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Comparing vildagliptin/metformin 50 mg/1000 mg film-coated tablets (Sensityn®) vs Galvusmet® 50 mg/1000 mg film-coated tablets in healthy adults, under fed conditions

Submission date
12/04/2023

Recruitment status
No longer recruiting

Registration date
02/05/2023

Overall study status
Completed

Last Edited
13/06/2023

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Bioequivalence is when two drugs with identical active ingredients or two different dosage forms of the same drug produce the same effect. This study was carried out to demonstrate bioequivalence between vildagliptin/metformin 50 mg/1000 mg film-coated tablets (test product, Alpha Pharma, Saudi Arabia) and Galvusmet® 50 mg/1000 mg film-coated tablets (reference product, Novartis Pharma, Switzerland) following a single 50 mg/1000 mg oral dose to healthy adults under fed conditions.

Who can participate
Healthy volunteers from Jordan, aged 18 to 50 years (inclusive)

What does the study involve?
The total duration of study participation is about 10 days from the admission day of period I until giving the last sample in period II. The washout period is 7 days between doses. A single dose (one film-coated tablet) is taken orally with glucose solution after consuming a high-fat, high-calorie breakfast in the morning of day 0 of each period.

What are the possible benefits and risks of participating?
This study aims to examine whether the investigational product is comparable to the reference product under fed conditions and does not aim to treat any medical/disease state. The participants do not clinically benefit from participating in this study. As a result of this study, information about the study drug may be generated that could be beneficial to the participants or others in the future.

Where is the study run from?
Triumpharma (Jordan)

When is the study starting and how long is it expected to run for?
May 2020 to December 2020

Who is funding the study?
Alpha Pharma (Saudi Arabia)

Who is the main contact?
Alpha Pharma

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
VIME.50.1000/357

Study information

Scientific Title
A randomized, two-treatment, two-period, crossover, open-label, laboratory-blind, single-dose bioequivalence study between vildagliptin/metformin 50 mg/1000 mg film-coated tablets (test product) and Galvusmet® 50 mg/1000 mg film-coated tablets (reference product), in healthy, adult, human subjects under fed conditions

Acronym
VIME.50.1000/357

Study objectives
Primary objective:
To assess the bioequivalence between vildagliptin/metformin 50 mg/1000 mg film-coated tablets (test product, Alpha Pharma, Kingdom of Saudi Arabia) and Galvusmet® 50 mg/1000 mg film-coated tablets (reference product, Novartis Pharma, Switzerland), in healthy adult subjects under fed conditions.

Secondary objective:
To monitor the safety and tolerability of a single dose administered in healthy human adult subjects under fed conditions.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/08/2020, Institutional Review Board of Triumpharma (07 Building Al-Yarout Street, Opposite Al-Jubiaha Circle, PO Box 2233, Amman-11941, Jordan; +962 (0)795178552; PI@Triumpharma.com), ref: TRI-20288 Rev 00, ICF Rev 00

Primary study design
Interventional

Study design
Randomized two-treatment two-period crossover open-label laboratory-blind single-dose study with 7 days washout period (between doses) under fed conditions

Study type(s)
Other

Health condition(s) or problem(s) studied
Bioequivalence between vildagliptin/metformin 50 mg/1000 mg film-coated tablets (test product) and Galvusmet® 50 mg/1000 mg film-coated tablets (reference product), in healthy, adult, human subjects under fed conditions

Interventions
The randomization plan is prepared by the Triumpharma pharmacy unit using SAS ® 9.4 program as per Triumpharma internal SOP no.: PHU-1104 "SOP title: Randomization plan preparation and drug assignment to clinical study participants and code breaking (blinded trials)". The subjects are randomized into two sequences (AB and BA).

The total duration of study participation was approximately 10 days from the admission day of period I until giving the last sample in period II. The washout period was 7 days between doses.

A single dose (one film-coated tablet containing vildagliptin/metformin 50 mg/1000 mg) was administered orally to each subject with 240 ± 2 ml of 20% glucose solution after consuming a high-fat, high-calorie breakfast in the morning of day 0 of each period according to the randomization plan.

Test Drug (A)/Study Drug A: vildagliptin/metformin 50 mg/1000 mg film-coated tablets, Batch No.: P-20004, Expiry date: July/2021.
Reference Drug (B)/Study Drug B: Galvusmet® 50 mg/1000 mg film-coated tablets, Batch No.: KT736, Expiry date: May/2021.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Vildagliptin, metformin

Primary outcome(s)
The bioequivalence of vildagliptin/metformin 50 mg/1000 mg film-coated tablets (test product, Alpha Pharma, Kingdom of Saudi Arabia) and Galvusmet® 50 mg/1000 mg film-coated tablets (reference product, Novartis Pharma, Switzerland), in healthy adult subjects under fed conditions. A validated (liquid chromatography with tandem mass spectrometry [LC-MS/MS]) method of analysis is used to analyze vildagliptin and metformin in human plasma samples with a lower limit of quantification (LLOQ) of 0.50 ng/ml for vildagliptin and 20.00 ng/ml for metformin. A total of 19 blood samples were collected for this study in tubes containing lithium-heparin according to the following schedule: pre-dose (BK) "1 sample", 0.25, 0.50, 0.75, 1.00, 1.50, 2.00, 2.25, 2.50, 2.75, 3.00, 3.50, 4.00, 5.00, 6.00, 8.00, 10.00, 12.00, 24.00 hours post-dosing in each study period.

Key secondary outcome(s)
The safety and tolerability of a single dose administered in healthy human adult subjects under fed conditions, measured using:
1. Full vital signs (blood pressure, pulse rate, and body temperature) measured, in a sitting position, at pre-dosing and at the following times: 0.50, 1.00, 1.50, 2.00, 3.00, 4.00, 6.00, 8.00,

12.00, and 24.00 hours post-dosing in each study period
2. Glucose blood test performed at 1 h before dosing, every 30 minutes during the first 4 hours post-dosing, and 5 h, 6 h, 7 h, 8 h, 12 h, and 24 h post-dosing
3. A final examination at the end of period II including vital signs, physical examination, ECG, and clinical laboratory examinations (full blood count, clinical chemistry, and urinalysis)

Completion date
17/12/2020

Eligibility

Key inclusion criteria
Healthy adult subjects from the Jordan population, 18 to 50 (inclusive) years old

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Male

Total final enrolment
36

Key exclusion criteria
1. The subject is pregnant or nursing (lactating), where pregnancy is defined as the state of the female after conception and until the termination of gestation, confirmed by a positive urine or serum pregnancy test at screening and on admission day (before admission) of period I.
2. The subject has evidence of psychiatric disorder, antagonistic personality, poor motivation, emotional or intellectual problems likely to limit the validity of the consent to participation in the study or limit the ability to comply with the protocol requirements at screening or on admission day (before admission) of period I.
3. The subject has a known history or presence of any clinically significant abnormality/pathology /disease in any of the body systems at screening or on admission day (before admission) of period I.
4. The subject has any significant physical or organ abnormality as determined by the principal investigator/clinical sub-investigator at screening or on admission day (before admission) of period I.
5. The subject has difficulty swallowing at screening or on admission day (before admission) of period I.
6. The subject has a clinically significant history or presence of any clinically significant pathology (e.g. chronic diarrhea), unresolved gastrointestinal symptoms (e.g. diarrhea, vomiting), or other

conditions known to interfere with the absorption, metabolism or excretion of the drug as determined by the principal investigator/clinical sub-investigator at screening or on admission day (before admission) of period I.
7. The subject has a known allergy to the drug under investigation (vildagliptin/metformin), or to any ingredient in the preparation (sodium starch glycolate, Avicel DG “dry granulation excipient-microcrystalline cellulose and anhydrous dibasic calcium phosphate”, hydroxypropyl cellulose, magnesium stearate, titanium dioxide, triacetin, iron oxide yellow, hypromellose, lactose monohydrate, fd&c yellow #6 sunset yellow aluminium lake, d&c yellow #10 aluminium lake, ferric oxide red, polyethylene glycol, and talc).
8. The subject has a history of hypersensitivity to heparin as checked at screening.
9. The subject suffered from a major illness (as per the principal investigator/clinical sub-investigator judgment) within one month preceding the screening procedure.
10. The subject has a history of or current compulsive abuse of alcohol or regular exposure to other substances of abuse at screening and on admission day (before admission) of period I.
11. The subject has a positive test for illicit drugs or alcohol on admission day (before admission) of the first period.
12. The subject is a moderate smoker (more than 10 cigarettes per day) at screening and on admission day (before admission) of period I.
13. The subject is on a special diet (for example the subject is a vegetarian, low salt food), or dieting (on a weight-lowering plan) during the month preceding the first dosing as checked at screening.
14. The subject as checked at screening and on admission day (before admission) of period I will consume alcohol or caffeine or related xanthine-containing foods or beverages such as caffeine in tea, coffee, chocolates, cola and Pepsi within 48 hours prior to first dosing.
15. The subject will use any prescribed medication during the last four weeks or OTC medicinal products, vitamins or herbal medications during the last two weeks preceding first dosing as checked at screening and on admission day (before admission) of period I.
16. The subject has consumed grapefruit or pomelo-containing beverages and foods 7 days prior to first dosing as checked at screening and on admission day (before admission) of period I.
17. The subject participated in a comparative bioavailability/ bioequivalence study within the last 80 days before the first dosing as checked at screening.
18. The subject participated in a clinical study within the last 80 days before first dosing as checked at screening and on admission day (before admission) of period I.
19. The subject donated blood or any of its constituents within 80 days before first dosing as checked at screening and on admission day (before admission) of period I.
20. The subjects who, through completion of this study, would have donated more than 900 ml of blood in 20 weeks as checked at screening and on admission day (before admission) of period I.
21. The subject has positive testing for HIV I & II and/or Hepatitis B and/or Hepatitis C using ELISA or CLIA method at screening.
22. The subject suffered from acute infection within one week preceding first study drug administration as checked at screening and on admission day (before admission) of period I.
23. The subject is diabetic as confirmed by HbA1c (HbA1c value is higher than or equal to 6.5%), and suffers from diabetic ketoacidosis, or diabetic pre-coma.
24. The subject’s glucose level is below 70 mg/dl at screening or before the first dosing.
25. The subject is suffering from acute or chronic disease which may cause tissue hypoxia such as: cardiac or respiratory failure, recent myocardial infarction, shock.
26. The subject has a history of acute pancreatitis (characteristic symptom is persistent, severe abdominal pain).
27. The subject is receiving cationic medicinal products that are eliminated by renal tubular secretion (e.g., cimetidine).
28. The subject is receiving glucocorticoids, beta-2-agonists, diuretics, or ACE inhibitors.

29. The subject knows that he/she is suffering from COVID-19 and confirmed by a diagnostic test.
30. The subject has a history of COVID-19 infection and is being treated for COVID-19.
31. The subject has any of the following signs and symptoms: “fever, tiredness, dry cough, aches and pains, nasal congestion, runny nose, sore throat, diarrhea, vomiting, difficulty breathing, or loss of smell or taste” that make him/her as a suspected case of COVID-19 patient before screening, during screening, or during admission of period I “as per PI/SI judgement.
32. The subject has a family member, friend, neighbor, work colleague, or other person, with whom he/ she was in contact with during the last months, who is infected with and/ or being treated for COVID-19.
33. The subject, or a family member, friend, neighbor, work colleague, or other person with whom the subject was in contact with during the last 6 months, has been in an area with ongoing community spread (e.g. hospital, working environment etc), or has recent travel from or residence in an area with ongoing community spread of COVID-19 as declared by local authority.
34. The subject has positive result for COVID-19 PCR test performed on the day before admission day of period I (day -2)”.

Date of first enrolment
08/12/2020

Date of final enrolment
17/12/2020

Locations

Countries of recruitment
Jordan

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Study participating centre
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Jordan
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Sponsor information

Organisation
Alpha Pharma

Funder(s)

Funder type
Industry

Funder Name
Alpha Pharma

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed during the current study will be available upon request from Dr Rana Jaouni (r.jaouni@triumpharma.com) and /or Iyad Eqtefan (i.s. eqtefan@alphapharma.com.sa).
Consent from participants was required and obtained.
Please refer to section 13. “Confidentiality and Personal Data Protection “ in the ICF: to protect the participants' anonymity, identification data was protected by using a single reference number/code (pseudonymization) during processing and transmission to the Sponsor, the Contract Research Organization (Triumpharma) and the supervisory authorities, including the Jordan Food and Drug Administration.
Only the investigator and other designated members of the investigating team are in control of the single reference number/code and are able to identify the participant.
To ensure the quality of clinical trial procedures, authorized representatives of the Sponsor, the Contract Research Organization (Triumpharma) and the supervisory authorities were allowed by the principal investigator to have access to the full data collected, including identification data. During quality controls, such authorized representatives used data only for verifying that the clinical trial is conducted in accordance with the approved procedures and protocols and did not take copies of any data collected. Data is not used for other purposes.
All persons who will have access to participant’s data were trained professionals and are bound by a confidentiality obligation and/or obligation to professional secrecy. Apart from quality controls, the Sponsor, the Contract Research Organization (Triumpharma) and the supervisory authorities received and processed pseudonymized data only.
There are no special relevant ethical or legal restrictions.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			13/06/2023	No	No