A PILOT PHASE 1, REPEATED SINGLE DOSE STUDY EVALUATING THE VARIABILITY OF PHARMACOKINETICS AND PHARMACODYNAMICS OF LONG ACTING FILGRASTIM FOLLOWING SUBCUTANEOUS ADMINISTRATION TO HEALTHY VOLUNTEERS

Published: 26-09-2012
Last updated: 26-04-2024

To evaluate the inter- and intra-subject variability in pharmacokinetics (PK) and pharmacodynamics (PD) of study drug following a two-period repeated single dose of 2 mg delivered by subcutaneous (SC) injection in healthy volunteers.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	White blood cell disorders
Study type	Interventional

Summary

ID

NL-OMON37064

Source
ToetsingOnline

Brief title
Perseus Phase I Pilot Study

Condition

- White blood cell disorders

Synonym
Neutropenia

Research involving
Human

Sponsors and support

Primary sponsor: Mylan GmbH
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: long acting filgrastim, Neutropenia

Outcome measures

Primary outcome

Pharmacokinetics / Pharmacodynamiek and safety, adverse events, laboratory

data, vital signs, ECG and physical examination

Secondary outcome

PK: AUC0-inf, Cmax, Tmax, kel and half waardetijd.

PD: (AUC), (Tmax), (CD34+ Cmax).

Study description

Background summary

The study drug is a drug registered for treatment of a shortage of white blood cells in order to prevent infections. It is used mostly for cancer patients to treat the side effects of chemotherapy. The study drug is a protein which is very similar to the human *granulocyte colony stimulating factor* (filgrastim). It is produced with the help of bacteria which have received a gene which makes them able to produce this protein.

Study objective

To evaluate the inter- and intra-subject variability in pharmacokinetics (PK) and pharmacodynamics (PD) of study drug following a two-period repeated single

dose of 2 mg delivered by subcutaneous (SC) injection in healthy volunteers.

Study design

This study is a phase I, pilot, open-label, single-centre, two-period repeated single-dose study assessing the PK and PD of study drug in healthy volunteers. Subjects will receive a 2 mg single dose delivered by SC injection on two separate occasions with a washout period of 6 weeks between doses.

Treatment:
Single-dose SC injection of 0.2mL (2 mg)

Procedures and assessments
Screening and follow-up: Clinical laboratory pregnancy test (females only), full physical examination, vital signs , 12-lead electrocardiogram (ECG), and previous and concomitant medication.

PK/PD blood sampling;
For PK of PEG-GCSF in serum: blood samples will be collected at regular intervals in both treatment periods.
For PD of ANC in whole blood: blood samples will be collected at screening, at admission and at regular intervals in both treatment periods.
For PD of CD34+ cell count in whole blood: blood samples will be collected at regular intervals in both treatment periods.

Safety: recorded from the time the Informed Consent Form is signed until completion of the follow up visit. clinical laboratory tests (including clinical chemistry, hematology and urine tests), vital signs (including body weight and height, systolic and diastolic blood pressure, pulse, respiratory rate and body temperature), 12-lead electrocardiogram (ECG).

Bio-Analysis:
analysis of serum samples for PEG-GCSF using a validated Enzyme-linked immunosorbent assay method; analysis of whole blood for ANC using a validated haematology method, CD34+ cells using a validated flow cytometry cell sorter method by PRA.

Intervention

Repeated single dose of 2 mg study drug delivered by 0.2mL subcutaneous (SC) injection.

Study burden and risks

During the investigation, various assessments will be done that can be experienced as more or less stressfull.

Blood draw, SC injections and the ECG can be experienced as stressfull in this respect.

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

1. Willingness and able to provide Informed Consent ;2. Gender : male or female;3. Age : 18 - 65 years, inclusive;4. Weight : minimal 60 kg;5. BMI : 19.0 - 30.0 kg/m2, inclusive [Body Mass Index (BMI) (kg/m2) <= Body weight (kg) / Height2 (m2)] ;6. Vital signs showing no clinically relevant deviations ;7. Computerised (12-lead) electrocardiogram (ECG) recording without signs of clinically relevant pathology;8. Nonsmoker or light smoker, i.e. smokes maximal 5 cigarettes per day; and ability and willingness to refrain from smoking from 24 hours prior to dosing and on Day 1 of each period, and to limit smoking from Day 2 onwards up to 5 cigarettes per day. ;9. Ability and willingness to abstain from alcohol from 48h prior to study

drug administration and prior to ambulatory visits, and during the stays in the clinic until discharge;10. Willingness to use adequate (e.g. double barrier) contraception from screening until 90 days after the follow-up visit, or being surgically sterile for at least 6 months, or (for females) at least 1 year postmenopausal (amenorrhoea duration of at least 12 months);11. Females must not lactate and have a negative pregnancy test at screening and each admission;12. Differentiation of leukocytes, platelet count, haematocrit and haemoglobin results within the reference ranges ;13. All other values for haematology and for clinical chemistry tests of blood and urine within the normal range or showing no clinically relevant deviations as judged by the Medical Investigator

Exclusion criteria

1. Mental handicap;2. Any past or concurrent medical conditions potentially increasing the subject*s risks. Examples of these include medical history with evidence of clinically relevant pathology (e.g. sickle cell disease, spleen pathologies, hematologic malignancies, and pulmonary illnesses such as Acute Respiratory Distress Syndrome (ARDS), interstitial pneumonia, pulmonary oedema, pulmonary infiltrates and pulmonary fibrosis) History of relevant drug and/or food allergies;3. Hypersensitivity to Neulasta® or its constituents (sorbitol E420 and sodium acetate) and/or hypersensitivity to E. coli derived proteins and/or history of previous exposure to PEG-GCSF;4. Subjects with any infections, cough or fever within 1 week prior to study drug administration ;5. Fructose intolerance;6. First grade relatives with haematological malignancy;7. Treatment with non-topical medications (including over the counter medication, and herbal remedies such as St. John*s Wort extract) within 7 days prior to study drug administration, with the exception of hormonal contraceptives, multivitamins, vitamin C, food supplements and a limited amount of acetaminophen, which may be used throughout the study. ;8. Participation in a drug study within 12 weeks prior to study drug administration. ;9. Donation of more than 50 mL of blood within 12 weeks prior to study drug administration. Donation of more than 1.5 litres of blood (for men) / more than 1.0 litres of blood (for women) in the 10 months preceding the start of this study.;10. History of alcohol abuse or drug addiction (including soft drugs like cannabis products);11. Regular intake of more than 24 units of alcohol per week (one unit of alcohol equals approximately 250 mL of beer, 100 mL of wine or 35 mL of spirits);12. Positive drug screen (opiates, methadone, cocaine, amphetamines, cannabinoids, barbiturates, benzodiazepines, tricyclic antidepressants and alcohol);13. Positive screen on Hepatitis B surface antigen (HBsAg), anti-Hepatitis C virus antibodies (HCV), or anti-human immunodeficiency virus 1/2 antibodies (HIV)

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):	09-10-2012
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lang acting filgrastim
Generic name:	Lang acting filgrastim
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	26-09-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	05-10-2012
Application type:	First submission
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	EUCTR2012-003956-36-NL
CCMO	NL42144.056.12