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Aspirin esomeprazole chemoprevention trial

Submission date 17/01/2005	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 15/02/2005	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 27/03/2019	**Condition category** Digestive System	[_] Individual participant data

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-aspirin-and-esomeprazole-as-a-way-of-preventing-cancer-of-the-foodpipe

Background and study aims
Barrett's oesophagus is a condition where the cells that line the lower part of the (oesophagus) (gullet) are damaged by acid and bile travelling upwards from the stomach. Patients with Barrett's oesophagus have an increased risk of developing oesophageal cancer. This study uses two drugs with the aim of reducing the risk of progression of Barrett's oesophagus to oesophageal cancer. All participants receive a drug called a proton pump inhibitor which reduces stomach acidity and may stop the cells in the oesophagus from being damaged more and becoming cancerous. Some participants also receive aspirin because there is some evidence that aspirin reduces the risk of developing oesophageal, stomach and colon cancer.

Who can participate?
Patients aged over 18 with Barrett's oesophagus

What does the study involve?
Participants are randomly allocated to one of four groups to take one of two doses of the proton pump inhibitor either with or without aspirin. Participants take tablets every day for at least 8 years and have annual follow up visits either at the hospital or by telephone. Participants also have endoscopies every 2 years which are the same as the standard monitoring endoscopies for patients with Barrett's oesophagus, although some additional samples are taken for the study.

What are the possible benefits and risks of participating?
Participants have regular follow up visits and endoscopies and receive their study tablets free of charge. The benefit of the drugs in preventing the progression of Barrett's oesophagus to oesophageal cancer will not be known until after the end of the study. Both of the study drugs have potential side effects but generally patients tolerate the treatment well. There are small risks to having an endoscopy but there is no greater risk to having an endoscopy in this study than there is to having an endoscopy as part of standard Barrett's monitoring.

Where is the study run from?
University of Oxford (UK) and 85 hospitals listed at https://aspect.octru.ox.ac.uk/all-sites-3

When is the study starting and how long is it expected to run for?
March 2005 to October 2018

Who is funding the study?
Cancer Research UK (CRUK) (UK)

Who is the main contact?
Prof. Janusz Jankowski
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Contact information

Type(s)
Scientific

Contact name
Prof Janusz Jankowski

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Additional identifiers

Clinical Trials Information System (CTIS)
2004-003836-77

ClinicalTrials.gov (NCT)
NCT00357682

Protocol serial number
N/A

Study information

Scientific Title
A phase III, randomised, study of Aspirin and Esomeprazole Chemoprevention in Barrett's Metaplasia (BM)

Acronym
AspECT

Study objectives
Study objectives as of 24/08/2016:
Primary objectives:
1. To assess whether intervention with aspirin result in a decreased mortality or conversion rate from Barretts metaplasia to adenocarcinoma or high grade dysplasia
2. To assess whether high dose PPI therapy decreases the mortality or conversion rate from Barretts Metaplasia to adenocarcinoma or high grade dysplasia

Secondary objectives:
1. To assess whether there are there clinical and molecular risk factors than can be identified in BM for the development of BA
2. To assess the cost effectiveness of aspirin and/or PPI treatment in the prevention of BA.
3. To assess whether intervention with PPI and/or aspirin induces changes in the expression of molecular markers for BA
4. To assess how quality of life is affected by the different treatments
5. To assess what the biological risk factors are for cardiac disease and aspirin resistance
6. To assess gender differences in outcomes

Tertiary/exploratory objectives:
1. To assess aspirin's role on the development of colorectal adenomas and cancer
2. To collect and bank samples for use in future ethically approved studies

Study objectives from 22/05/2007 to 24/08/2016:
Primary objectives:
1. To assess whether intervention with aspirin result in a decreased mortality or conversion rate from Barretts metaplasia to adenocarcinoma or high grade dysplasia
2. To assess whether high dose PPI therapy decreases the mortality or conversion rate from Barretts Metaplasia to adenocarcinoma or high grade dysplasia

Secondary objectives:
1. To assess whether there are there clinical and molecular risk factors than can be identified in BM for the development of BA
2. To assess the cost effectiveness of aspirin and/or PPI treatment in the prevention of BA.
3. To assess whether intervention with PPI and/or aspirin induces changes in the expression of molecular markers for BA
4. To assess whether molecular markers can be used to monitor disease and identify groups at high risk of conversion
5. To investigate new genes important in the progression of BA, as a unique tissue bank will be available with a complete endoscopic, histological, physiology and pharmaceutical history
6. To investigate host susceptibility genes and environmental (diet) versus gene interactions
7. To investigate how intervention with PPI and/or aspirin influences the timing and severity of acid reflux into the oesophagus and the change in concentrations of bile acids in the oesophageal aspirates

Study hypothesis provided at time of registration:
The aim of this trial is to see if high or low dose esomeprazole alone, or esomeprazole and aspirin together can help stop Barrett's oesophagus developing into oesophageal cancer.

Ethics approval required

Old ethics approval format

Ethics approval(s)
East London and the City Research Ethics Committee 1, 08/06/2004, ref: 04/Q0603/1

Study design
Phase III multi-centre randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Barrett's oesophagus due to chronic reflux in the gullet

Interventions
Please note that the doses of the drugs below were added as of 22/05/2007:
Arm A (Standard Therapy): 20 mg esomeprazole
Arm B (Strong Acid Suppression): 80 mg esomeprazole
Arm C (Standard Therapy + Aspirin): 20 mg esomeprazole + 300 mg aspirin
Arm D (Strong Acid Suppression + Aspirin): 80 mg esomeprazole + 300 mg aspirin

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Aspirin, esomeprazole

Primary outcome(s)
Primary outcome measures as of 24/08/2016:
A composite primary endpoint of all-cause mortality and conversion to adenocarcinoma and conversion to high grade dysplasia, assessed after all patients have completed at least 8 years of follow up

Primary outcome measures from 22/05/2007 to 24/08/2016:
The following will be assessed at 4 and 8 years and four yearly until the end of study:
1. Conversion to adenocarcinoma of the oesophagus
2. Conversion to high grade dysplasia
3. Death by all causes

Key secondary outcome(s))
Secondary outcome measures as of 24/08/2016:
1. All-cause mortality, assessed after all patients have completed at least 8 years of follow up
2. Conversion to oesophageal adenocarcinoma, assessed after all patients have completed at least 8 years of follow up
3. Conversion to high grade dysplasia, assessed after all patients have completed at least 8 years

of follow up
4. Death from oesophageal cancer, assessed after all patients have completed at least 8 years of follow up
5. Cost/oesophageal adenocarcinoma prevented, assessed after all patients have completed at least 8 years of follow up
6. Cost/quality adjusted life year saved, assessed after all patients have completed at least 8 years of follow up
7. Molecular markers to be identified at the end of the trial, assessed after the end of the trial following sample analysis

Secondary outcome measures from 20/06/2007 to 24/08/2016:
The following will be assessed at 4 and 8 years and four yearly until the end of study:
1. Incidence of oesophagectomy
2. Stage of adenocarcinoma
3. Incidence of ablation therapy
4. Incidence of endoscopic mucosal resection
5. Quality of life, assessed by The Reflux Disease Questionnaire and the Euroqol-5 Dimensions (EQ-5D) Questionnaire
6. Molecular endpoints including genotype and mutational status

Secondary outcome measures added as of 22/05/2007:
1. Oesophagectomy
2. Stage of adenocarcinoma
3. Ablation therapy
4. Endoscopic mucosal resection

Completion date
31/10/2018

Eligibility

Key inclusion criteria
Inclusion criteria as of 24/08/2016:
1. Patients aged over 18 years
2. Circumferential Barrett's metaplasia of at least 1 cm in length (≥C1M1) or a tongue of Barrett's metaplasia of at least 2 cm in length (≥C0M2) (irrespective of the presence now or historically of histologically proven intestinal metaplasia)
3. Patients able to give written consent
4. Patients with World Health Organization (WHO) activity profile of 0 or 1 i.e. fully active and self-caring

Inclusion criteria from 22/05/2007 to 24/08/2016:
1. Patients aged over 18 years
2. Patient with circumferential Barretts Metaplasia at least 1 cm long, and histologically proven intestinal metaplasia in at least one sample
3. Patients able to give written consent
4. Patients with World Health Organization (WHO) activity profile of 0 or 1 i.e. fully active and self-caring

Inclusion criteria provided at time of registration:
1. Male between 40 - 75 years

2. At least 2 cm from the gastro-oesophageal junction of circumferential BM (histologically proven by intestinal metaplasia in at least one sample)
3. Able to give written consent
4. World Health Organization (WHO) activity profile of 0 i.e. fully active and self-caring

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Exclusion criteria as of 24/08/2016:
1. Patients with high grade dysplasia or carcinoma at enrolment
2. Medical conditions which would make completing endoscopies or completing the trial difficult, including:
2.1. Frequent transient ischaemic attacks (3 or more) or severe cerebral vascular accident in the previous 6 months (patients answering yes were eligible for the PPI-only (non-aspirin) arms of the trial)
2.2. Severe respiratory disease with arterial oxygen saturation of less than 90% at rest
2.3. Severe ischaemic heart disease (exercise tolerance less than 100 yards or life expectancy < 4 years) or myocardial infarction in the previous 3 months
2.4. Severe inflammatory bowel disease requiring at least one hospital admission of 5 days in the last year or bowels open > 6 times/day
3. Patients with absolute contraindications to PPIs, aspirin or their excipients i.e. allergies, ulcers, renal impairment or use of oral anticoagulants.
4. Pregnant or lactating women will not undergo endoscopy and may be given dispensation to stop drug therapy for a year. This should be discussed with the Trial Office.

Exclusion criteria from 22/05/2007 to 24/08/2016:
1. Patients with high grade dysplasia or carcinoma at enrolment;
2. Patients with medical conditions which would make completing endoscopies or the trial difficult to complete including:
2.1. Previous transient ischaemic attacks or cerebral vascular disease
2.2. Severe respiratory disease
2.3. Severe ischaemic heart disease or myocardial infarction in the previous 6 months
2.4. Inflammatory bowel disease
3. Patients who are on continuous aspirin or non-steroidal anti-inflammatories or Cox-2 inhibitors (more than 3 courses/year)
4. Patients with absolute contraindications to PPIs, aspirin or their excipients such as allergies, ulcers, renal impairment or use of oral anticoagulants
5. Pregnant or lactating women

Exclusion criteria provided at time of registration:
1. High grade dysplasia or carcinoma at enrolment
2. Medical conditions which would make endoscopy or the trial difficult or failure to complete including transient ischaemic attacks or cerebral vascular disease, severe respiratory disease, severe ischaemic heart disease or recent myocardial infarction or inflammatory bowel disease
3. Patients who are on continuous aspirin or non-steroidal drugs (more than 3 courses/year)
4. Absolute contraindications (ulcers) or allergies to PPIs or aspirin such as renal impairment and oral anticoagulants

Date of first enrolment
01/03/2005

Date of final enrolment
28/02/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Oxford
Oxford
United Kingdom
OX3 7DQ

Study participating centre
85 active sites
United Kingdom
-

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK)

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Janusz Jankowski (Chief Investigator) (jjankowski@uclan.ac.uk) and Sharon Love (Statistician) (Sharon.Love@csm.ox.ac.uk). The TMG assess applications for the data and the DSMC give permission for distribution of the data. All data may be made available after the study's laboratory endpoints have been completed.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	04/08/2018		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes