ISRCTN12728443 https://doi.org/10.1186/ISRCTN12728443

A study in healthy volunteers to assess how the test medicine ODM-111 is taken up, broken down and removed from the body when taken by mouth as a tablet, and when given radiolabelled in the form of an oral solution and by short infusion into a vein

Submission date 20/06/2024	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol
Registration date 29/07/2024	**Overall study status** Stopped	[ ] Statistical analysis plan [ ] Results
Last Edited 07/11/2024	**Condition category** Other	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims

The Sponsor is developing the test medicine, ODM-111, as a potential treatment for short and long-term pain. Pain is one of the most common reasons for patients to visit healthcare providers. Currently available medicines to treat pain only provide partial pain relief and can have troublesome side effects.

In this study healthy volunteers will receive three single doses of the test medicine to find out how the body breaks down and gets rid of it. Two doses of the test medicine will be 'radiolabelled' - it will contain a small amount of radioactivity (Carbon-14) so that it can be tracked in the body.

In this study in healthy volunteers, the aim is to answer these questions:

1. Does the test medicine cause any important side effects?
2. What are the blood levels of the test medicine and how quickly does the body get rid of it?
3. How much of the test medicine gets into the bloodstream?
4. How does the body break down and get rid of the test medicine?

Who can participate?

Healthy men aged 30-65 years

What does the study involve?

In Part 1, volunteers will receive a single oral dose of test medicine, and then 2.75 hours later a dose of test medicine containing a very tiny amount of radiolabel by injection into a vein. In Part 2, volunteers will receive a dose of test medicine also containing a radiolabel, by mouth. In Part 1 volunteers will stay in the clinic for 4 nights and in Part 2 they will stay for up to 10 nights. There will be a minimum 14-day gap between each study part, and it will take up to 8 weeks to finish

the study. The researchers will collect blood and urine samples to do safety tests, take blood samples throughout the volunteers' stay in clinic and collect all their urine and faeces to measure the amount of test medicine and its breakdown products.

What are the possible benefits and risks of participating?
Volunteers may experience side effects from the test medicine. The test medicine is early in development so there is little information about its effects in humans. Full information on possible side effects is in the Participant Information Sheet and Informed Consent Form. There is always a risk of unexpected side effects or an allergic reaction. To mitigate the risk, we'll ensure that volunteers meet the entry criteria for the study and monitor volunteers closely throughout the study.
From both doses of the radiolabelled test medicine (IV and oral), volunteers will be exposed to not more than a total of 2.4 milliSieverts (mSv) (to 1 decimal place) of radioactivity during the study (IV dose = 0.0052 mSv, oral dose = 2.4 mSv). This is about 11 months' exposure to average background radiation in the UK (2.7 mSv). This equates to slightly more than the radiation dose that would result from five abdominal X-rays or slightly less than two CT scans of the head for example. That amount of radiation poses negligible risk to the volunteers' health but volunteers should not have taken part in any other absorption, distribution, metabolism and excretion (ADME) study involving radiation for at least 1 year before this study.
The screening tests might be of benefit if they find an important medical problem, but they might reveal something that the volunteer would prefer not to know about. If there are medically important findings in our tests at screening, or during the study, the researchers will inform the volunteer's GP (having obtained their consent to do so).
Volunteers will be confined to the clinic during each of the study parts (volunteers will be discharged and able to return home in between each study part) and must make outpatient visits and comply with the lifestyle restrictions described in the PIS/ICF, including periods of fasting from food and drink except water, and short periods during which they'll be allowed no fluids.
The test medicine might harm unborn children, so all volunteers must follow the restrictions on the donation of sperm and use acceptable contraception. Were a partner of a volunteer to become pregnant during the study, we would ask permission to follow up on the pregnancy.
Volunteers will undergo many tests and procedures during the study. The side effects of these are listed below:
Blood sampling can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks. Susceptible volunteers may faint when we take blood samples; volunteers must lie down when we take blood samples to mitigate that risk.
ECG stickers may cause local skin irritation.
Volunteers may experience irritation at the site of infusion, but this will usually be mild.
Healthy volunteers will get no medical benefit from the test medicine; however, the aims of the study can be most efficiently met in volunteers with no concurrent medical conditions and who do not need to take concomitant medication that might interfere with the study objectives or increase the risk of the study. The risk/benefit evaluation in this study supports the use of healthy volunteers.
Volunteers will receive payment for participating in the study. There is always a risk that payment could represent coercion. However, payment will be based on committed time, inconvenience, and travel and other expenses, not on risk. An ethics committee will review the payment to ensure that it is fair.

Where is the study run from?
Quotient Sciences Limited (United Kingdom)

When is the study starting and how long is it expected to run for?
June 2024 to January 2025

Who is funding the study?
Orion Corporation (Finland)

Who is the main contact?
Clinical Study Director, clinicaltrials@orionpharma.com

Contact information

Type(s)
Principal investigator

Contact name
Dr Nand Singh

Contact details
Mere Way
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS
+44 (0)03303031000
recruitment@weneedyou.co.uk

Additional identifiers

Integrated Research Application System (IRAS)
1009963

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
NAVAME 3133005, IRAS 1009963

Study information

Scientific Title
Pharmacokinetics, absolute bioavailability and excretion balance after a single oral dose and IV microtracer dose of [14C]ODM-111; an open-label, non-randomised, single centre study in healthy male subjects

Acronym
QSC301595

Study objectives

Primary objectives:
Part 1:
To evaluate the absolute bioavailability of ODM-111

Part 2:
To determine the mass balance, routes and rates of elimination after a single oral dose of [14C] ODM-111

Secondary objectives:
Part 1:
1. To evaluate the plasma pharmacokinetics (what the body does to the test medicine; PK) of ODM-111, the metabolites (breakdown products) and total radioactivity
2. To provide additional safety and tolerability information for ODM-111

Part 2:
1. To perform metabolite profiling and structural identification from plasma, urine and faecal samples
2. To identify the chemical structure of each metabolite accounting for more than 10% of circulating total radioactivity or accounting for 10% or more of the dose in excreta
3. To evaluate the extent of distribution of total radioactivity into blood cells
4. To evaluate the pharmacokinetics of ODM-111, the metabolites in plasma, and total radioactivity in plasma and whole blood
5. To determine concentrations of ODM-111 and its metabolites in urine
6. To provide additional safety and tolerability information for ODM-111

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 26/07/2027, HSC REC B (Unit 5, Lissue Industrial Estate West, Rathdown Walk, Moira Road, Lisburn, Co. Antrim, BT28 2RF, United Kingdom; +44 (0)28 9536 1400; recb@hscni.ne), ref: 24/NI/0060

Study design
Single-center open-label non-randomized multiple-dose study in eight healthy male volunteers

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Acute and chronic pain. Study to be conducted in healthy volunteers

Interventions
In Part 1 participants will receive a single oral dose of ODM-111 as a tablet, and a single 5 ml IV dose of [14C]ODM-111.

In Part 2 participants will receive a single oral dose of [14C]ODM-111 as an oral solution.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ODM-111

Primary outcome(s)
Part 1:
Absolute bioavailability (F) of ODM-111 based on AUC(0-inf) of oral administration of ODM-111 compared to radiolabelled IV microtracer dose of ODM-111, adjusted for dose.

Part 2:
Mass balance recovery of total radioactivity in all excreta (urine and faeces) and in urine and faeces separately: Ae, %Ae, CumAe and Cum%Ae and by interval.

Part 1:
Plasma samples for ODM-111 will be taken from pre-dose on Day 1 until 72 h post oral dose on Day 4.
Part 2:
Mass balance recovery will be measured in urine and faecal samples collected from pre-dose on Day 1 until discharge (up to Day 10), and potentially also including additional home collections if required.

Key secondary outcome(s))
Part 1:
1. PK parameters for ODM-111, [14C]ODM-111 and metabolites, and total radioactivity in plasma after a single IV microtracer dose of [14C]ODM-111. Including, but not limited to the following as applicable: Tmax, Cmax, AUC(0-last), AUC(0-inf), T1/2 and metabolite ratios. Plasma samples for ODM-111 taken from pre-dose (Day 1) until 72 h post oral dose (Day 4)
2. Adverse events (AEs), physical examinations, vital signs, ECGs, and laboratory safety tests. Monitoring for AEs occurs from signing the informed consent form until discharge (prior to Day -1 to Day 4). Results from physical examinations, vital sign measurements, ECGs and safety tests at screening and from pre-dose (Day 1) until 75 h post oral dose (Day 4)

Part 2:
1. Collection of plasma, urine and faecal samples for metabolite profiling, structural identification, and quantification analysis. Analysis of blood, urine and faecal samples for ODM-111 taken from pre-dose (Day 1) until discharge (up to Day 10)
2. Identification of the chemical structure of each metabolite accounting for more than 10% by AUC of circulating total radioactivity or accounting for 10% or more of the dose in excreta. Performed by analysing blood, urine and faecal samples for ODM-111 taken from pre-dose (Day 1) until discharge (up to Day 10). Urine and faecal home collections may also be required.
3. Evaluation of whole blood:plasma concentration ratios for total radioactivity. Performed by analysing blood, urine and faecal samples for ODM-111 taken from pre-dose (Day 1) until discharge (up to Day 10). Urine and faecal home collections may also be required.
4. PK parameters for ODM-111, metabolites, and total radioactivity in plasma after a single oral dose of [14C]ODM-111. Including, but not limited to the following as applicable: Tmax, Cmax, AUC(0-last), AUC(0-inf), T1/2 and metabolite ratios. Performed by analysing plasma samples for

ODM-111, metabolites and total radioactivity taken from pre-dose (Day 1) until discharge (up to Day 10).
5. Determination of ODM-111 and metabolite concentration in urine. Performed by analysing urine samples for ODM-111 and metabolites taken from pre-dose (Day 1) until discharge (up to Day 10). Urine home collections may also be required.

Completion date
31/01/2025

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria
1. Must provide written informed consent.
2. Must be willing and able to communicate and participate in the whole study.
3. Aged 30 to 65 years inclusive at the time of signing informed consent.
4. Must agree to and adhere to the contraception requirements defined in the clinical protocol.
5. Males who are healthy as determined by medical evaluation including medical history, physical or neurological examination, vital signs, 12-lead ECG, screening clinical laboratory profiles (haematology, biochemistry, coagulation, and urinalysis), as deemed by the Investigator or designee.
6. Body mass index (BMI) of 18.5 to 32.0 kg/m2 as measured at screening.
7. Weight 55 to 100 kg at screening.
8. Must have regular bowel movements (i.e. average stool production of ≥1 and ≤3 stools per day).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
30 years

Upper age limit
65 years

Sex
Male

Total final enrolment
0

Key exclusion criteria

1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients.
2. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active.
3. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or GI disease, neurological or psychiatric disorder, as judged by the investigator.
4. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening.
5. Any clinically significant physical examination finding, as judged by the investigator.
6. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are not allowed.
7. Subjects who exhibit any first, second or third degree atrioventricular (AV) block at screening.
8. Subjects who have systolic BP <90 mmHg or >140 mmHg or diastolic BP <45 mmHg or >90 mmHg after 5 min in a supine position at screening.
9. Abnormal 12-lead ECG finding of clinical relevance at the screening visit or at pre-dose, (after 5 min rest in supine position), confirmed by a repeat measurement.
10. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results.
11. Evidence of renal impairment at screening, as indicated by an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m2 using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI; 2009) equation.
12. ALT or aspartate aminotransferase greater than the upper limit of normal (ULN) at screening.
13. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer.
14. Radiation exposure, including that from the present study, excluding background radiation but including diagnostic x-rays and other medical exposures, exceeding 5 mSv in the last 12 months or 10 mSv in the last 5 years. No occupationally exposed worker, as defined in the Ionising Radiation Regulations 2017, shall participate in the study.
15. Subjects who have been administered IMP in an ADME study in the last 12 months.
16. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood.
17. Subjects who are taking, or have taken, any prescribed or over-the-counter drug or herbal remedies (other than up to 4 g of paracetamol per day) in the 14 days before IMP administration. Exceptions may apply, as determined by the investigator, if each of the following criteria are met: medication with a short half-life if the washout is such that no PD activity is expected by the time of dosing with IMP; and if the use of medication does not jeopardise the safety of the trial subject; and if the use of medication is not considered to interfere with the objectives of the study. COVID-19 vaccines are accepted concomitant medications.
18. Subjects who have had a COVID 19 vaccine 72 h before admission.
19. History of any drug or alcohol abuse in the past 2 years.
20. Regular alcohol consumption in males >21 units per week (1 unit = ½ pint beer, or a 25 mL shot of 40% spirit, 1.5 to 2 units = 125 mL glass of wine, depending on type).
21. A confirmed positive alcohol breath test at screening or admission.
22. Current smokers and those who have smoked within the last 12 months.
23. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months.
24. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission.
25. Confirmed positive drugs of abuse test result at screening or admission.
26. Male subjects with pregnant or lactating partners.
27. Subjects who are, or are immediate family members of, a study site or sponsor employee.
28. Failure to satisfy the investigator of fitness to participate for any other reason.

Date of first enrolment
14/10/2024

Date of final enrolment
04/12/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
Ruddington Fields
Ruddington
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Orion Corporation (Finland)

ROR
https://ror.org/0296s4x19

Funder(s)

Funder type
Industry

Funder Name
Orion Corporation (Finland)

Results and Publications

Individual participant data (IPD) sharing plan

Participant-level data is not expected to be made available due to this being a Phase I study whereby the results are commercially very sensitive and it would not be appropriate to share the results publically at this time. Data will be stored by the Sponsor in line with international regulations and guidance, and by Quotient in a secure off-site archive.

IPD sharing plan summary

Not expected to be made available