Study of Safety and Efficacy of LNP023 in Patients With Kidney Disease Caused by Inflammation

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Main Information

Primary registry identifying number
LBCTR2020023394

Protocol number
CLNP023X2203

MOH registration number
4352/2020

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
07/02/2020

Primary sponsor
Novartis Pharmaceuticals

Primary sponsor: Country of origin
Novartis Pharmaceuticals

Date of registration in primary registry
04/01/2021

Date of registration in national regulatory agency
07/02/2020

Public title
Study of Safety and Efficacy of LNP023 in Patients With Kidney Disease Caused by Inflammation

Acronym

Scientific title
An Adaptive Seamless Randomized, Double-blind, Placebo-controlled, Dose Ranging Study to Investigate the Efficacy and Safety of LNP023 in Primary IgA Nephropathy Patients

Acronym

Brief summary of the study: English
Efficacy and safety of LNP023 in IgAN patients

Brief summary of the study: Arabic
دراسة تكييفيّة موحّدة عشوائيّة التوزيع مزدوجة التعمية مستندة على المقارنة بدواء وهميّ متفاوتة الجرعات للبحث في فعاليّة وسلامة دواء LNP023 لدى المرضى المصابين باعتلال الكلية الأساسي الناتج عن الغلوبولين المناعي أ

Health conditions/problem studied: Specify
Patients with IgA nephropathy

Interventions: Specify
•Drug: LNP023
LNP023 b.i.d. Dose 1, Dose 2 and Dose 3

•Drug: Placebo
Placebo to LPN023 b.i.d

Key inclusion and exclusion criteria: Inclusion criteria
Inclusion Criteria:
•Female and male patients above 18 years of age with a biopsy-verified IgA nephropathy and where the biopsy was performed within the prior three years.
•Patients must weigh at least 35 kg to participate in the study, and must have a body mass index (BMI) within the range of 15 - 38 kg/m2. BMI =

Body weight (kg) / [Height (m)]2
•Measured Glomerular Filtration Rate (GFR) or estimated GFR (using the CKD-EPI formula) ≥30 mL/min per 1.73 m2
•Urine protein ≥1 g/24hr at screening and ≥0.75 g / 24h after the run- in period
•Vaccination against Neisseria meningitidis types A, C, Y and W-135 is required at least 30 days prior to first dosing with LNP023. Vaccination against N. meningitidis type B, S. pneumoniae and H. influenzae should be conducted if available and acceptable by local regulations, at least 30 days prior to first dosing with LNP023
•All patients must have been on supportive care including a maximally tolerated dose of ACEi or ARB therapy for the individual, antihypertensive therapy or diuretics for at least 90 days before dosing

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

18

Key inclusion and exclusion criteria: Age maximum

99

Key inclusion and exclusion criteria: Exclusion criteria

Exclusion criteria
1.Presence of crescent formation in ≥50% of glomeruli assessed on renal biopsy
2.Patients previously treated with immunosuppressive agents such as cyclophosphamide or mycophenolate mofetil (MMF), or cyclosporine, systemic corticosteroids exposure within 90 days prior to start of LNP023/Placebo dosing
3.Use of other investigational drugs at the time of enrollment, or within 5 half-lives of enrollment, or within 30 days, whichever is longer; or longer if required by local regulations
4.All transplanted patients (any organ, including bone marrow)

5.History of immunodeficiency diseases, or a positive HIV (ELISA and Western blot) test result.

Chronic infection with Hepatitis B (HBV) or Hepatitis C (HCV). A positive HBV surface antigen (HBsAg) test, or if standard local practice, a positive HBV core antigen test, excludes a patient. Patients with a positive HCV antibody test should have HCV RNA levels measured. Subjects with positive (detectable) HCV RNA should be excluded

6.Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of drugs, or which may jeopardize the subject in case of participation in the study. The Investigator should make this determination in consideration of the subject's medical history and/or clinical or laboratory evidence of any of the following:
◦A history of invasive infections caused by encapsulated organisms, e.g. meningococcus or pneumococcus
◦Splenectomy
◦Inflammatory bowel disease, peptic ulcers, severe gastrointestinal disorder including rectal bleeding;
◦Major gastrointestinal tract surgery such as gastrectomy, gastroenterostomy, or bowel resection;
◦Pancreatic injury or pancreatitis;
◦Liver disease or liver injury as indicated by abnormal liver function tests. ALT (SGPT), AST (SGOT), GGT, alkaline phosphatase and serum bilirubin will be tested.
◦Any single parameter of ALT, AST, GGT, alkaline phosphatase or serum bilirubin must not exceed 3 x upper limit of normal (ULN)
◦PT/INR must be within the reference range of normal individuals
◦Evidence of urinary obstruction or difficulty in voiding any urinary tract disorder other than IgNA that is associated with hematuria at screening and before dosing; [If necessary, laboratory testing may be repeated on one occasion (as soon as possible) prior to randomization, to rule out any laboratory error]

7.Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test.

8.A history of clinically significant ECG abnormalities, or any of the following ECG abnormalities at screening or baseline:
◦PR > 200 msec
◦QRS complex > 120 msec
◦QTcF > 450 msec (males)
◦QTcF > 460 msec (females)
◦History of familial long QT syndrome or known family history of Torsades de Pointes
◦Use of agents known to prolong the QT interval unless they can be permanently discontinued for the duration of the study

9.History of severe allergic reactions as per Investigator decision
10.Plasma donation (> 200mL) within 30 days prior to first dosing.
11.Donation or loss of 400 mL or more of blood within eight (8) weeks prior to initial dosing, or longer if required by local regulation

12.Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during dosing and for 1 week after stopping of investigational drug. Highly effective contraception methods include:
◦Total abstinence from heterosexual intercourse (when this is in line with the preferred and usual lifestyle of the subject). Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.
◦Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy), total hysterectomy or tubal ligation at least six weeks before taking investigational drug. In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment.
◦Male sterilization (at least 6 months prior to screening). For female subjects on the study the vasectomized male partner should be the sole partner for that subject.
◦Use of oral (estrogen and progesterone), 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 <1%), for example hormone vaginal ring or transdermal hormone contraception In case of use of oral contraception women should have been stable on the same pill for a minimum of 3 months before taking investigational drug.

If local regulations deviate from the contraception methods listed above and require more extensive measures to prevent pregnancy, local regulations apply and will be described in the ICF.

Women are considered post-menopausal and not of child bearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or have had surgical bilateral oophorectomy (with or without hysterectomy), total hysterectomy or tubal ligation at least six weeks ago. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment is she considered not of child bearing potential.

13.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, regardless of whether there is evidence of local recurrence or metastases
14.History of any porphyria metabolic disorder
15.History of drug or alcohol abuse within the 12 months prior to dosing, or evidence of such abuse as indicated by the laboratory assays conducted during screening and baseline.
16.History of hypersensitivity to any of the study treatments or excipients or to drugs of similar chemical classes

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Safety

Trial scope: Specify scope

N/A

Study design: Allocation

Randomized controlled trial

Study design: Masking

Blinded (masking used)

Study design: Control

Placebo

Study phase

2

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Parallel

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

LNP023

Year of authorization

Month of authorization

Type of IMP

Others

Pharmaceutical class

LNP023 is a first-in-class, oral, low molecular weight (LMW) inhibitor of Factor B (FB)

Therapeutic indication

Patients with:
IgA Nephropathy

Therapeutic benefit

LNP023 has not been previously administered with therapeutic intent to patients with IgAN. Therefore, no statement can be made at this time on the actual clinical benefits of LNP023 in this patient population. However, given the mechanism of action of LNP023 targeting the complement system, there is good rationale to believe that a therapeutic response can be achieved with the compound in patients with IgAN.

Study model
N/A

Study model: Explain model
N/A

Study model: Specify model
N/A

Time perspective
N/A

Time perspective: Explain time perspective
N/A

Time perspective: Specify perspective
N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention
Samples with DNA**

Biospecimen description
Samples are shipped to Q2 central Lab

Target sample size
4

Actual enrollment target size

Date of first enrollment: Type
Anticipated

Date of first enrollment: Date
29/05/2020

Date of study closure: Type
Anticipated

Date of study closure: Date
28/10/2021

Recruitment status
Other

Recruitment status: Specify
Recruitment reached globally - study will not start in Lebanon

Date of completion

IPD sharing statement plan
Yes

IPD sharing statement description
Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data availability is according to the criteria and process described on www.clinicalstudydatarequest.com

Additional data URL
https://www.clinicaltrials.gov/ct2/show/record/NCT03373461?term=LNP023&recrs=a&cond=IgA+Nephropathy&rank=1&view=record

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinical Trials.gov	NCT03373461

Sources of Monetary or Material Support

Name
Novartis Pharmaceuticals

Secondary Sponsors

Name
NA

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Hilal AbuZeinab	Saida	Lebanon	9613811611	hilal@abouzeinab.com	Hammoud Hospital University Medical Center
Scientific	Hind Khairallah	Sin El Fil	Lebanon	00961512002#271	Hind.Khairallah@fattal.com.lb	Khalil Fattal et Fils s.a.l.

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hammoud Hospital UNiversity Medical Center	Hilal Abu Zainab	Nephrologist	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hammoud Hospital University Medical Center	20/12/2019	Ahmad Zaatari	zaatari@hammoudhospital.com	961 (0) 7 723111 ext 1160

Countries of Recruitment

Name
Lebanon
Argentina
Australia
Belgium
China
Denmark
Finland
France
Germany
Hungary
Japan
Netherlands
Norway
Singapore
Spain
Sweden
Taiwan
Thailand
Turkey
United Kingdom
United States of America

Health Conditions or Problems Studied

Condition	Code	Keyword
IgA nephropathy	Kidney (D41.0)	IgA nephropathy

Interventions

Intervention	Description	Keyword
ICF, Lab tests, Physical Assessment, IMP addministration, kidney biopsy if applicable	ICF, Lab tests, Physical Assessment, IMP addministration, kidney biopsy if applicable	ICF, Lab tests, Physical Assessment, IMP addministration, kidney biopsy if applicable

Primary Outcomes

Name	Time Points	Measure
change from baseline of urine protein to creatinine concentration	Baseline and Day 90	Baseline and Day 90
baseline of urine protein to creatinine concentration ratio	90 days	90 days

Key Secondary Outcomes

Name	Time Points	Measure
•The effect of LNP023 on renal function - Estimated Glomerular Filtration Rate eGFR	Baseline, Day 1, 8, 15, 30, 90, 120	Baseline, Day 1, 8, 15, 30, 90, 120
•The effect of LNP023 on renal function - Serum creatinine	Baseline, Day 1, 8, 15, 30, 90, 120	Baseline, Day 1, 8, 15, 30, 90, 120
•The effect of LNP023 on renal function - Hematuria	Baseline, Day 1, 8, 15, 30, 60, 90, 120, 180	Baseline, Day 1, 8, 15, 30, 60, 90, 120, 180
•The effect of LNP023 on renal function - 24h-UP, 24h-UA, UACR (urine albumin to creatinine concentration ratio)	Baseline, Day 1, 30, 60, 90, 120, 180	Baseline, Day 1, 30, 60, 90, 120, 180

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files