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A Phase I, non-randomized, open-label, crossover study designed to evaluate the pharmacokinetic profile of iptacopan (LNP023) following single-dose administration of iptacopan modified-release formulations in comparison to a reference capsule formulation in healthy participants

Submission date 22/03/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 23/03/2023	**Overall study status** Deferred	
Last Edited 21/07/2026	**Condition category** Other	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, iptacopan (also known as LNP023), to treat diseases in which the immune system damages parts of the body. Examples of diseases that iptacopan (the test medicine) may be used to treat include paroxysmal nocturnal hemoglobinuria (PNH), immunoglobulin A nephropathy (IgAN), and C3 glomerulopathy.
This study in healthy volunteers aims to answer this question: how do blood levels of the test medicine compare when it's given in different formulations (recipes)?
This study will also provide more information on the safety and tolerability of the test medicine and any side effects.

Who can participate?
Healthy male and female participants who are unable to have a baby, aged 18 to 55 years

What does the study involve?
Participants will take part in seven study periods. In six of those study periods they will take a single oral dose of new formulations (recipes) of the test medicine, as tablets, and in one period they will take a single oral dose of the existing formulation of the test medicine, as capsules. In three of the study periods, the dose of test medicine may be taken with food. They'll stay in the clinic for 5 nights in each study period, and there will be a minimum of 7 days between each dose of test medicine. Volunteers will have a follow-up phone call about 30 days after their final dose of test medicine and will take up to 12 months to finish the study.

What are the possible risks and benefits of participating?
1. As this is a Phase I study, the most relevant population is healthy volunteers. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. Women of childbearing potential are excluded from this study.
2. There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation.
3. 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.
4. 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 Forms.
5. There may be an extended period of fasting for the volunteers taking part in this study. To ensure an adequate fluid intake, the volunteers will be placed under a strict fluid intake regime, with no fluids to be consumed 1 hour pre/post dosing, after which water can be consumed freely. Volunteers will be monitored for signs of dehydration and fatigue.
6. 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.
7. 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 Limited (UK)

When is the study starting and how long is it expected to run for?
March 2023 to January 2024

Who is funding the study?
Novartis Pharma AG (Switzerland)

Who is the main contact?
recruitment@weneedyou.co.uk

Contact information

Type(s)
Principal investigator

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Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-02525-10

Integrated Research Application System (IRAS)
1006182

Protocol serial number
Quotient Code: QSC205832

Study information

Scientific Title
A Phase I, non-randomized, open-label, crossover study designed to evaluate the pharmacokinetic profile of iptacopan (LNP023) following single-dose administration of iptacopan modified-release formulations in comparison to a reference capsule formulation in healthy participants

Study objectives
The trial will meet the following primary and secondary objectives:

Primary:
1. To evaluate the pharmacokinetic (PK) profile of iptacopan following single oral dosing of iptacopan modified release (MR) prototype tablet formulations in healthy participants in the fasted state.
2. To estimate the relative oral bioavailability of iptacopan following administration of single oral doses of iptacopan MR prototype tablet formulations, compared to a reference iptacopan immediate release (IR) capsule formulation in healthy participants in the fasted state.

Secondary:
1. To provide information on the safety and tolerability of single oral doses of iptacopan MR

prototype tablet formulations in healthy participants.
2. To estimate the relative bioavailability of iptacopan following administration of a single oral dose of iptacopan MR prototype tablet formulations in the fed (test) versus fasted state (reference; optional).

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 03/03/2023, HSC REC A (Office for Research Ethics Committees in Northern Ireland (ORECNI), Business Services Organisation, Lissue Industrial Estate West, Rathdown Walk, Moira Road, Lisburn, Co. Antrim BT28 2RF, UK; +44 (0)28 95 361400; reca@hscni.net), ref: 22/NI/0169
2. Approved 03/03/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 04935/0231/001-0001

Primary study design
Interventional

Allocation
Non-randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Crossover

Purpose
Pharmacokinetic, relative bioavailability, safety and tolerability trial in healthy volunteers

Study type(s)
Other

Health condition(s) or problem(s) studied
Complement alternative pathway disorders

Interventions
This is a non-randomised, open-label study. Healthy volunteers will receive single oral doses of a new tablet formulation of the test medicine in up to six study periods and a single oral dose of the existing capsule formulation in one study period. Up to three doses of the new tablet formulation may be given with food. In total, volunteers will receive up to seven doses of the test medicine. Volunteers will take their doses of test medicine on Day 1 of each study period and will be discharged from the clinical unit 4 days after each dose. There will be a minimum of 7 days between doses of test medicine.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
LNP023 MR Prototype X Tablet, 100 mg to 500 mg; LNP023 200 mg Capsule, hard

Primary outcome(s)
1. Pharmacokinetic parameters of iptacopan (including but not limited to Cmax, AUClast, AUCinf, AUC0-24h, C24h and Tmax) measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints until Period 7 Day 5
2. Relative bioavailability (Frel) for Cmax, C24h, AUClast, AUCinf and AUC0-24h (Tmax may be measured) of the iptacopan mmodified-release prototype tablets in comparison to the reference immediate-release capsule measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints until Period 7 Day 5

Key secondary outcome(s)
1. Safety endpoints measured using vital signs, electrocardiogram parameters, safety laboratory parameters and the incidence of adverse events at screening and at multiple post-dose timepoints until Period 7 Day 5
2. Relative bioavailability (Frel) for Cmax, C24h, AUClast, AUCinf and AUC0-24h (Tmax may be measured) of the iptacopan modified-release prototype tablet formulation(s) in the fed (test) versus fasted state (reference) measured using plasma drug concentration assay at pre-dose and at multiple post-dose timepoints until up to Period 7 Day 5 in applicable study periods

Completion date
28/01/2024

Eligibility

Key inclusion criteria
1. Signed informed consent must be obtained prior to participation in the study.
2. Healthy male and non-childbearing potential female participants, 18 to 55 years of age, inclusive.
3. In good health as determined by past medical history, physical examination, ECG, and laboratory tests at screening and first baseline (admission).
4. Participants must weigh at least 50 kg at screening to participate in the study and must have a body mass index (BMI) within the range of 18.0 to 30.0 kg/m² at screening.
5. Normal or abnormal without clinical significance vital sign measurements at first baseline (admission) and first pre-dose. Supine vital signs should be within the following ranges:
5.1. Body temperature: ≤37.5°C
5.2. Pulse rate: 45-100 bpm
5.3. Systolic blood pressure: 90-140 mmHg
5.4. Diastolic blood pressure: 40-90 mmHg
If the vital signs are out of range at first baseline and/or first pre-dose, two additional readings can be obtained so that up to three consecutive assessments are made, with the participant lying supine quietly for approximately 5 minutes preceding each repeat assessment. The last reading must be within the specified range for the participant to qualify.
6. Able to communicate well with the investigator to understand and comply with the requirements of the study.

Participant type(s)

Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
16

Key exclusion criteria
1. Participants who have received any IMP in a clinical research study within the 90 days or 5 half-lives, whichever is longer, prior to Period 1 Day 1.
2. Participants who are, or are immediate family members of, a study site or Sponsor employee.
3. History of hypersensitivity to the investigational compound/compound class or excipients being used in this study.
4. History or current diagnosis of ECG abnormalities indicating significant risk of safety for participants participating in the study at screening or first baseline (admission) or first pre-dose such as:
4.1. Concomitant clinically significant cardiac arrhythmias, e.g., sustained ventricular tachycardia, and clinically significant second or third degree atrioventricular (AV) block without a pacemaker.
4.2. History of familial long QT syndrome or known family history of Torsades de Pointe.
4.3. QT interval corrected by Fridericia's formula (QTcF) >450 milliseconds (ms) (males) or >460 ms (females)
5. History of symptomatic orthostatic hypotension or syncope.
6. A history of recurrent invasive infections caused by encapsulated organisms, e.g., meningococcus or pneumococcus.
7. Active systemic bacterial, viral (including SARS-CoV-2), parasitic or fungal infection within 14 days prior to study drug administration.
8. History of malignancy of any organ system (other than localized basal cell carcinoma of the skin or in situ cervical cancer), treated or untreated, within the past 5 years of screening, regardless of whether there is evidence of local recurrence or metastases.
9. Participants with a history of cholecystectomy or gall stones.
10. History or evidence of testicular disease (males).
11. Sexually active males unwilling to adhere to the contraception requirements of the study as detailed below:
11.1. A condom is required for all sexually active male participants to prevent them from fathering a child and to prevent delivery of the investigational drug via seminal fluid to their partner.
11.2. Males with partners of childbearing potential must use a condom during intercourse while taking investigational drug and for 95 days after stopping investigational drug (duration to cover

one spermatogenesis cycle plus 5 half-lives) as a precautionary measure.
11.3. In addition to condoms, as a precaution, if a male has a female partner of childbearing potential, the partner must use a method of effective contraception from the list below whilst the male participant is taking the investigational drug for 95 days after he stops taking the investigational drug (duration to cover one spermatogenesis cycle plus 5 half-lives):
11.3.1. Partner's bilateral tubal occlusion.
11.3.2. Partner's use of oral (estrogen and progesterone; or progesterone only), injected, or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS) or other forms of hormonal contraception that have comparable efficacy (failure rate < 1%), for example, a hormone vaginal ring or transdermal hormone contraception.
11.3.3. Male participant sterilization (vasectomy; at least 6 months prior to screening) is also appropriate.
11.3.4. Progesterone-only contraception where inhibition of ovulation is not the primary mechanism of action.
11.4. Female cap, diaphragm or sponge with spermicide.
11.5. Total abstinence (when this is in line with the preferred and usual lifestyle of the participant). Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.
11.6. Males with partners of non-childbearing potential must use a condom during intercourse while taking the investigational drug and for 5 days after stopping the investigational drug (duration to cover 5 half-lives) as a precautionary measure.
11.7. In addition, male participants should not donate sperm for 95 days after stopping the investigational drug.
12. Women of childbearing potential, defined as all women physiologically capable of becoming pregnant. Women are considered not of childbearing potential if they are post-menopausal or have had surgical bilateral salpingectomy or bilateral oophorectomy (with or without hysterectomy) or total hysterectomy at least six weeks before screening. Women are considered post-menopausal if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g., age-appropriate, history of vasomotor symptoms) and serum follicle-stimulating hormone (FSH) concentration of ≥40 IU/L. Follicle-stimulating hormone testing is required for post-menopausal female participants at screening.
13. Participants who do not have suitable veins for multiple venipunctures/cannulation as assessed by the Investigator or delegate at screening.
14. History or evidence of use of any tobacco or other nicotine-containing products in the 3 months prior to screening including but not limited to cigarettes, cigars, chewing tobacco, vaporizers, and electronic cigarettes.
15. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or first baseline (admission).
16. Participants who have received a COVID-19 vaccine, or any other vaccine, within the 2 weeks prior to the first IMP administration.
17. Use of any medications (including prescription drugs and dietary supplements) known to induce or inhibit CYP2C8 or OATP or any herbal remedies within the four weeks prior to first IMP administration.
18. Use of any other prescription drugs; dietary supplements or vitamins within the two weeks prior to first IMP administration. Hormone replacement therapy (HRT) is permitted. If needed, paracetamol/acetaminophen up to 4 g per 24 hours is acceptable, but must be documented in the Concomitant medications / Significant non-drug therapies page of the case report form (CRF). 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 pharmacodynamic activity is expected by the time of dosing with IMP; and if the use of medication does not jeopardize the safety of the trial participant; and if the use of medication is not considered to

interfere with the objectives of the study.
19. Donation of blood or plasma or loss of greater than 400 ml of blood within the previous 3 months.
20. Hemoglobin below the lower limit of the reference range at screening or first baseline (admission).
21. Significant illness, which has not resolved within 2 weeks prior to initial dosing.
22. Recent (within the last three years prior to screening) and/or recurrent history of autonomic dysfunction (e.g., recurrent episodes of fainting, palpitations, etc) or symptoms of postural hypotension.
23. Recent (within the last 3 years prior to screening) and/or recurrent history of acute or chronic bronchospastic disease (including asthma and chronic obstructive pulmonary disease, treated or not treated). Hay fever is allowed unless it is active.
24. Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of drugs, or which may jeopardize the participant in case of participation in the study, e.g., significant cardiovascular, chronic respiratory, neurological or psychiatric disorder. The Investigator should make this determination in consideration of the participant's medical history and/or clinical or laboratory evidence of any of the following:
24.1. Inflammatory bowel disease, peptic ulcers, GI disease including rectal bleeding.
24.2. Major GI tract surgery such as gastrectomy, gastroenterostomy, or bowel resection.
24.3. Pancreatic injury or pancreatitis.
24.4. Any single parameter of ALT, AST, GGT, or ALP exceeding 1.2 x upper limit of normal (ULN) and ≥ 1.5 x ULN total bilirubin (TBL) or any elevation above the ULN of more than one parameter of ALT, AST, GGT, ALP or serum bilirubin.
24.5. Evidence of renal impairment at screening.
24.6. Evidence of urinary obstruction or difficulty in voiding at screening.
24.7. Participants with Gilbert's syndrome are not allowed.
25. History or evidence of immunodeficiency or a confirmed positive human immunodeficiency virus (HIV) 1 and 2 test result (e.g., enzyme-linked immunosorbent assay (ELISA) and Western blot) at screening regardless of immune status.
26. Infection with Hepatitis B virus (HBV) or Hepatitis C virus (HCV) at screening. A positive HBV surface antigen (HBsAg) or HCV test.
27. History of drug abuse or unhealthy alcohol use within the 12 months prior to dosing. Unhealthy alcohol use is defined as a history of or current alcohol misuse/abuse defined as >21 units per week for males and >14 units for females (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).
28. Confirmed positive drugs of abuse test result at screening or first baseline (admission).
29. A confirmed positive alcohol breath test at screening or first baseline (admission).
30. Failure to satisfy the Investigator's assessment for fitness to participate for any other reason.

Date of first enrolment
29/03/2023

Date of final enrolment
28/01/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences
Mere Way
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Sponsor information

Organisation
Novartis (Switzerland)

ROR
https://ror.org/02f9zrr09

Funder(s)

Funder type
Industry

Funder Name
Novartis Pharma

Alternative Name(s)
Novartis Deutschland GmbH, Novartis Pharma GmbH, Novartis Deutschland

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available