A multi-center, randomized, double-blind, placebocontrolled, parallel group, phase III study to evaluate the efficacy and safety of LNP023 in primary IgA nephropathy patients

Published: 17-11-2020
Last updated: 25-09-2024

This study has been transitioned to CTIS with ID 2024-511067-29-00 check the CTIS register for the current data. The purpose of the study is to evaluate the efficacy and safety of LNP023 compared to placebo on proteinuria reduction and slowing renal...

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

Summary

ID

NL-OMON56184

Source
ToetsingOnline

Brief title
CLNP023A2301 (APPLAUSE)

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

The primary objective at the time of interim analysis is:

To demonstrate superiority of LNP023 vs. placebo in the reduction of

proteinuria at 9 months by measuring UPCR sampled from a 24h urine collection.

The primary objective at the time of final analysis is:

To demonstrate superiority of LNP023 vs. placebo in slowing IgAN progression

measured by the annualized total slope of eGFR decline over 24 months.

The primary clinical questions of interest at the Interim and Final Analysis

respectively are:

What is the treatment effect of LNP023 (200 mg b.i.d oral administration) vs.

placebo on

a) proteinuria reduction as measured by UPCR (sampled from 24h urine

collection) at the Interim analysis, and

b) slowing IgAN progression as measured by the annualized total eGFR slope at

the Final analysis

In primary IgAN patients with eGFR >= 30 mL/min/1.73m2 who are on background

ACEi/ARB treatment, as though corticosteroids, immunosuppressant therapy, or other newly approved drugs or new background therapy for IgAN and Kidney Replacement Therapy (KRT) were not available and regardless of unforeseen changes in permitted/concomitant medications or treatment discontinuation for any reason.

Secondary outcome

The secondary objectives at the time of interim analysis are:

To evaluate the effect of LNP023 vs. placebo on slowing eGFR decrease as measured by the change from baseline in eGFR at 9 months.

To assess the effect of LNP023 vs. placebo on the proportion of study participants reaching proteinuria below 1g/g of UPCR (sampled from 24h urine collection) at 9 months.

To evaluate the effect of LNP023 vs. placebo on slowing IgAN progression measured by the annualized total slope of eGFR decline over 1 year.

To assess the effect of LNP023 vs. placebo on the change from baseline to 9 months in the fatigue scale measured by the Functional Assessment Of Chronic Illness Therapy (FACIT-Fatigue) questionnaire.

To evaluate the safety and tolerability of LNP023 vs. placebo.

The secondary objectives at the time of final analysis are:

To demonstrate superiority of LNP023 vs. placebo in the reduction of proteinuria at 9 months by measuring UPCR sampled from a 24h urine collection.

To demonstrate the superiority of LNP023 vs. placebo on the proportion of study participants reaching proteinuria below 1g/g of UPCR (sampled from 24h urine collection) at 9 months.

To demonstrate the superiority of LNP023 vs. placebo on delaying the time to first occurrence of a composite kidney failure endpoint of reaching either at least 30% decline in eGFR, eGFR <15 mL/min/1.73 m2, dialysis, kidney transplantation or death from kidney failure.

To demonstrate the superiority of LNP023 vs. placebo on the change from baseline to 9 months in the fatigue scale measured by FACIT-Fatigue questionnaire.

To evaluate the safety and tolerability of LNP023 vs. placebo.

Study description

Background summary

The study is designed as a multicenter, randomized , double-blind, placebo controlled study to demonstrate the superiority of LNP023 at a dose of 200 mg b.i.d. compared to placebo on top of maximally tolerated or maximal locally approved ACEi or ARB on reduction of proteinuria and slowing renal disease progression in primary IgAN patients. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend long-term supportive therapy with an ACEi or ARB with or without high dose CS or IS for blood pressure control and proteinuria reduction. In this double-blind, randomized study, the efficacy and safety of LNP023 will be assessed in comparison to placebo on top of the maximally tolerated or maximal locally approved doses of an ACEi or ARB.

Study objective

This study has been transitioned to CTIS with ID 2024-511067-29-00 check the CTIS register for the current data.

The purpose of the study is to evaluate the efficacy and safety of LNP023 compared to placebo on proteinuria reduction and slowing renal disease progression in primary IgAN patients

Study design

This is a multi-center, randomized, double-blinded, placebocontrolled study, which comprises a screening visit, followed by a run in period of 14 to

approximately 90 days. Thereafter, eligible participants will be randomized in a 1:1 ratio to either LNP023 200mg or matching placebo b.i.d. for a 24 month treatment period.

Intervention

Study participants will be randomized to LNP023 200 mg b.i.d. or placebo in 1:1 ratio, while
remaining on the maximally tolerated or locally approved maximal daily doses of ACEi or ARB
throughout the treatment period.

Study burden and risks

The study lasts 24 to 27 months. The study starts with a screening period followed by a run-in phase of maximum 90 days. After that there is a treatment period of about 24 months in which the research medication is used. Three months after the last administration of the
research medication there is a final check, unless the patient immediately switches to the Roll-over Extension protocol.

Assuming 13 visits, the load will be as follows:
Collection of 24-hour urine: 5x
Collecting First Morning Void: 12x
Blood and urine test: 13x
Measure weight, pulse, blood pressure and temperature: 13x
Measuring the length: 1x
Questionnaires: 6x
Physical examination: 4x
ECG: 3x
Pregnancy test: 3 times if participant is in fertile period.
Kidney biopsy (if needed): 1x

Optional:
Pharmacogenetics (1x blood collection)

Side effects of research medication and inconvenient research procedures.
Prohibited co-medication.

Contacts

Public
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL
Scientific
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Male and female patients >= 18 years of age with an eGFR level and biopsy-confirmed IgA nephropathy as follows
o For patients eGFR* >= 45mL/min/1.73m2, a qualifying biopsy performed within the last 5 years is required
o For patients with eGFR* 30 to <45mL/min/1.73m2, a qualifying biopsy performed within 2 years with < 50% tubulointerstitial fibrosis is required
o For patients with eGFR* 20 to <30mL/min/1.73m2, a qualifying biopsy performed at any time. In all cases, if a historical biopsy is not available, one may be performed during screening.
• Proteinuria due to primary diagnosis of IgA nephropathy as assessed at screening by UPCR >=1 g/g (113 mg/mmol) sampled from FMV or 24h urine collection, as well as at the completion of the run-in period by UPCR >=1 g/g (113 mg/mmol) calculated as the (geometric) mean of two 24h urine collections obtained within 14 days of each other at baseline.
• Vaccination against Neisseria meningitidis and Streptococcus pneumoniae infection is required prior to the start of study treatment. If the patient has not been previously vaccinated, or if a booster is required, vaccine should be given according to local regulations at least 2 weeks prior to first study drug administration. If study treatment has to start earlier than 2 weeks post

vaccination, prophylactic antibiotic treatment should be initiated.
• If not previously vaccinated, vaccination against Haemophilus influenzae infection should be given, if available and according to local regulations, at least 2 weeks prior to first study drug administration.
• All patients must have been on supportive care including stable dose regimen of ACEi or ARB at either the locally approved maximal daily dose or the maximally tolerated dose (per investigators* judgment) for approximately 90 days before first study drug administration. In addition, if patients are taking diuretics, other antihypertensive medication or other background medication for IgAN, the doses should also be stabilized for approximately 90 days prior to the first dosing of study treatment.

Exclusion criteria

• Any secondary IgAN as defined by the investigator; secondary IgAN can be associated with cirrhosis, celiac disease, Human Immunodeficiency Virus (HIV) infection, dermatitis herpetiformis, seronegative arthritis, small-cell carcinoma, lymphoma, disseminated tuberculosis, bronchiolitis obliterans, and inflammatory bowel disease, familial mediterranean fever, etc.
• Sitting office SBP >140 mmHg or DBP >90 mmHg at the randomization visit
• Patients previously 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, or systemic corticosteroids exposure (>7.5 mg/d prednisone/prednisolone equivalent) within 90 days (or 180 days for rituximab) prior to first study drug administration. Participants previously or currently treated with oral budesonide. Participants treated with endothelin (receptor) antagonists within 90 days prior to first study drug administration.
• Prior use of LNP023 or prior enrollment in any other LNP023 clinical trial where study drug was taken, including matching placebo
• History of recurrent invasive infections caused by encapsulated organisms, such as meningococcus and pneumococcus.
• Active systemic bacterial, viral (including COVID-19) or fungal infection within 14 days prior to study drug administration.

Study design

Design

Study phase: 3

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-07-2021
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nog niet bekend
Generic name:	iptacopan

Ethics review

Approved WMO Date:	17-11-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-05-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	16-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-08-2022
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-10-2023
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:	15-04-2024
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	CTIS2024-511067-29-00
EudraCT	EUCTR2020-001049-38-NL
ClinicalTrials.gov	NCT04578834
CCMO	NL75457.056.20