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A study in healthy male volunteers to investigate how the test medicine is taken up, processed, and removed from the body

Submission date 28/01/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 09/03/2022	**Overall study status** Completed	
Last Edited 23/05/2023	**Condition category** Other	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, NRD135S.E1, for the potential treatment of painful diabetic peripheral neuropathy (PDPN). Peripheral neuropathy develops over time because high blood sugar levels associated with diabetes can damage the nerves in the body which can lead to spontaneous pain.

This healthy volunteer study will try to assess how the test medicine is taken up, processed and removed by the body when given as an oral solution at steady state. To help investigate how this happens, the test medicine will be radiolabelled. 'Radiolabelled' means the test medicine has a radioactive component (Carbon-14), which enables the test medicine to be tracked in the body. The safety and tolerability of the test medicine will also be studied.

Who can participate?
Healthy male volunteers aged 30-65 years

What does the study involve?
On Days 1 to 13, volunteers will receive single doses of the non-radiolabelled test medicine in the form of an oral capsule, in the morning. On Day 7, 30 minutes following the non-radiolabelled dose, volunteers will receive a single dose of the radiolabelled test medicine in the form of an oral solution.
Volunteers will be dosed after breakfast every day. Blood samples will be taken throughout the study for analysis of the test medicine and for safety. Saliva, urine and faecal collection will begin after the radiolabelled dose. Volunteers will stay in the clinic up to Day 14. If relevant radioactivity criteria have not been met, the stay may be extended until Day 16. If relevant criteria are still not met at this point, home collections of urine and/or faeces may be required. Volunteers are expected to be involved in this study for approximately 7 weeks from screening to the follow-up call.

What are the possible benefits and risks of participating?
Benefits:

Participants will get no medical benefit from taking part in this study. We hope that the development of a product to improve the treatment of painful diabetic peripheral neuropathy will be of benefit to patients with this condition.
Risks:
When investigating new medicines there is always a risk of unexpected side effects and occasionally allergic reactions. Volunteers will be closely monitored during the study.
Hazards predictable: Volunteers may experience side effects from the test medicine in this study. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form. All volunteers will be closely monitored during the study and safety assessments including vital signs, ECGs and clinical laboratory tests will be performed at regular intervals. The risks will be further mitigated by ensuring that only volunteers who meet all of the inclusion/exclusion criteria are included and that if the safety of any subject represents a concern they will be withdrawn.
There will be an extended period of fasting for the volunteers taking part in this study. To ensure an adequate fluid intake, the volunteers will be allowed ad libitum fluids and will be monitored for signs of dehydration and fatigue. The volunteers will always be dosed after consumption of food.
Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks.
ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist.

Where is the study run from?
Quotient Sciences (UK)

When is the study starting and how long is it expected to run for?
January 2022 to April 2022

Who is funding the study?
Novaremed AG (Switzerland)

Who is the main contact?
Dr Dalma Seboek, clinical@novaremed.com
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2021-006502-76

IRAS number
1004636

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
NRD135S.E1-104, IRAS 1004636

Study information

Scientific Title
Open-label study to investigate pharmacokinetics, mass balance and metabolite profiles of NRD135S.E1 in healthy adult male volunteers

Acronym
QSC203557

Study objectives
- To determine routes/rates of elimination and mass balance recovery after a single oral dose of [14C]-NRD135S.E1 under condition of steady-state exposure to unlabelled NRD135S.E1
- To provide metabolite profiles for known metabolites and tentative structures for new metabolites
- To determine single and multiple doses PK of NRD135S.E1
- To determine concentration-time profiles of drug-related material
- To determine major metabolites (metabolites with an AUC ≥10% relative to the AUC of total

radioactivity)
- To evaluate the extent of distribution of total radioactivity, parent compound and metabolites
- To evaluate the safety and tolerability of NRD135S.E1

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/02/2022, HRA Fast Track REC (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom), ref: 22/FT/0015

Study design
Interventional non-randomized

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Pharmacokinetics, mass balance and metabolite profiles of NRD135S.E1 in healthy adult male volunteers

Interventions
There is a single treatment arm, and all 8 healthy male participants will receive the same treatment. There is no placebo. Participants will take the test medicine for 13 days. They will take a capsule of test medicine, by mouth, each morning on Days 1–13. On Day 7, 30 minutes after taking the capsule of test medicine, participants will swallow a single dose of a solution of radiolabelled test medicine containing [14C]. Participants will be involved in the study for about 7 weeks (from screening to final follow-up). They will visit the ward to be screened before they take part, to check that they are healthy. They will stay on the ward for 14–16 nights while they are taking the test medicine. They will have a follow-up telephone call 3 to 7 days after they have left the ward, to check on their wellbeing.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
NRD135S.E1

Primary outcome measure
The rates and routes of elimination of the test medicine from the body, and the ways in which the body processes the test medicine will be assessed by taking whole blood, plasma, urine, faeces and saliva samples for liquid scintillation counting to measure the amount of radioactivity, and to identify breakdown products of the test medicine by liquid chromatography with radio detection and high resolution mass spectrometry, between Day 7 and Day 14. Participants stay may be extended an additional two days and they may need to continue collections of urine and faeces for a few days at home after they have left the ward.

Secondary outcome measures
1. The pharmacokinetics of the test medicine in plasma after single and repeated doses will be assessed by taking blood samples for LC-MS/MS assay of the test medicine between Day 1 and Day 14.
2. Adverse events (to assess tolerability of the test medicine) will be collected by often asking volunteers how they are feeling, from the start of the trial until follow up.
3. Other safety measures (including vital signs, ECGs and laboratory safety tests) will be assessed by standard phase 1 unit monitoring, at screening, from Day –1 to discharge from the ward

Overall study start date
18/01/2022

Completion date
15/04/2022

Eligibility

Key inclusion criteria
1. Healthy males
2. Aged 30 to 65 years inclusive at the time of signing informed consent
3. Body mass index (BMI) of ≥18.0 kg/m² and <30.0 kg/m² as measured at screening
4. Must be willing and able to communicate and participate in the whole study
5. Must be willing to consume the drug formulation that contains a small amount of alcohol
6. Must have regular bowel movements (i.e. average stool production of ≥1 and ≤3 stools per day)
7. Must provide written informed consent
8. Must agree to adhere to the contraception requirements defined in the clinical protocol

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
30 Years

Upper age limit
65 Years

Sex
Male

Target number of participants
8

Total final enrolment
8

Key exclusion criteria
1. 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
2. Subjects who are, or are immediate family members of, a study site or sponsor employee
3. Evidence of current SARS-CoV-2 infection within 2 weeks of first IMP administration or current ongoing symptoms from previous SARS-CoV-2 infection
4. History of any drug or alcohol abuse in the past 2 years
5. 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)
6. A confirmed positive alcohol breath test at screening or admission
7. Current smokers and those who have smoked within the last 6 months. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
8. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
9. Male subjects with pregnant or lactating partners
10. 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
11. Subjects who have been administered IMP in an ADME study in the last 12 months prior to screening
12. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
13. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are allowed
14. Confirmed positive drugs of abuse test result
15. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) antibody results
16. Evidence of renal impairment at screening, as indicated by an estimated eGFR of <60 mL/min using Chronic Kidney Disease Epidemiology Collaboration (CKD EPI) equation
17. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease, neurological or psychiatric disorder, as judged by the investigator
18. Serious adverse reaction or serious hypersensitivity to any drug or the formulation excipients
19. Subjects with history of intolerance to alcohol
20. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
21. Donation of blood or plasma or loss of greater than 400 mL of blood within the previous 3 months
22. Subjects with a haemoglobin lower than the lower limit of normal at screening
23. 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 NRD135S.E1

administration. Exceptions may apply on a case by case basis, if considered not to interfere with the objectives of the study, 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 trial
24. Subjects who have had a COVID-19 vaccine 72h before admission
25. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
10/03/2022

Date of final enrolment
15/04/2022

Locations

Countries of recruitment
United Kingdom

Study participating centre
Quotient Sciences Limited
Mere Way
Ruddington Fields
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Sponsor information

Organisation
Novaremed AG (Switzerland)

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Novaremed AG

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Publication on website
Submission to regulatory authorities

Intention to publish date
23/05/2024

Individual participant data (IPD) sharing plan
The findings of this Phase I study will be shared with the Sponsor, Novaremed AG, only. As these findings are confidential due to commercial sensitivity, it is not appropriate to share the results of this study with other researchers at this time.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No