A randomized, open-label, parallel group, two arm, proof-of-concept clinical trial to investigate the efficacy and safety of LNP023 compared with rituximab in the treatment of subjects with idiopathic membranous nephropathy.

Published: 22-08-2019
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The purpose of this study is to ascertain the efficacy, safety, tolerability and pharmacokineticsof LNP023 over a 24-week treatment period compared with rituximab in subjects with MN.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON52636

Source
ToetsingOnline

Brief title
CLNP023D12201

Condition

- Nephropathies

Synonym
Ideopathic membranous nephropathy, Membranous nephropathy

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: Efficacy, LNP023, Membranous nephropathy, Safety

Outcome measures

Primary outcome

To assess the efficacy of LNP023 compared with rituximab

Secondary outcome

Objective 1: To assess the safety and tolerability of dose of LNP023

Objective 2: To assess the relationship between LNP023 systemic

drug exposure and pharmacodynamics, mode-of-action markers

and clinical efficacy

Objective 3: To assess the effect of LNP023 compared with

rituximab on proteinuria remission and renal function

Objective 4: To assess the pharmacokinetics of LNP023

Study description

Background summary

Idiopathic (primary) membranous nephropathy (MN) is a glomerular disease in 40-70 year old adults very frequently associated with nephrotic syndrome and significant morbidity, including the progressive loss of renal function leading to End Stage Renal Disease (ESRD).
The estimated prevalence is around 550 per million, giving a total of approximately 100,000 patients in the US and about twice

that in the EU. There is also evidence that the prevalence of MN is increasing in certain regions,for example in China.
Current recommended therapies include the Ponticelli regimen (oral and i.v.corticosteroids and alkylating agents) or calcineurin inhibitors, though both of these are associated with significant adverse effects. There is increasing use of the B-cell depleting
monoclonal antibody rituximab, though this agent is not licensed for this indication and does not feature in any current treatment guidelines.

There is a high-unmet medical need for new therapies and therapies targeting the complement system represent a promising approach.

Study objective

The purpose of this study is to ascertain the efficacy, safety, tolerability and pharmacokinetics
of LNP023 over a 24-week treatment period compared with rituximab in subjects with MN.

Study design

This is a randomized, treatment open-label, dose blinded, parallel group, three arm proof-ofconcept,
non-confirmatory study evaluating the efficacy and safety of LNP023 compared with
rituximab in subjects with MN at high risk of disease progression defined on the basis of anti-
PLA2R antibody titre (>= 60 RU/mL) and proteinuria (>= 3.5 g/24h)

Intervention

LNP023 or rituximab

Study burden and risks

Minimum of 14 visites, duration 4 hours per visit, but for two visits patients have to stay 10 hours in hospital, total study time is minimum 65 weeks.
Physical examination: 7 times
ECG: 14 times
Renalbiopt: 1 time (if hospital has a biopt of the patient older than 36 months)
3 Vaccines (Meningokokken, pnuemokokken en haemophilus influenza): 1 time
24 hours urine collection (at home): 4 times
Collecting first morning urine (at home): 11 times
Questionnaires: 6 times
Patient diary: Every day during treatment phase.

Taking bloodsamples:12 times

Contacts

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Scientific
Novartis

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Female or male adult (>=18 years) subjects at screening visit with a diagnosis of idiopathic (primary) MN confirmed by renal biopsy within 36 months prior to screening. A renal biopsy may be taken at any time during the run-in period to confirm the diagnosis of MN and facilitate subject eligibility, if the most recent biopsy was performed greater than 36 months prior to the screening visit.
• Anti-PLA2R antibody titer of >= 60 RU/mL at screening visit (based on the EuroImmun ELISA test)
• Urine protein >= 3.5 g/24h at run-in and baseline visits
• <=50% reduction in both anti-PLA2R level and 24h urine protein between first

measurement at screening or run-in visit and baseline
• Estimated GFR (using the CKD-EPI formula) >= 30 mL/min per 1.73 m2 at screening visit
• Receiving stable dose at the maximum recommended dose according to local guidelines or maximum tolerated dose of ACEi and/or ARB and/or statins and/or diuretics for at least 8 weeks prior to Day 1
• Vaccination against Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae (in accordance with local guidelines) at least 28 days prior to Day 1 and no longer than 5 years prior to Day 1

Exclusion criteria

• Secondary causes of MN, e.g. systemic autoimmune diseases, solid or haematological malignancies, infections or chronic intake of drugs (e.g. gold salts, NSAIDs, penicillamines)
• Diagnostic renal biopsy showing evidence of crescent formation in glomeruli, suggestive of an alternative or additional diagnosis to primary idiopathic MN
• Previous treatment with B-cell depleting or B-cell modifying agents such as, but not limited to rituximab, belimumab, daratumomab or bortezomib
• Previous treatment with immunosuppressive agents such as cyclophosphamide, chlorambucil, mycophenolate mofetil (or equivalent), cyclosporine, tacrolimus or azathioprine within 90 days prior to Day 1. Low dose systemic corticosteroid therapy is permitted, though the subject should have been on stable dose equivalent to <=10 mg prednisolone for at least 90 days prior to Day 1
• Previous treatment with gemfibrozil or strong CYP2C8 inhibitors such as clopidogrel within 7 days prior to Day 1
• Presence or suspicion (based on judgment of the investigator) of active infection within 30 days prior to Day 1, or history of severe recurrent bacterial infections

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-10-2021
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	LNP023
Generic name:	LNP023
Product type:	Medicine
Brand name:	Rituximab
Generic name:	Rituximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-08-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-04-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-04-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-09-2020
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-10-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-04-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-12-2021
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-07-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-07-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-08-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-08-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2019-001734-34-NL
ClinicalTrials.gov	NCT04154787
CCMO	NL70845.091.19