ISRCTN60358675 https://doi.org/10.1186/ISRCTN60358675

Oral delivery of semaglutide to the colon for improved absorption

Submission date
18/10/2023

Recruitment status
No longer recruiting

Registration date
27/10/2023

Overall study status
Completed

Last Edited
21/12/2023

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Semaglutide is a medication used to treat type 2 diabetes. Semaglutide is not a new medication, it is widely prescribed for patients with type 2 diabetes under the brand name Rybelsus®. Currently available preparations of Semaglutide release the medication in the stomach. BDD Pharma has developed two new tablet formulations of semaglutide which are designed to release semaglutide further along in the digestive tract, in the small intestine and/or in the colon (large intestine). The aim of this study is to determine when, where and how the tablets break up in the body and how long they take to travel through the gut. In addition, the study will also confirm how well the medication is absorbed into the body.

Who can participate?
Healthy male volunteers aged 18-60 years

What does the study involve?
Three treatments will be assessed in this study:
Treatment A: One Rybelsus® 7 mg semaglutide tablet
Treatment B: Two 3.5 mg semaglutide enteric coated Oralalogik tablets designed to release in the first part of the large bowel (colon)
Treatment C: Two 3.5 mg semaglutide enteric coated delayed release Oralogik tablets designed to release in the middle of the small intestine
Follow-up took place 21-35 days after final dosing.

What are the possible benefits and risks of participating?
There are no direct benefits to participants in taking part in this study.
All materials used in the tablets are standard pharmaceutical ingredients which are generally regarded as safe. These materials will be incorporated in quantities usually found in pharmaceutical formulations.
The safety of oral semaglutide is well established and is currently available as the marketed product Rybelsus®. The most common adverse reactions seen after taking semaglutide are nausea, vomiting, diarrhoea and reflux. Up to 15% of individuals treated with semaglutide (about 1 in 6 people) will experience these symptoms which are more likely at higher, regular doses of the medication. The symptoms are usually mild in severity and resolve without the need

for any treatment. There is a risk of semaglutide causing low blood sugar levels, but this only occurs when the medication is taken with other drugs to treat diabetes such as insulin. Increased heart rate has been observed with semaglutide use. This is minor, usually a small increase of up to 4 beats per minute and has not been shown to be associated with any symptoms or complications.
The researchers will be taking blood samples for testing at the medical assessments before and after the study. At each medical assessment, they will take 20 ml (about four teaspoons). They will also take blood samples during the assessment visits. The total amount of blood removed during the study will be about 275 ml (about 20 tablespoons). There may be some bruising at the site where the needle goes in and some people feel faint when having blood taken.

Where is the study run from?
BDD Pharma Ltd (UK)

When is the study starting and how long is it expected to run for?
June 2022 to February 2023

Who is funding the study?
Scottish Enterprise (UK)

Who is the main contact?
Lyn Corry, lyn.corry@bddpharma.com

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-002566-32

Integrated Research Application System (IRAS)
1006243

Protocol serial number
BDD21302

Study information

Scientific Title
An exploratory pharmacoscintigraphic single centre, open-label, crossover study in healthy volunteers to evaluate novel oral modified release semaglutide tablets

Study objectives
Assess the potential to enhance absorption of peptides and proteins through targeted delivery within the GI tract.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 13/10/2022, London - Hampstead Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, United Kingdom; +44 (0)207 104 8248; hampstead.rec@hra.nhs.uk), ref: 22/LO/0596

Primary study design
Interventional

Study design
Exploratory single-centre open-label crossover study in healthy volunteers

Study type(s)
Other

Health condition(s) or problem(s) studied
Oral delivery of semaglutide to the colon

Interventions
Treatment A: One radiolabelled Rybelsus® 7 mg semaglutide tablet (comparator)
Treatment B: Two radiolabelled 3.5 mg semaglutide EC OralogiKTM tablets (designed to release in the proximal colon)
Treatment C: Two radiolabelled 3.5 mg semaglutide EC OralogiKTM tablets (designed to release in the mid small intestine)

Follow-up took place 21-35 days after final dosing. There was no randomisation process.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
The performance of two early prototype targeted release semaglutide formulations, using gamma scintigraphy to monitor their location in the gastrointestinal tract with time in the fasted state. Imaging carried out every 15 min until a maximum of 12 h post dose.

Key secondary outcome(s)
1. The absorption of semaglutide in blood plasma from targeted release semaglutide formulations and scintigraphic data. Blood samples taken pre-dose and at specified intervals as follows: Treatment B: 3, 4, 5, 6, 7, 8, 10, 11, 12, 13, 14, 16, 20 and 24 h; and Treatment C: 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12 and 24 h
2. The pharmacokinetic profiles of the prototype formulations and Rybelsus® 7 mg Semaglutide tablet in the fasted state. Blood samples taken pre-dose and at specified intervals as follows: Treatment A: 0.5, 1, 1.5, 2, 3, 4, 6, 12 and 24 h

Completion date
28/02/2023

Eligibility

Key inclusion criteria
1. Male
2. Aged between 18 and 60 years inclusive
3. BMI between 18 and 30 kg/m², inclusive. Body weight ≥50 kg
4. Understands and is willing, able, and likely to comply with all study procedures including consumption of meals provided and restrictions
5. Demonstrates understanding of the study and willingness to participate as evidenced by voluntary written informed consent (signed and dated) obtained before any trial-related activities
6. Good general health with (in the opinion of the Principal Investigator (PI), or medically qualified designee) no clinically significant and/or relevant abnormalities of medical history or prior to dosing evaluations, including physical examination, vital signs, ECG and screening clinical laboratory results
7. Unless you have had a vasectomy more than 12 weeks prior to the study starting you must be willing to use a condom with spermicide or practice sexual abstinence with any male partner for the duration of the trial and for 90- days after the last assessment visit. Unless you have had a vasectomy more than 12 weeks prior to study starting you must be willing to abstain from sexual intercourse with women of childbearing potential for the duration of the trial and for 90 days after the last assessment visit OR agree to use a condom in addition to having your female partner use a form of hormonal contraception such as the oral contraceptive pill, implant, hormonal contraceptive injection or an intrauterine device (coil).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Male

Total final enrolment
10

Key exclusion criteria
1. Medical history:
1.1. Current or recurrent disease/condition that, in the opinion of the PI or medically qualified designee responsible, could affect study conduct; the safety of the subject as a result of participation; and/or the ability of the subject to complete the study or laboratory assessments. For example: hepatic disorders, renal insufficiency, congestive heart failure, conditions known to impact gastric emptying such as migraine or diabetes mellitus and relevant non-self-limiting GI disorders.
1.2. A history of acute pancreatitis regardless of aetiology
1.3. Family history of pancreatic cancer
1.4. Personal or family history of Multiple Endocrine Neoplasia type 2 or medullary thyroid tumour
1.5. Current or relevant previous history of serious, severe or unstable psychiatric illness, that may require treatment or make the subject unlikely to fully complete the study, or that presents undue risk from the study medication or procedures
1.6. History of previous surgical intervention which could affect GI transit and/or function for example gastric surgery, vagotomy or known adhesions with previous obstructive symptoms
1.7. Haematological or biochemical blood test at screening outside normal ranges and deemed clinically significant by the PI or medically qualified designee
1.8. Amylase and lipase values from blood tests outside normal ranges
1.9. Has a diagnosis of an immunosuppressive disorder or a condition requiring chronic immunosuppression
1.10. Any contraindication to the gamma scintigraphy procedure
1.11. As a result of a physical examination or screening investigations available prior to dosing evaluations, the PI or medically qualified designee/physician responsible considers the volunteer unfit for the study
1.12. Measured body temperature >38°C at screening visit (COVID-19 risk reduction procedure)
2. Medications:
2.1. Subject is scheduled to take prescribed medication within 14 days prior to the first or any subsequent assessment visit which, in the opinion of the PI or medically qualified designee responsible, will interfere with the study procedures or has the potential to affect gastric emptying and/or gut transit or compromise safety
2.2. Subject is scheduled to take over-the-counter (OTC) medication, including vitamins, pro and prebiotics and natural or herbal remedies, within 48 hours prior to the first or any subsequent assessment visit
3. Alcohol/substance abuse:

3.1. Recent history (within the last year) of alcohol or other substance abuse
3.2. Subject has an average weekly alcohol intake of greater than 14 units
3.3. Subject has positive urine drugs of abuse test at screening or prior to dosing evaluation
3.4. Subject has a positive breath alcohol test at screening or prior to dosing evaluation
4. Smoking:
4.1. Subject has recently discontinued smoking (less than 3 months).
4.2. Subject is currently a smoker or user of nicotine-containing products
4.3. Subject has a positive urine cotinine test at screening or prior to dosing evaluation
5. Allergy/intolerance:
5.1. Subject has a history of allergy to any component of the dosage form or any other allergy, which, in the opinion of the PI or medically qualified designee responsible, contraindicates their participation
5.2. Subject has an allergy to any of the contents of the standardised meals
5.3. Subject is vegetarian or vegan
6. Clinical studies:
6.1. Participation in another clinical study (inclusive of final post-study examination) or receipt of an investigational drug within the 12 weeks before the screening visit, or five elimination half-lives of the previous study drug, whichever is longer
6.2. Subject whose participation in this study will result in participation in more than four studies over a 12-month period
7. Personnel:
7.1. An employee of the Sponsor, client or study site or members of their immediate family.
8. Radiation exposure:
8.1. Subject has a total dosimetry value which, in the opinion of the PI or medically qualified designee/physician responsible, contraindicates their participation
9. Family planning:
9.1. Subjects who are intending to father a child in the 90 days following the study or are unwilling or unable to follow the precautions outlined in inclusion criteria 7
10. Blood:
10.1. Blood donation or significant blood loss within 3 months of screening and for the duration of the study
10.2. Difficulty accessing forearm veins for cannulation or blood sampling
11. Other:
11.1. Subject has any non-removable metal objects such as metal plates, screws etc in their chest or abdominal area which in the opinion of the PI or medically qualified designee/responsible physician could affect the study conduct

Date of first enrolment
17/11/2022

Date of final enrolment
07/12/2022

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
BDD Pharma Ltd
Bio-Imaging Centre
Basement Medical Block
Within Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Sponsor information

Organisation
BDD Pharma Ltd

Funder(s)

Funder type
Government

Funder Name
Scottish Enterprise

Alternative Name(s)
SE

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			21/12/2023	No	No