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Study to assess the amount of drug that reaches the blood circulation of two new tablets containing mesalazine in comparison with the tablet on the market called Lialda, in healthy volunteers in fasting conditions

Submission date	Recruitment status	[ ] Prospectively registered
10/05/2021	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
18/05/2021	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
18/05/2021	Digestive System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
DPL Pharma S.p.A., Italy, recently developed 2 novel formulations of mesalazine, i.e. mesalazine gastro-resistant tablets in sachets 1.2 g and Mesalazine prolonged-release tablets in sachets 1.2 g. Both mesalazine gastro-resistant tablets in sachets 1.2 g and mesalazine prolonged-release tablets in sachets 1.2 g are formulated with a multi-particulate-matrix system that allows the delivery of the active ingredient directly inside the colon.
This pilot study is aimed to preliminary compare the bioavailability of the two novel Test formulations versus the Reference product (Lialda® 1.2 g delayed release tablets, Shire US Inc., USA) when administered under fasting conditions.

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

What does the study involve?
A single 1.2 g oral dose of Test 1, Test 2 and Reference products will be administered to each study subject under fasting conditions in 3 subsequent study periods according to a randomised cross-over design, with a wash-out interval of at least 7 days between consecutive administrations.
During the study, blood samples will be collected from participants for the measurement of mesalazine (5-ASA) and its metabolite N-acetyl-5-aminosalicylic acid (N-Ac-5-ASA) in the bloodstream. The subject heart rate and blood pressure will be measured and laboratory tests on blood and urine will be performed to test the safety of the medications.

What are the possible benefits and risks of participating?
No potential benefits are foreseen for subjects participating in this study except for the medical screening. 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.

Where is the study run from?
DPL Pharma S.p.A., Italy

When is the study starting and how long is it expected to run for?
January 2019 to November 2019

Who is funding the study?
DPL Pharma S.p.A., Italy

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CRO-PK-18-333 - Sponsor code DPL-734-01-2018

Study information

Scientific Title
Bioavailability study of two new mesalazine formulations versus the marketed formulation Lialda® administered to healthy volunteers in fasting conditions

Study objectives
To compare the bioavailability of two new mesalazine Test formulations (Mesalazine gastro-resistant tablets in sachets 1.2 g, Test 1 and Mesalazine prolonged-release tablets in sachets 1.2 g, Test 2) versus the Reference product (Lialda® 1.2 g delayed release tablets) when administered under fasting conditions

Ethics approval required

Old ethics approval format

Ethics approval(s)
Approved 07/01/2019, Cantonal Ethics Committee Canton Ticino (c/o Health Office, Via Orico 5, 6501 Bellinzona, Switzerland; +41 (0)91 8143057; dss-ce@ti.ch), ref: 2018-02350 CE 3436

Primary study design
Interventional

Study design
Single-centre single-dose open-label fasting conditions 3-way cross-over randomized bioavailability pilot study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Mild to moderate ulcerative colitis

Interventions
A single 1.2 g oral dose of Test 1, Test 2 and Reference products will be administered under fasting conditions in 3 subsequent study periods according to the study randomised cross-over design, with a wash-out interval of at least 7 days between consecutive administrations. Test 1, Test 2 and Reference products will be orally administered in the morning of day 1 at 08:00±1 h.

For the administration of the Test products, the content of one sachet will be dispersed in a glass containing 25 mL of still mineral water, shaken for 10 sec and immediately drunk, without chewing. The glass will be rinsed with 25 mL of still mineral water, the rinse will be shaken for 10 sec and immediately drunk. Finally, additional 190 mL of still mineral water will be drunk by the subject.

For the Reference product administration, one tablet will be swallowed without chewing with 240 mL of still mineral water.

Regarding the randomisation procedure, subjects will be assigned to the sequence of treatments in the 3 study periods (T1T2R, T1RT2, T2RT1, T2T1R, RT1T2 or RT2T1) according to the randomisation list. Randomisation number will be given to the subjects on study day -1, period 1, and will be used to assign the treatment sequence according to the randomisation list.

During the interventional phase, blood samples will be collected for pharmacokinetic analysis at pre-dose (0), 1, 2, 4, 6, 8, 10, 11, 12, 13, 14, 16, 24, 36, 48, 60 and 72 h post-dose in each of the 3 study periods. Each sample will be processed for the determination of the concentration of mesalazine (5-ASA) and its metabolite N-Acetyl-5-aminosalicylic acid (N-Ac-5-ASA) in plasma.

Safety and general tolerability of the investigational products will be based on adverse events, physical examinations including body weight, vital signs and routine haematology, blood chemistry and urinalysis laboratory tests.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Mesalazine, also called 5-aminosalicylic acid [5-ASA] or mesalamine

Primary outcome(s)
The bioequivalent rate (Cmax) and extent (AUC0-t) of absorption of mesalazine calculated from the corresponding plasma concentrations after single dose administration of Test 1, Test 2 and and Reference products under fasting conditions (Cmax = Maximum plasma concentration and AUC0-t = Area under the concentration-time curve from administration to the last observed concentration time t, calculated with the linear trapezoidal method)

Key secondary outcome(s)
1. The description of the pharmacokinetic (PK) profile of mesalazine (5-ASA) and its metabolite N-acetyl-5-aminosalicylic acid (N-Ac-5-ASA) after single dose administration of Test 1, Test 2, and Reference products under fasting conditions
2. The collection of safety and tolerability data after single dose administration of Test 1, Test 2, and Reference products under fasting conditions (adverse events, vital signs (blood pressure and heart rate), body weight, ECG, laboratory parameters) using case report forms

Completion date
15/11/2019

Eligibility

Key inclusion criteria
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and Age: men and women, 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: ability to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to co-operate with the Investigator and to comply with the requirements of the entire study
7. Contraception and fertility (women only): women 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
Women of non-child-bearing potential or in post-menopausal status for at least 1 year will be admitted.
For all women, pregnancy test result must be negative at screening and at each scheduled evaluation

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
18

Key exclusion criteria
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 products, 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 women 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 women and >2 drinks /day for men, defined according to the USDA Dietary Guidelines 2015 - 2020), caffeine (>5 cups coffee/tea/day) or tobacco abuse (>10 cigarettes/day)
10. Drug test: positive result at the drug test at screening or day -1 (all study periods)
11. Alcohol test: positive alcohol breath test at day -1 (all study periods)
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 (women only): positive or missing pregnancy test at screening or day -1 (all study periods), pregnant or lactating women

Date of first enrolment
03/05/2019

Date of final enrolment
11/06/2019

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research S.A. - Phase I Unit
Via F. A. Giorgioli 14
Arzo
Switzerland
6864

Sponsor information

Organisation
DPL Pharma S.p.A.

Funder(s)

Funder type
Industry

Funder Name
DPL Pharma S.p.A.

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