Japan) and FOB GoldTM (Sentinel, Milan, Italy);
in the detection of advanced neoplasia compared to colonoscopy in a surveillance population.

2. To model various strategies of surveillance based on colonoscopy or alternative surveillance tools using the obtained accuracy data from the molecular stool test (Cologuard®) and FIT.

Study design

The current project is designed as a prospective observational cross-sectional cohort study.

Through this design, rates of advanced neoplasia as detected by the molecular stool test (Cologuard®) and FIT will be compared to the results as detected by colonoscopy. Colonoscopy in combination with histology is considered the gold standard for the diagnosis of advanced neoplasia. All subjects scheduled for (elective) colonoscopy surveillance in the participating centres (i.e. AMC, Antoni van Leeuwenhoek Hospital, Slotervaart Hospital, MUMC, Kennemer Gasthuis Haarlem and Flevoziekenhuis Almere) who are eligible for this study according to the in- and exclusion criteria, will be invited to participate. Necessary faeces collection is scheduled at home just before the surveillance colonoscopy and before bowel preparation. Participants receive a questionnaire before the scheduled colonoscopy to assess risk-factors for CRC.

Study burden and risks

Burden for participant consists of at home faeces collection and the completion of a questionnaire.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Subjects in the age group 50-75 years.
- Subjects with an indication for surveillance colonoscopy according to the previous guideline (*Follow up after polypectomy*, 2002; summarized in 2008) or current (*Colonoscopy Surveillance*, 2013) guideline, i.e. subjects with a history of CRC or polypectomy, as well as subjects under surveillance for familial colorectal carcinoma (FCC).
- Subjects who have sufficient comprehension of the Dutch language.
- Subjects who have given their informed consent.

Exclusion criteria

- Subjects with inflammatory bowel disease (IBD)
- Subjects with Lynch syndrome, familial adenomatous polyposis (FAP), attenuated FAP (AFAP), MUTYH associated polyposis (MAP) and serrated polyposis syndrome (SPS)
- Subjects with a previous colonoscopy < 6 months (rescopy)
- Subjects with proctocolectomy
- Subjects with life expectancy < 3 years

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-11-2015
Enrollment:	4000
Type:	Actual

Ethics review

Approved WMO Date:	09-07-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	03-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-03-2019
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	NL52708.018.15