A randomized, open-label, 4-group, 2-period replicate design study to evaluate within- and between-subject variability in exposure of two lots of E5501 20 mg tablets administered as single doses of 40 mg, in the fasted and fed conditions to healthy subjects.

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Primary :to determine whether concomitant administration of the study drug with food reduces within- and between-subject variability in exposure as measured by area under the plasma concentration-time course profile (AUC) and maximum observed plasma...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON36548

Source
ToetsingOnline

Brief title
E5501 BA and FE study

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
low blood platelet number, Thrombocytopenia

Research involving
Human

Sponsors and support

Primary sponsor: Eisai
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: E5501, Trombocytopenia

Outcome measures

Primary outcome

Criteria for evaluation

Pharmacokinetics: plasma E5501 concentrations, pharmacokinetic parameters

Safety : adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination

Secondary outcome

Not applicable.

Study description

Background summary

The drug to be given is an *investigational drug*. *Investigational* means that the drug being tested in this study has not been approved by the United States Food and Drug Administration (FDA) or the European Medicines Agency (EMA). The drug is being developed for treatment of thrombocytopenia (low blood platelet numbers). Platelets are blood cells that are involved in blood clotting; when platelet numbers are low, the blood doesn*t clot normally and there is an increased risk of bleeding. This drug is expected to improve the clotting of the blood. The drug is still being researched.

Study objective

Primary :

to determine whether concomitant administration of the study drug with food reduces within- and between-subject variability in exposure as measured by area under the plasma concentration-time course profile (AUC) and maximum observed plasma concentration (Cmax).

Secondary :
to evaluate the bioavailability (BA) of the study drug 20 mg tablet Lot P01008ZZA (test) relative to the study drug 20 mg tablet Lot P01009ZZA (reference) under fasted and fed conditions to evaluate the overall effect of food on the BA of the study drug relative to the fasted condition.

Study design

Design :
A randomized, open-label, 4-group, 2-period replicate design study to evaluate within- and between-subject variability in exposure of two lots of study drug 20 mg tablets administered as single doses of 40 mg, in the fasted and fed conditions to healthy subjects.; a washout of at least five days between dosing.

In total 4 Groups of 21 subjects will participate.

Groep A: 21 subjects will receive batch 1 (Lot P01008ZZA) of the drug on Day 1 and Day 6 underfasted conditions
Groep B: 21 subjects will receive batch 1 (Lot P01008ZZA) of the drug on Day 1 and Day 6 fed conditions
Groep C: 21 subjects will receive batch 2(Lot P01009ZZA) of the drug on Day 1 and Day 6 underfasted conditions
Groep D: 21 subjects will receive batch 2 (Lot P01009ZZA) of the drug on Day 1 and Day 6 fed conditions

After a screening visit the subjects will be in-house for a total of 11 Days, followed by 8 short visits and end with a follow-up visit 2 Days after the last ambulantory visit.

Procedures and assessments:
Screening and follow up: clinical laboratory, vital signs, physical examination, weight, ECG, serum pregnancy test (females only); at eligibility screening: medical history, height, urine alcohol and drug screen, HBsAg, anti HCV, anti-HIV 1/2; vital signs, physical examination, 12-lead ECG, urine pregnancy test (females only), clinical laboratory, urine alcohol and drug screen to be repeated upon admission
follow-up on Day 35

Observation period:
one period in clinic from -17 h before drug administration on Day 1 up to 96 h after drug administration on Day 6 and ambulatory visits on Days 12, 13, 16, 19, 22, 26, 29 and 33 (Treatment Period 2 starts on Day 6)

Blood sampling:
for pharmacokinetics of the study drug in plasma: pre-dose and 1, 2, 3, 4, 5, 6, 7, 8, 12, 18, 24, 36, 48, 72 and 96 h post-dose on Day 1 (Treatment Period 1) and pre-dose and 1, 2, 3, 4, 5, 6, 7, 8, 12, 18, 24, 36, 48, 72 and 96 h post-dose on Day 6 (Treatment Period 2)
for platelet counts: pre-dose and 48, 72 and 96 h post-dose on Day 1 (Treatment Period 1) and pre-dose and 48, 72 and 96 h post-dose and once on Days 10, 12, 13, 16, 19, 22, 26, 29 and 33 (Treatment Period 2)

Safety:
adverse events: throughout the study; vital signs: once on Days -1, 1, 6, 10, 12, 13, 16, 19, 22, 26, 29 and 33; abbreviated physical examination: once on Days -1 and 10; ECG: once on Days -1 and 10; clinical laboratory: once on Days -1 and 10

Bioanalysis:
analysis of plasma study drug samples using a validated method by Sponsor
platelet count determinations by Sponsor

Intervention

Study Medication
Active substance : E5501
Activity : c-Mpl agonist
Indication: adult chronic immune thrombocytopenic purpura (ITP), thrombocytopenia associated with chronic liver disease (TLD) and prevention and treatment of chemotherapy-induced thrombocytopenia
Strength : 20 mg
Dosage form : Lot P01008ZZA and Lot P01009ZZA tablets

Treatments
Treatment A: a single oral dose of 40 mg (2 x 20 mg tablets) Lot P01008ZZA in the fasted state in each period
Treatment B: a single oral dose of 40 m (2 x 20 mg tablets) Lot P01008ZZA in the fed state in each period
Treatment C: a single oral dose of 40 mg (2 x 20 mg tablets) Lot P01009ZZA in the fasted state in each period
Treatment D: a single oral dose dose of 40 mg (2 x 20 mg tablets) Lot P01009ZZA in the fed condition in each period

Each subject will be dosed for 2 periods.

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibly an infection.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Age : 18-55 yrs, inclusive
BMI : 18-32 kg/m2, inclusive
Blood platelet count: *120 x 10E9/L and *250 x 10E9/L
Roken: non- or light smokers

Exclusion criteria

1) Evidence of clinically significant cardiovascular, hepatic, gastrointestinal, renal, respiratory, endocrine, hematologic, neurologic, or psychiatric disease or abnormalities or a known history of any gastrointestinal surgery that could impact the PK of study drug

2) Agents associated with thrombotic events (including oral contraceptives) must be discontinued within 30 days of first study drug administration
3) Evidence of organ dysfunction or any clinically significant deviation from normal in their medical history, e.g., history of splenectomy
4) History of venous or arterial thrombotic disease or other hypercoaguable state
5) Hemoglobin less than lower limit of normal (LLN) levels (females 7.1 mmol/L, males 8.1 mmol/L)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-02-2011
Enrollment:	84
Type:	Actual

Ethics review

Approved WMO Date:	25-01-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-02-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	25-02-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-02-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-03-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EudraCT	EUCTR2010-024174-19-NL
CCMO	NL35386.056.11