Chemopreventive effects of mesalazine in patients at high risk of recurrent (nonfamilial) colorectal adenomas

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1) Identify chemopreventive properties of mesalazine in patients at high risk of recurrent (nonfamilial) colorectal adenomas by evaluating the effect of treatment on apoptosis and proliferation in histologically normal sigmoid and rectal mucosa...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Benign neoplasms gastrointestinal
Study type	Interventional

Summary

ID

NL-OMON38274

Source
ToetsingOnline

Brief title
mesalazine effects in sporadic colorectal adenoma patients

Condition

- Benign neoplasms gastrointestinal
- Gastrointestinal neoplasms benign

Synonym
sporadic colorectal adenoma, sporadic colorectal adenomatous polyps

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Dr. Falk Pharma Benelux B.V.

Intervention

Keyword: anti-proliferative, chemoprevention, pro-apoptotic, sporadic colorectal adenomatous polyp

Outcome measures

Primary outcome

The effect of treatment with mesalazine on apoptotic and proliferation indices

and distribution of proliferating cells relative to the placebo group.

Secondary outcome

The effect of treatment with mesalazine on the mRNA and protein expression of β-

catenin signalling pathway components relative to the placebo group.

Study description

Background summary

Patients with sporadic colorectal adenomatous polyps removed by polypectomy have a high rate of polyp recurrence and carry an increased risk for the development of colorectal carcinoma (CRC). Chemoprevention may lower the rate of adenoma recurrence after polypectomy, thereby reducing the risk of CRC development. Unlike NSAIDs mesalazine is an attractive candidate for chemoprevention, since even during long-term use it has only limited systemic adverse effects and no gastrointestinal toxicity. In a prospective trial a trend towards reduced adenoma recurrence has been observed in high risk patients with a history of at least 3 sporadic colorectal adenomas treated with mesalazine. Identification of biologically relevant antineoplastic properties of mesalazine in patients with sporadic adenomatous polyps will support further investigation of mesalazine as chemopreventive agent against colorectal neoplasia in the sporadic setting. Growth inhibition of colonic epithelial cells through induction of apoptosis and inhibition of proliferation is widely recognized as a potential mechanism for chemoprevention of colorectal cancer. In vivo data suggest that mesalazine exerts pro-apoptotic and anti-proliferative effects on normal colorectal epithelial cells. Furthermore, there is in vitro evidence in CRC cells that mesalazine inhibits Wnt/β-catenin signalling, an early and common inappropriately activated pathway in colorectal carcinogenesis and molecular target for chemoprevention.

Study objective

1) Identify chemopreventive properties of mesalazine in patients at high risk of recurrent (nonfamilial) colorectal adenomas by evaluating the effect of treatment on apoptosis and proliferation in histologically normal sigmoid and rectal mucosa relative to the placebo group.
2) Identify chemopreventive properties of mesalazine in patients at high risk of recurrent (nonfamilial) colorectal adenomas by evaluating the effect of treatment on expression of beta-catenin signalling pathway components in histologically normal sigmoid and rectal mucosa relative to the placebo group.

Study design

double-blind, randomized placebo-controlled study

Intervention

Treatment with 3.0 g mesalazine or placebo once daily for 6 months. At baseline and after 6 months of treatment, a sigmoidoscopy will be performed and biopsies of normal appearing sigmoid and rectal mucosa will be collected.

Study burden and risks

Very rarely renal and liver disorders occur as a result from using mesalazine. In general these resolve after the use of mesalazine is discontinued. Four times during the study period blood samples will be drawn to check renal and liver function.
Five additional hospital visits are required for this study; one for screening and informed consent, twice to undergo a sigmoidoscopy and twice for adverse effects evaluation and compliance monitoring. During four of these visits a questionnaire concerning use of concomitant medication and nutritional supplements has to be completed.
A sigmoidoscopy is in general a safe examination with rarely complications occuring. Risk increase due to biopsy taking is negligible.

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

- Within 6 months before study entry having undergone complete colonoscopy with polypectomy for removal of sporadic adenomatous polyps. This should be 2 or more adenomas, irrespective of size, and/or one adenoma with a diameter of at least 1 cm and/or with proximal localization and/or with villous aspects or high-grade dysplasia.
- age 50-75 years

Exclusion criteria

- inflammatory bowel disease
- familial colorectal cancer syndrome
- history of colorectal carcinoma
- history of surgery to the large bowel (except appendectomy)
- chronic renal insufficiency
- chronic hepatic insufficiency
- allergy to salicylates
- asthma
- diabetes mellitus
- coagulation disorder or anticoagulant use, which cannot be temporarily discontinued
- regular intake of thiopurines, methotrexate or cyclosporin
- prescription use of aspirin (high- and low-dose) or other NSAIDs

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-07-2012
Enrollment:	68
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Salofalk granules
Generic name:	mesalazine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-08-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	11-11-2011
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-12-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-01-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	04-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
EudraCT	EUCTR2011-001815-29-NL
CCMO	NL36557.041.11