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Multiple-dose tolerability and effect of food

Submission date 29/01/2013	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 18/02/2013	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 18/02/2013	**Condition category** Other	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Dulamin is an alcoholic extract of Filipendula ulmaria. The objective of the study is to obtain information on the safety, tolerability, and pharmacokinetics of repeated oral doses of Dulamin in healthy subjects as well as information on the bioavailability and effects of food on pharmacokinetics.

Who can participate?
Adult healthy Caucasian males and females (aged 18 45 years) can participate in the study.

What does the study involve?
One group of the patients will receive Dulamin once and for 15 days in two cohorts of 1200 mg daily dose and 2400 mg daily dose. Safety assessments are performed during the whole study and blood sampling will be made at the specified time points after the first dose and after the last dose of Dulamin for 48 hours.
In another group, single doses of 1200 mg Dulamin will be investigated on three occasions: once as tablets with no meal, once as drinking suspension with no meal, once as tablets after administration of a meal.

What are the possible benefits and risks of participating?
The participants are healthy people and there will be no direct benefits in participating. Filipendula ulmaria is a traditional herbal medicine in Europe. According to the German monograph, treatment with Filipendula ulmaria holds no risk of adverse drug reactions.

Where is the study run from?
The study will be performed in a specialised phase 1 unit in Germany.

When is the study starting and how long is it expected to run for?
The study will start in February 2013 and will run for about 6 months.

Who is funding the study?
Dr. Willmar Schwabe GmbH & Co. KG, Germany

Who is the main contact?
Dr. Stephan Klement
Stephan.klement@schwabe.de

Contact information

Type(s)
Scientific

Contact name
Dr Wolfgang Timmer

Contact details
Grenadierstraße 1
Mannheim
Germany
68167

Additional identifiers

Protocol serial number
561501.01.002

Study information

Scientific Title
A phase I study to assess the safety and tolerability of repeated oral doses of 1200 mg and 2400 mg Dulamin once daily for 2 weeks in healthy volunteers as well as to evaluate the relative bioavailability of film-coated tablets containing 1200 mg Dulamin and to evaluate effects of food on its pharmacokinetics

Study objectives
The aim of this study is to evaluate the safety and tolerability of repeated oral doses of 1200 and 2400 mg Dulamin in healthy subjects as well as to evaluate the bioavailability and the effect of food on pharmacokinetics.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Commission of the State Medical Association of Baden-Württemberg [Ethik-Kommissin der Landesärztekammer Baden -Württemberg], 16 October 2012

Study design
Single-centre randomized placebo-controlled double-blind dose-ascending study with an open-label 3-period 3-way cross-over part

Primary study design

Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Safety / pharmacokinetics of Dulamin

Interventions
One single day and 15 days in the multiple ascending dose part of the study; Three single doses separated by a washout of at least 1 week in the food effect/bioavailability part of the study.

Multiple dosing part
Cohort 1= 1200mg. Single dose of 2 tablets 600 mg Dulamin on Day 1, followed by intake of 2 tablets 600 mg Dulamin once daily from day 3 day 17
Cohort 2= 2400mg. Single dose of 4 tablets 600 mg Dulamin on Day 1, followed by intake of 4 tablets 600 mg Dulamin once daily from day 3 day 17.
Blood sampling PK: at predose and at 0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 8, 10, 12, 24, and 48 h after administration on Days 1 and 17; Days 15 and 16: predose
ECG: at predose and on Day 17 at predose, and at 1, 2, 4, 8, 12, 24, and 48 h after administration.
Bioavailability and effects of food part
Cohort 3= 1200mg. Single dose of 2 tablets 600 mg Dulamin two times and once 1200 mg drinking suspension of extract; intake times separated by a wash out of at least one week
Blood sampling PK: at predose and at 0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 1.75, 2, 2.5, 3, 4, 5, 6, 8, 10, 12, 24, and 48 h after administration
ECG: at predose and 24 and 48 h after administration

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Dulamin

Primary outcome(s)
1. Adverse events
2. Laboratory data
3. Blood pressure
4. Pulse rate
5. Electrocardiogram (ECG)

Adverse events, ECG and vital signs daily, Laboratory values: at screening visit, pre-dose, day 3, day 10, day 17, day 19, follow up visit.

Key secondary outcome(s))
Plasma pharmacokinetics

Completion date
30/06/2013

Eligibility

Key inclusion criteria
1. Age 18-45 years
2. Caucasian
3. Informed consent
3. Healthy men and women
4. Body mass index between 18 and 29 kg/m2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
All

Key exclusion criteria
1. More than moderate smoker
2. Demonstrating excess in xanthine consumption
3. More than moderate alcohol consumption
4. Any history of alcohol or drug abuse
5. Demonstrating any active physical disease, acute or chronic
6. History or any current evidence of clinically relevant allergies or idiosyncrasies to drugs or food
7. History (within the last 2 years) of drug hypersensitivity, asthma, urticaria or other severe allergic diathesis as well as current hay fever 8. Proneness to orthostatic dysregulation, fainting, or blackouts
9. ECG abnormalities of clinical relevance
10. History (within the last 2 years) of chronic gastritis or peptic ulcers
11. History (within the last 2 years) of chronic or recurrent metabolic, renal, hepatic, pulmonary, gastrointestinal, neurological (especially history of epileptic seizures), endocrine, immunological, psychiatric or cardiovascular diseases, myopathies, or bleeding tendency
12. History (within the last 2 years) of malignancy
13. Pregnant or nursing women
14. Women of childbearing potential who are not using a highly-effective method of birth control
15. Laboratory values outside the reference range that are of clinical relevance
16. Positive test for human immunodeficiency virus (HIV) antibodies and antigens
17. Positive Hepatitis B-virus surface antigen (HBsAg) test
18. Positive Anti-hepatitis C-virus antibodies (Anti-HCV) test
19. Any history or suspicion of barbiturate, amphetamine, benzodiazepine, cocaine, opiates and

cannabis abuse
20. Ethanol consumption within 48 h before administration of IMP
21. Consumption of xanthine-containing food or beverages within 48 h before administration of IMP
22. Any gastrointestinal complaints within 7 days before first administration of IMP
23. Use of any medication within 4 weeks before first administration of IMP

Date of first enrolment
05/02/2013

Date of final enrolment
30/06/2013

Locations

Countries of recruitment
Germany

Study participating centre
Grenadierstraße 1
Mannheim
Germany
68167

Sponsor information

Organisation
Dr. Willmar Schwabe GmbH & Co. KG (Germany)

ROR
https://ror.org/043rrkc78

Funder(s)

Funder type
Industry

Funder Name
Dr. Willmar Schwabe GmbH & Co. KG (Germany)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration