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A study of a new gastro-resistant prolonged-release mesalazine tablet formulation

Submission date	Recruitment status	[_] Prospectively registered
21/12/2022	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
07/08/2023	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
07/08/2023	Digestive System	

Plain English summary of protocol

Background and study aims
A new formulation containing mesalazine, i.e., Mesalazine 1200 mg gastro-resistant prolonged-release tablets, has been recently developed. Mesalazine is an anti-inflammatory drug used to treat inflammatory bowel disease since it reduces the symptoms of mild to moderate ulcerative colitis. The aim of the development is to obtain a generic version of the originator drug, currently marketed in Italy as Mesavancol® and in the rest of the world under different brand names. This study aims to produce a preliminary comparison of the amount of the active ingredient that reaches the blood circulation after the administration of the new formulation Mesalazine 1200 mg gastro-resistant prolonged-release tablets versus the reference marketed product (Mesavancol® 1200 mg gastro-resistant prolonged-release tablets) when administered to healthy men and women under fed conditions.

Who can participate?
Healthy men and women aged 18-55 years old

What does the study involve?
The study will be conducted at the CROSS Research S.A. Phase I Unit Clinical Centre, in Arzo, Switzerland. Study participants will receive a single dose of Mesalazine 1200 mg gastro-resistant prolonged-release tablets and a single dose of Mesavancol® 1200 mg gastro-resistant prolonged-release tablets in 2 subsequent study periods, with a wash-out interval of at least 8 days between consecutive administrations. Participants will have blood samples taken and vital parameters recorded at regular intervals.

What are the possible benefits and risks of participating?
Participating in this study will not bring any direct benefit to participants, with the exception of the medical tests that will be performed during it. No particular risks are expected for the study subjects originating from the mesalazine dose regimen scheduled in the present study, considering the favourable safety profile of the drug. However, as with all products, the appearance of allergic reactions or side effects that are known or not yet known cannot be ruled out.

Where is the study run from?
The study will be conducted at the CROSS Research S.A. Phase I Unit Clinical Centre, in Arzo, Switzerland.

When is the study starting and how long is it expected to run for?
May 2022 to December 2022

Who is funding the study?
Mogon Pharmaceuticals Sagl

Who is the main contact?
Dr. Milko Radicioni, clinic@croalliance.com

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
01-22

Study information

Scientific Title
Bioavailability study of a mesalazine formulation of 1200 mg gastro-resistant prolonged-release tablets versus the marketed product Mesavancol® administered to healthy volunteers under fed conditions

Study objectives
To compare the bioavailability of the Mesalazine 1200 mg gastro-resistant prolonged-release tablets versus the Mesavancol® 1200 mg gastro-resistant prolonged-release tablets when administered to healthy volunteers under fed conditions.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Approved 09/08/2022, Canton Ticino Ethics Committee (c/o Ufficio di Sanità, Via Orico 5, 6501 Bellinzona, Switzerland; +41(0)91.814.30.57; beatrice.giberti-gai@ti.ch), ref: 2022-01347 CE 4143

Primary study design
Interventional

Study design
Single-centre single-dose open-label fed-conditions two-way cross-over randomized bioavailability pilot study

Study type(s)
Other

Health condition(s) or problem(s) studied
Chronic inflammation of the intestinal epithelium

Interventions
A single oral dose of Mesalazine 1200 mg gastro-resistant prolonged-release tablets and Mesavancol® 1200 mg gastro-resistant prolonged-release tablets will be administered under fed conditions in 2 subsequent study periods according to the study randomised cross-over design, with a wash-out interval of at least 8 days between consecutive administrations. The investigational medicinal products will be orally administered on the morning of day 1 at 08: 00±1 h after a standardised high-fat high-caloric breakfast. The volunteers will completely eat their breakfast within 30 min and before investigational product administration. For both products administration, one tablet will be swallowed without chewing with 150 ml of still mineral water.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
5-aminosalicylic acid (5-ASA; mesalazine, mesalamine)

Primary outcome(s)
Area under the concentration-time curve from administration to the last observed concentration time t (AUC0-t) and maximum plasma concentration (Cmax) of mesalazine (5-ASA) calculated from the concentrations of plasma samples taken at pre-dose (0) and 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 20, 24, 28, 36, 48, 60 and 72 h post-dose after single dose administration of the two treatments (Mesalazine 1200 mg gastro-resistant prolonged release tablets and the Mesavancol® 1200 mg gastro-resistant prolonged release tablets) under fed conditions

Key secondary outcome(s)
1. Time to peak (tmax), relative bioavailability (Frel) and, if feasible, area under the concentration-time curve extrapolated to infinity (AUC0-inf), half-life (t1/2) and percentage of the residual area extrapolated to infinity in relation to the total AUC0-inf (%AUCextra) of

mesalazine (5-ASA) after single-dose administration of the two treatments (Mesalazine 1200 mg gastro-resistant prolonged-release tablets and the Mesavancol® 1200 mg gastro-resistant prolonged-release tablets) under fed conditions
2. All adverse events occurring after the informed consent signature but before (PTAEs) or after (TEAEs) the first dose of the investigational medicinal product, vital signs (blood pressure and heart rate, measured at the screening visit, on Day 1 of each study period at pre-dose (0) and at 10 h post-dose, on Day 4 of each study period at 72 h post-dose and at early termination visit [ETV] as applicable), body weight (measured at screening and final visit/ETV as applicable), physical examination (performed at screening and final visit/ETV as applicable), clinical laboratory parameters (haematology, blood chemistry and urine analysis performed at screening and final visit/ETV as applicable; virology performed at screening; urine drug test performed at screening; a serum pregnancy test at screening; urine pregnancy test at the entrance of each study period).

Completion date
16/12/2022

Eligibility

Key inclusion criteria
To be enrolled in this study, subjects must fulfil all the following criteria:
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and Age: males/females, 18-55 years old inclusive
3. Body Mass Index: 18.5-30 kg/m2 inclusive
4. Vital signs: systolic blood pressure 100-139 mmHg, diastolic blood pressure 50-89 mmHg, heart rate 50-90 bpm, measured after 5 min at rest in the sitting position
5. Salicylates drugs: intake of salicylates drugs (such as aspirin) at least once in life without any allergic reactions
6. Full comprehension: the ability to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to cooperate with the investigator and to comply with the requirements of the entire study
7. Contraception and fertility (females only): females of child-bearing potential must be using at least one of the following reliable methods of contraception:
7.1. Hormonal oral, implantable, transdermal, or injectable contraceptives for at least 2 months before the screening visit
7.2. A non-hormonal intrauterine device or female condom with spermicide or contraceptive sponge with spermicide or diaphragm with spermicide or cervical cap with spermicide for at least 2 months before the screening visit
7.3. A male sexual partner who agrees to use a male condom with spermicide
7.4. A sterile sexual partner
Female participants of non-child-bearing potential or in post-menopausal status for at least 1 year will be admitted. For all female subjects, pregnancy test results must be negative at screening and on day -1.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
16

Key exclusion criteria
Subjects meeting any of these criteria will not be enrolled in the study:
1. Electrocardiogram (ECG, 12-leads, supine position): clinically significant abnormalities
2. Physical findings: clinically significant abnormal physical findings which could interfere with the objectives of the study
3. Laboratory analyses: clinically significant abnormal laboratory values indicative of physical illness
4. Allergy: ascertained or presumptive hypersensitivity to the active principle, salicylates, aminosalicylates, formulations ingredients or related drugs (sulfasalazine); history of anaphylaxis to drugs or allergic reactions in general, which the investigator considers may affect the outcome of the study
5. Diseases: significant history of renal, hepatic, gastrointestinal, cardiovascular, respiratory, skin, haematological, endocrine, or neurological diseases that may interfere with the aim of the study. Known renal dysfunction
6. Medications: medications, including over-the-counter medications and herbal remedies, in particular aspirin and other salicylates, nephrotoxic agents including non-steroidal anti-inflammatory drugs, azathioprine, 6-mercaptopurine and coumarin-type anticoagulants e.g., warfarin, for 2 weeks before the start of the study. Hormonal contraceptives for females will be allowed
7. Investigative drug studies: participation in the evaluation of any investigational product for 3 months before this study. The 3-month interval is calculated as the time between the first calendar day of the month that follows the last visit of the previous study and the first day of the present study
8. Blood donation: blood donations for 3 months before this study
9. Drug, alcohol, caffeine, tobacco: history of drug, alcohol [>1 drink/day for females and >2 drinks/day for males, defined according to the USDA Dietary Guidelines 2020-2025], caffeine (>5 cups coffee/tea/day) or tobacco abuse (10 cigarettes/day)
10. Drug test: a positive result at the drug test at screening
11. Alcohol test: positive alcohol test on day -1
12. Diet: abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before this study; vegetarians
13. Pregnancy (females only): positive or missing pregnancy test at screening or on day -1, pregnant or lactating women.

Date of first enrolment
25/10/2022

Date of final enrolment
02/11/2022

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research S.A.
Via F.A. Giorgioli 14
Arzo
Switzerland
6864

Sponsor information

Organisation
Mogon Pharmaceuticals Sagl

Funder(s)

Funder type
Industry

Funder Name
Mogon Pharmaceuticals Sagl

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		07/08/2023	07/08/2023	No	No