Summary Attachment for

Mesacol: The effect of mesalazine on molecular pathways of cell adhesion in ulcerative colitis

1) Trial Information

Active Ingredient: 5-ASA (Mezavant MSR Retardtbl. 1200 mg)
Phase: II; Pilot study
Sponsor: Medical University of Vienna

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Study code: MESACOL
EudraCT number: 2012-002023-15
Principal investigator: Ao. Univ. Prof. Dr. Christoph Gasche
Study centers: single center study; Christian Doppler Laboratory for Molecular Cancer Chemoprevention; Division of Gastroenterology and Hepatology, Department of Medicine III, Medical University of Vienna
Main objective: To evaluate the changes in molecular pathways of cell adhesion (cellular localization of E-cadherin and ß-catenin) in ulcerative colitis prior to and after treatment with mesalazine (5-ASA)
General information about the trial

- Start of recruitment: Jul 2nd 2012
- Primary completion date May 11th 2018
- Global end of trial date: May 11th 2018
- Premature ending: yes, due to low recruitment
- Long term follow-up planned: no
- Independent data monitoring committee (IDMC) involvement: no
- Paediatric regulatory details: the trial is not part of an agreed paediatric investigation plan
- Substantial protocol amendments: none
- Interruptions: none

Analysis stage: final analysis, 06.05.2020
Limitations and caveats: the trial was discontinued prematurely because of low recruitment
Online references: the trial results have not been published

2) Trial subjects

First patient enrolled: May 23rd 2013
Last patient enrolled: Feb 18th 2015
Last patient completed study: Mar 3rd 2015
Planned number of subjects: 12
Actual number of subjects enrolled: 3
Study discontinued on May 11th 2018 due to low recruitment.

Baseline characteristics:

Age: mean 39 y, range 28-49
Age < 18y: 0 patients

Age ≥ 65 y: 0 patients
Female : Male: 1:2
Endoscopic Mayo score at baseline: 2, range 2-2

Patients who discontinued study: none

Exclusion from FAS (s. below) due to other reasons: none

3) Results

Reporting groups:

- Full analysis set (FAS; i.e., all patients who received at least one dose of the study drug and underwent both endoscopic procedures including tissue collection), n=2
  The primary endpoint was evaluated based on the FAS
- Safety set (SS; i.e., all patients who received at least one dose of the study drug)
  The SS was used for adverse event reporting

Primary endpoint

- Definition: difference between post-treatment and pre-treatment membranous expression of E-cadherin in inflamed mucosa, evaluated by the immunoreactivity score (IRS) ranging from 0 (no staining) to 4 (strongest staining)
- Results: Mean difference: +1.3 (range: 0.5-2.0)
- Statistics: p=0.094 (not significant) by two-tailed paired sample t-test

Secondary endpoints:

- Increase of the immune reactivity score of membranous E-cadherin in the normal mucosa before and after 5-ASA treatment: could not be obtained due to insufficient tissue amount and missing data for pairwise analysis
- Change in the immune reactivity score of membranous ß-catenin in inflamed mucosa before and after 5-ASA treatment
  - Results: Mean difference: + 1.3 (range: 0-2.0)
  - Statistics: p=0.184 (not significant) by two-tailed paired sample t-test
- Change in the immune reactivity score of membranous ß-catenin in normal mucosa before and after 5-ASA treatment: could not be obtained due to insufficient tissue amount and missing data for pairwise analysis
- Changes in related chemopreventive pathways (Rac1/PAK-1, PI3K/Akt, ras/raf) prior to and after treatment with 5-ASA: not analyzed due to low sample size
- Change in Mayo-Score (clinical and endoscopic ulcerative colitis activity score) from baseline to study end:
  - Results: Mean difference: -1.3 (range: -1 - -2)
  - Statistics: p=0.057 (not significant) by two-tailed paired sample t-test

4) Adverse events

Timeframe for adverse event reporting: during study

Assessment type: non-systematic

Frequency threshold for reporting non-serious adverse events: 5%

Dictionary name: none used

Serious adverse events: none

Non-serious adverse events: none