A multicenter rollover extension program (REP) to evaluate the long-term safety and tolerability of open label iptacopan in adult participants with primary IgA nephropathy who have completed a Novartis-sponsored iptacopan parent study in IgAN

Published: 23-07-2021
Last updated: 25-09-2024

This study has been transitioned to CTIS with ID 2023-508690-92-00 check the CTIS register for the current data. The primary objective is to evaluate the long-term safety and tolerability of iptacopan in eligible participants. The primary clinical...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON56438

Source
ToetsingOnline

Brief title
CLNP023A2002B IgA Rollover

Condition

- Nephropathies

Synonym
IgA kidney disease, IgAN

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V.

Intervention

Keyword: chronic kidney disease, IgA nephropathy, LNP023, proteinuria

Outcome measures

Primary outcome

• Safety and tolerability endpoints (including but not limited to AEs/SAEs,

safety laboratory parameters, vital signs).

Secondary outcome

• Annualized total eGFR slope

• Change from baseline in eGFR

• Log transformed ratio to baseline in UPCR, UACR

Study description

Background summary

The purpose of this study is to evaluate the long-term safety and tolerability, of open label iptacopan 200 mg b.i.d. in primary IgA nephropathy adult participants who have completed one of the Novartis-sponsored parent studies in IgAN with biopsy-confirmed IgAN, an eGFR >= 20 mL/min/1.73m2 and per Investigator*s clinical judgement may benefit from receiving open-label iptacopan, despite optimal supportive treatment. The trial will enroll approximately 500 participants. The open-label design of the current study is appropriate to provide study participants the opportunity to receive treatment with iptacopan until marketing authorizations are received and the drug product becomes commercially available while enabling collection of long-term safety and tolerability data for the investigational drug. Furthermore, efficacy assessments conducted every 6 months will afford the opportunity to evaluate

the clinical effects of iptacopan on long-term disease progression.

Study objective

This study has been transitioned to CTIS with ID 2023-508690-92-00 check the CTIS register for the current data.

The primary objective is to evaluate the long-term safety and tolerability of iptacopan in eligible participants.
The primary clinical question of interest is: what is the long-term safety and tolerability of iptacopan in IgAN participants including but not limited to adverse events/serious adverse events (AEs/SAEs), safety laboratory parameters, and vital signs.

The secondary objective is to characterize the clinical benefit (efficacy) of iptacopan in eligible participants receiving open-label iptacopan.
The secondary clinical question of interest addresses the rate of IgAN progression as measured by annualized total Estimated Glomerular Filtration Rate (eGFR) slope in participants treated with open-label iptacopan.

Study design

This is an open-label, non-randomized, multicenter rollover extension program (REP) to:
• CLNP023X2203, a Phase II trial investigating the dose ranging effects of LNP023 on efficacy, pharmacokinetics (PK), pharmacodynamics (PD), safety and tolerability in primary IgAN patients,
• CLNP023A2301, a Phase III trial, investigating the efficacy, pharmacokinetics (PK), pharmacodynamics (PD), safety and tolerability of LNP023 in patients with primary IgAN.
• Any other Novartis-sponsored clinical trial of iptacopan in IgAN.
Once enrolled in the study, participants will commence study treatment with iptacopan at 200 mg b.i.d. and may continue on treatment until:
• 3 years after LPFV of this study CLNP023A2002B or,
• the participant no longer derives benefit from iptacopan according to the Investigator, or
• the benefit-risk profile of the product in IgAN is no longer positive, or
• initiation of maintenance dialysis (defined as dialysis performed for at least 4 weeks), kidney transplantation or sustained eGFR < 15 mL/min/1.73m2 over at least 4 weeks, or
• the product becomes commercially available in a specific country following product launch and subsequent reimbursement for IgAN, where applicable, or
• if a marketing application or reimbursement of an investigational product is rejected/not pursued in a region/country for the indication under study whichever is sooner.

Intervention

Iptacopan at 200 mg b.i.d.

Study burden and risks

Disadvantages of participating include the potential for side effects of iptacopan and inconveniences of study procedures.
The possible side effects of iptacopan include:
- Infections. Iptacopan may make you more susceptible to infections. You can be vaccinated against some infectious diseases. This may help reduce the chance of infections.
- Delayed sperm maturation. During studies in animals, a delayed maturation of sperm cells has been observed, combined with a reduction in the normal motility of sperm. These phenomena were partially reversible during the observation period. It is unknown whether these phenomena can also occur in humans. Blood is regularly examined for certain hormones.
- Discomforts of examination tests:
- Venapuncture; local pain, bruise, crust, infection.

Vaccination: If a booster is needed
Collection of morning urine: 2-16x
Blood and urine tests: 6-20x
Measuring weight, pulse, blood pressure and temperature: 8-21x
Measuring height: 1x
Physical examination: 6-19x
ECG: 2-9x
Pregnancy test: 4-17x if participant is in fertile period.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Signed informed consent must be obtained prior to participation in the REP; participants should be able to communicate well with the Investigator, understand and comply with the requirements of the study.
• For CLNP023X2203, participants must have completed Part 1 or Part 2 of the trial. For other parent trials participants must have completed the entire parent trial duration defined by the respective protocol.
• eGFR* >= 20 mL/min/1.73m2
*eGFR calculated using the CKD-EPI formula (or modified MDRD formula according to specific ethnic groups and local practice guidelines)
• Per Investigator*s clinical judgment, the participant may benefit from receiving the open-label treatment of iptacopan 200 mg b.i.d.
• Prior vaccination against Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae infections should be up to date (i.e. any boosters required administered according to local regulations).
• All participants must be on supportive care regimen of stable dose of ACEi or ARB* as per KDIGO guidelines (KDIGO 2021).
* Participants with allergies or intolerance to ACEi and ARB are eligible for the study but the Investigator should clearly document the reasons for not being on maximal ACEi/ARB dose in the source documents.

Exclusion criteria

• Participants who are screen or baseline failed in any of the iptacopan parent studies in IgAN or who prematurely withdrew from iptacopan parent studies in IgAN for any reason.
• Evidence of severe urinary obstruction or difficulty in voiding; any urinary tract disorder other than IgAN at screening and before dosing with iptacopan.
• Current (within 4 weeks prior to study treatment administration in the REP)

acute kidney injury (AKI) defined by AKIN criteria).
• Presence of Rapidly Progressive Glomerulonephritis (RPGN) as defined by 50% decline in eGFR within the last 3 months.
• Participants treated with immunosuppressive or other immunmodulatory agents such as but not limited to cyclophosphamide, rituximab, infliximab, eculizumab, canakinumab, mycophenolate mofetil (MMF) or mycophenolate sodium (MPS), cyclosporine, tacrolimus, sirolimus, everolimus and/or systemic corticosteroids exposure (>7.5 mg/d prednisone/prednisolone equivalent) within 90 days prior to first study drug administration. Rituximab requires 180 days wash out. Participants treated with endothelin (receptor) antagonists within 90 days prior to first study drug administration.
• Use of other investigational drugs at the time of enrollment, or within 5 half-lives of enrollment or within 30 days whichever is longer.
• All transplanted participants (any solid organ, or bone marrow transplantation).
• History of recurrent invasive infections caused by encapsulated organisms, such as meningococcus, pneumococcus, and H. influenzae.
• Major concurrent comorbidities including but not limited to severe uncontrolled hypertension, other chronic kidney disease (with or without kidney failure), advanced cardiac disease (e.g., NYHA class IV), severe pulmonary disease (e.g., severe pulmonary hypertension (WHO class IV), or hepatic disease (e.g. active hepatitis) that in the opinion of the Investigator precludes participant's participation in the study.
• Any medical condition deemed likely to interfere with the participant*s participation in the study.
• Active systemic bacterial, viral (including COVID-19) or fungal infection within 14 days prior to study treatment administration.
• Presence of fever >= 38°C (100.4°F) within 7 days prior to study treatment administration.
• History of Human Immunodeficiency Virus (HIV) infection (known history of HIV or test positive for HIV antibody at Screening).
• Liver disease or liver injury as indicated by abnormal liver function tests (LFT) at screening as defined below. ALT (SGPT), AST (SGOT), GGT, alkaline phosphatase and serum bilirubin will be tested.
• Any single parameter of ALT, AST, GGT, alkaline phosphatase must not exceed 3 × upper limit of normal (ULN)
• Serum bilirubin must not exceed 2 × ULN
Participants from CLNP023X2203 study or any other parent study participants if required by local regulations will be additionally tested for HBsAg and HCV-RNA and are not eligible if the results are positive.
• History of hypersensitivity to any of the study treatments or its excipients or to drugs of similar chemical classes or any participant who discontinued study treatment in the parent study due to a suspected treatment related AE.
• History of malignancy of any organ system (other than localized basal cell carcinoma of the skin or in situ cervical cancer treated with curative intent), treated or untreated, within the past 5 years, regardless of whether there is evidence of local recurrence or metastases.

• Pregnant or breastfeeding females, where pregnancy is confirmed by a positive Human Chorionic Gonadotrophin (HCG) test.
• Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using effective methods of contraception during dosing of investigational drug and for 1 week after stopping of investigational drug.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-06-2023
Enrollment:	5
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Nog niet bekend
Generic name:	iptacopan

Ethics review

Approved WMO

Date:	23-07-2021
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	12-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-508690-92-00
EudraCT	EUCTR2020-002200-40-NL
ClinicalTrials.gov	NCT04557462

Register	ID
CCMO	NL78462.056.21