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A randomised controlled trial of colorectal polyp and cancer prevention using aspirin and resistant starch in carriers of hereditary nonpolyposis colorectal cancer

Submission date
18/05/2001

Recruitment status
No longer recruiting

Registration date
18/05/2001

Overall study status
Completed

Last Edited
15/06/2020

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.capp2.com

Contact information

Type(s)
Scientific

Contact name
Prof John Burn

Contact details
CAPP Office
Bioscience Centre
Times Square
Scotswood Road
Newcastle upon Tyne
United Kingdom
NE1 4EP
+44 (0)191 2331414
John.Burn@ncl.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
G0100496

Study information

Scientific Title
A randomised controlled trial of colorectal polyp and cancer prevention using aspirin and resistant starch in carriers of hereditary nonpolyposis colorectal cancer

Acronym
CAPP2

Study objectives
1. To study the effect of aspirin and/or resistant starch in a placebo controlled, double-blind randomised trial on carriers of Hereditary Non-Polyposis Colorectal Cancer (HNPCC) (Lynch Syndrome);
2. To assess the polyp, adenoma and/or cancer recurrence in these patients during a two to four year treatment period.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Hereditary non-polyposis colorectal cancer (HNPCC)

Interventions
Targets Lynch syndrome patients/600 mg enteric coated aspirin daily or placebo AND 30 g resistant starch or placebo:
1. 600 mg aspirin/30 g treatment starch
2. 600 mg placebo tablets/30 g treatment starch
3. 600 mg aspirin/30 g placebo starch
4. 600 mg placebo tablets/30 g placebo starch

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Aspirin and resistant starch

Primary outcome measure
The primary endpoint will be the number, size and histological stage of colorectal carcinomas found after a minimum of 2 years treatment.

Secondary outcome measures
1. Adenoma size and number:
Elective removal of polyps will make fully developed cancers rare. The main outcome measure will be the number, size, location, villosity and dysplasia of adenomatous polyps
2. Apoptosis in adenomata:
A recent observation in the histology of an adenoma from a participant in CAPP1 has led us to consider that the pattern of apoptosis within adenomata is worthy of study. This is in keeping with the evidence in vivo and in vitro for an effect of aspirin on apoptosis. We will therefore request histopathological assessment of adenomas snared at colonoscopy, with special interest in signet cells and undifferentiated medullary carcinoma.
3. Cell proliferation and apoptosis in flat mucosa:
In a sub-set of participants, biopsies of flat rectal mucosa will be collected before and after treatment to test the hypothesis that altered cell proliferation (see Mills et al. 2001) and/or apoptosis is a reliable biomarker of tumorigenesis.
4. Other cancers:
Gene carriers of Lynch syndrome are at increased risk of many extracolonic cancers, and these will be systematically reported in the study group. In particular, there is a 42% lifetime risk of endometrial cancers in female gene carriers (Dunlop et al., 1997; Watson et al., 1994). These data are important in monitoring any favourable or unfavourable change in all cancers within the different study groups. In particular, it will be important to ascertain if the interventions might reduce colonic tumours while at the same time increasing upper gastrointestinal (GI) or non GI tumours. In mouse studies parallel to CAPP1, we have found a significant increase in small bowel polyps in APC knockout mice fed excess resistant starch (Burn et al., 1996). Aspirin reversed the effect. Regular aspirin use is associated with a reduced incidence of gastric cancer, a malignancy reported with increased frequency in Lynch syndrome families.

Overall study start date
01/01/1999

Completion date
31/01/2008

Eligibility

Key inclusion criteria
A) Genetic diagnosis:
Proven carriers of pathological mutations in mismatch repair genes

B) Clinical diagnosis:
Belong to a recognised Lynch Syndrome family based on the modified Amsterdam criteria (see below) AND have had at least one of the following events:
1. A colorectal cancer
2. An adenoma of over 5 mm diameter
3. A related carcinoma; endometrial carcinoma is particularly predictive of gene carrier status but others include small bowel, uroepithelial, or stomach
4. An adenoma under 40 years of age
5. Two or more adenomas on more than one occasion
6. Also have had an intact colon or have had only a segmental resection and have normal bowel actions

Modified Amsterdam criteria:
1. Three cases of HNPCC related cancer in the family
2. One is a first degree relative of the other two
3. One under 50 years
4. At least two generations affected

All enrolees should also:
1. Be over 25 years old. There is no upper age limit.
2. Have intact colon or have had only a segmental resection and have normal (non-medicated) bowel actions (three or fewer formed bowel actions per day).

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
1,000

Total final enrolment
861

Key exclusion criteria
1. Pregnancy (note: there have been few reports of adverse effects associated with aspirin use in pregnancy and aspirin is not regarded as a teratogen so women of child bearing age may be

recruited. However, women should temporarily withdraw from the trial if they become pregnant. They can restart immediately after delivery if they are not breast feeding. If mothers are breast feeding they should not re-enter the trial until they have completed breast feeding.)
2. Medical contraindications for aspirin e.g. aspirin induced asthma, previous aspirin/Non-Steroidal Anti-Inflammatory Drug (NSAID) induced peptic ulcer, renal impairment beyond creatinine of 0.15 mmol/l, or haemorrhagic diathesis
3. Already taking NSAIDs or steroids (note: if, during participation in the trial, a participant needs to take a course of NSAIDs they should be temporarily withdrawn from all limbs of the trial)
4. Severe intercurrent disease
5. Known to be Human Immunodeficiency Virus (HIV) positive (routine testing not required)

Date of first enrolment
01/01/1999

Date of final enrolment
31/01/2008

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
CAPP Office
Newcastle upon Tyne
United Kingdom
NE1 4EP

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Trust (UK)

Sponsor details
R&D Department
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
England
United Kingdom
NE1 4LP
+44 (0)191 282 5959
craig.mackerness@trvi.nuth.northy.nhs.uk

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (UK)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Plain English results				No	Yes
Results article	results	11/12/2008		Yes	No
Results article	aspirin results	17/12/2011		Yes	No

Results article	resistant starch results	01/12/2012		Yes	No
Results article	results	13/06/2020	15/06/2020	Yes	No