CRC chemoprevention in UC.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24955

Source
NTR

Brief title
CRC chemoprevention

Health condition

Ulcerative colitis - Colitis ulcerosa
Chemoprevention - Chemopreventie
Colorectal cancer - Colorectaal carcinoom

Sponsors and support

Primary sponsor: University Medical Center Utrecht
Source(s) of monetary or material Support: Dr Falk Pharma GmbH, Germany: Preparation investigational product

Intervention

Outcome measures

Primary outcome

1. Study the chemopreventive potential of 5-ASA and UDCA in UC by evaluating the effect of treatment on ACF number, relative to the placebo group;

2. Gain mechanistic insight into the chemopreventive properties of 5-ASA and UDCA by

genome-wide array based mRNA expression analysis of UC normal colonic mucosa before and after treatment.

Secondary outcome

1. Study the chemopreventive potential of 5-ASA and UDCA in UC by evaluating the effect of treatment on ACF size and rate of dysplasia, relative to the placebo group;

2. Improve understanding of early events in colorectal carcinogenesis by genome-wide array based mRNA expression analysis of dysplastic ACF and UC normal colonic mucosa.

Study description

Background summary

Patients with Ulcerative Colitis (UC), have an increased risk of developing colorectal cancer (CRC). Endoscopic surveillance does not reduce inherent neoplastic potential of the colon and colectomy is associated with medical and psychological complications. The developement of a safe and effective chemopreventive treatment strategy for reducing the overall risk of neoplasia would thus be of substantial benefit to UC patients. Epidemiological case-control studies have indicated that the regular use of 5-aminosalicylic acid (5-ASA) may reduce the risk of developing CRC in UC. Furthermore, 5-ASA and ursodeoxycholic acid (UDCA) has been demonstrated to suppress colitis-associated colon carcinogenesis in mice. Moreover, two retrospective studies have shown that patients with Primary Sclerosing Cholangitis (PSC) and UC had a significantly lower risk of developing dysplasia and CRC than non-treated patients. A recent study in patients with IBD and PSC also suggested that de combined use of 5-ASA and UDCA further decreases the risk of colorectal dysplasia development. Aberrant crypt foci (ACF) are considered to be the earliest identifiable preneoplastic lesions in the multistep proces of colorectal carcinogenesis. Recently, it has been reported that the number of ACF in the rectum increases from patients with UC and no dysplasia, to those with dysplasia and further to UC patients with CRC. Using ACF as a biological end-point rather than the number of colonic tumours has the advantage of a shorter study duration with generation of quantifiable results. Insight into the mechanism of chemopreventive properties of 5-ASA and UDCA has come from studies using CRC cells or animal models of inflammation. We speculate however that identifying the molecular targets in human colonocytes will provide more powerful insight into the mechanisms by which these agents impact neoplastic transformation.

Study objective

5-ASA and UDCA have a chemopreventive potential in UC.

Study design

1. Baseline: Informed consent, Clinical Activity Index, Bloodsamples, Colonoscopy & staining, Rectal/Sigmoid biopsies NM;

2. 4 Weeks: Compliance, Adverse effects questionnaire, Bloodsamples;

3. 12 Weeks: Compliance, Adverse effects questionnaire, Bloodsamples;

4. 20 Weeks: Compliance, Adverse effects questionnaire, Bloodsamples;

5. 32 Weeks: Compliance, Adverse effects questionnaire, Bloodsamples;

6. 52 Weeks: Clinical Activity Index, Compliance, Adverse effects questionnaire, Bloodsamples, Colonoscopy & staining, Rectal/sigmoid biopsies NM, Rectal/sigmoid biopsies ACF.

Intervention

There are three groups:

1. This group will receive 5-ASA: 4 g a day (4 sachets of 1000mg granu-stix) and UDCA 20-25 mg/kg/day (500mg tablets);

2. This group will receive 5-ASA: 4 g a day (4 sachets of 1000mg granu-stix) and a placebo of UDCA 20-25 mg/kg/day(500mg tablets);

3. This group will receive a placebo of 5-ASA: 4 g a day (4 sachets of 1000mg granu-stix) and a placebo of UDCA 20-25 mg/kg/day (500mg tablets).

Medication will be used during 1 year.

Contacts

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Eligibility criteria

Inclusion criteria

1. Clinical activity index ¡Ü 4;

2. Long-standing extensive ulcerative colitis for more than 8 years;

3. Age 18-65 years;

4. Using 6-mercaptopurine or azathioprine to maintain remission;

5. For women only: sufficient anti-conception;

6. Signed informed consent.

Exclusion criteria

1. Dysplasia or colorectal cancer before study entry;

2. Coexistent liver disease (Primary Sclerosing Cholangitis (PSC), chronic hepatitis B or C infection);

3. Colectomy;

4. Family history of colorectal cancer;

5. Symptomatic cholelithiasis;

6. Cholecystitis;

7. Coagulation disorder or use anticoagulants that can not be temporarily discontinued, precluding the taking of biopsies;

8. Chronic renal impairment/failure;

9. Diabetes mellitus (higher risk for developing renal disease);

10. Hypertension (higher risk for developing renal disease);

11. Allergy to 5-ASA or UDCA;

12. Vertricular/gastric or duodenal ulcera;

13. Asthma;

14. For women only: Pregnancy, lactation or childbearing potential without adequate contraception;

15. Galactose-intolerance, Lapp lactasedeficience or glucose-galactose malabsorption;

16. Treatment with antacids containing hydroxide, hypolipidemics, high-dose calcium supplements (¡Ý 1200 mg/day), or any other medication disturbing the enterohepatic circulation;

17. Treatment with methotrexate, riphampicine, lactulose or glucocorticosteroids;

18. Unwillingness to be informed about accidental diagnostic findings.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2010
Enrollment:	45
Type:	Anticipated

Ethics review

Positive opinion

Date:	07-04-2010
Application type:	First submission

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
NTR-new	NL2150
NTR-old	NTR2274
Other	METC UMC Utrecht : 09/084
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A