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A study to evaluate the effectiveness and safety of obinutuzumab in Chinese participants with Class III or IV lupus nephritis

Submission date
27/10/2023

Recruitment status
No longer recruiting

Registration date
06/11/2023

Overall study status
Ongoing

Last Edited
04/12/2023

Condition category
Digestive System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Lupus is a disease in which the body's defence system (immune system) produces proteins called autoantibodies that attack the body's own tissues and organs, including the kidneys. Lupus nephritis (LN) occurs when these proteins (autoantibodies) attack and affect structures in the kidneys which causes kidney inflammation and may lead to blood in the urine, protein in the urine, high blood pressure, impaired kidney function or even kidney failure. This study is testing a drug called obinutuzumab (also known as Gazyva® or Gazyvaro®) which is an approved drug for certain types of blood cancers but is still an experimental drug for LN. An experimental drug means that Health Authorities have not yet approved obinutuzumab for the treatment of LN. The aim of this study is to compare the effects, good or bad, of obinutuzumab compared to a medication that looks like a drug but has no active ingredient (placebo) on participants with lupus nephritis.

Who can participate?
People with lupus nephritis between the ages of 18-75 years

What does the study involve?
Participants will need to be a part of the study for about 2 years (including the screening period and the safety follow-up visit). Participants may remain in the study for 5 years or longer to continue receiving treatment or if additional follow-up for safety is needed. The study has the following parts:
1. Screening period: Participants will be screened to check if they are eligible to participate in the study. The screening period will take place from 28 days to 1 day before the start of treatment.
2. Treatment period: During this period participants will have to be admitted to the clinic where they will be randomly assigned to three groups to receive obinutuzumab or placebo into the vein (infusion) up to Week 76. The participant and the study doctor will not know which treatment the participant is receiving.
Group 1a will receive obinutuzumab
Group 1b will receive obinutuzumab and one single dose of placebo

Group 2 will receive a placebo
After Week 76, participants will continue receiving treatment with obinutuzumab or placebo if the study doctor determines that the participant has adequately responded to treatment. Participants who do not respond adequately to treatment will receive open-label treatment with obinutuzumab after Week 76. Open-label means that the participant and the study doctor know that the participant is receiving obinutuzumab. During this period participants will also receive also receive corticosteroid (prednisone or a similar drug) as well as mycophenolate mofetil (MMF) by mouth in combination with obinutuzumab as standard treatment for LN.
3. Follow-up visit: Participants' overall health and occurrence of any side effects will be assessed during a follow-up visit that may take place for at least 12 months from the last dose of obinutuzumab or placebo.
During this study, participants will have 12 visits through Week 76, then subsequent visits approximately every 6 months and any additional visits if necessary for safety.

What are the possible benefits and risks of participating?
Participants will not receive any benefit from participating in this study, but the information learned from this study may be useful to treat future patients with LN. Participants may have side effects from the drug or procedures used in this study, and they can be mild to severe, and they can vary from person to person.
Very common side effects of obinutuzumab may include a decrease in red blood cells (anemia) with symptoms such as tiredness, weakness, shortness of breath, or poor ability to exercise, constipation, physical weakness, lack of energy (asthenia), pain in joints (arthralgia), back pain, cough, difficulty falling asleep (insomnia), baldness, pneumonia, decrease in platelet count, cells that help stop bleeding (thrombocytopenia), decrease in neutrophils, a type of blood cell that fights infections (neutropenia), decrease in leukocytes, a type of white blood cell (leukopenia), diarrhea, fever, cold, sinus infection (sinusitis), and/or infection of the nose and throat (nasopharyngitis), urinary tract infection, itching (pruritus).
Common side effects of obinutuzumab may include fever associated with a decrease in neutrophils, (febrile neutropenia), common form of skin cancers (squamous/basal cell skin cancer), trouble urinating (dysuria), sore throat, stuffy or running nose, high level of uric acid in the blood (hyperuricemia), high blood pressure (hypertension), severe infection in the blood (sepsis), low blood potassium (hypokalemia, irregular heart rate (atrial fibrillation), piles (hemorrhoids), indigestion, inflammation of the skin (eczema), and or feeling low or upset (depression).
Side effects of obinutuzumab with unknown frequency may include brain infection (progressive multifocal leukoencephalopathy), greater risk of developing infections due to removal of cells that help the body fight infections (B-cells) by obinutuzumab, worsening of preexisting heart (cardiac) conditions, and/ or abnormal blood clotting (coagulation abnormalities).
Kidney tissue sample (biopsy) may cause pain, redness, swelling, excessive bleeding, bruising, or draining at the needle site.
There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to the study drug. Participants who are pregnant, become pregnant, or are currently breastfeeding, cannot take part in this study.

Where is the study run from?
F. Hoffmann-La Roche Ltd (Switzerland)

When is the study starting and how long is it expected to run for?
May 2021 to August 2029

Who is funding the study?
F. Hoffmann-La Roche Ltd (Switzerland)

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
YA42816

Study information

Scientific Title
A Phase III, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of obinutuzumab in Chinese patients with ISN/RPS 2003 Class III or IV lupus nephritis

Study objectives
The primary purpose of this study is to evaluate the efficacy of obinutuzumab compared with placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 02/11/2021, General Hospital of Eastern Theater Command Ethics Committee (No. 305, East Zhongshan Road, Nanjing, 210002, China; +86 (0)25 8086 3234; wuqiong80863234@163.com), ref: N/A

Study design
Phase III randomized double-blind placebo-controlled multi-centre parallel group study

Primary study design
Interventional

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
ISN/RPS 2003 Class III or IV lupus nephritis (LN)

Interventions
Randomization will be carried out using the interactive web response system (IxRS).

Obinutuzumab Arm 1:
Participants will receive blinded obinutuzumab, 1000 milligrams (mg), intravenously (IV), at baseline (Day 1 of Week 0) and on Day 1 of Weeks 2, 24, 26, 50 and 52. At Week 76 participants who show an adequate response to study treatment, as assessed by the investigator will continue to receive blinded obinutuzumab, 1000 mg, IV from Day 1 of Week 80 and then every 6 months thereafter. Participants will also receive mycophenolate mofetil (MMF) and corticosteroid (oral) as background therapy on multiple days starting from Day 1. The dose of MMF and corticosteroid may be adjusted at the investigator's discretion beginning at Week 80.

Obinutuzumab Arm 2:
Participants will receive blinded obinutuzumab, 1000 mg, IV, at baseline (Day 1 of Week 0) and on Day 1 of Weeks 2, 24, 26, and 52. At Week 76 participants who show an adequate response to study treatment as assessed by the investigator will continue to receive blinded obinutuzumab, 1000 mg, IV from Day 1 of Week 80 and then every 6 months thereafter. Participants will receive a single dose of placebo, IV, on Day 1 of Week 50. Participants will also receive MMF, and corticosteroid (oral) as background therapy on multiple days starting from Day 1. The dose of MMF and corticosteroid may be adjusted at the investigator's discretion beginning at Week 80.

Placebo:
Participants will receive obinutuzumab matched placebo, IV, at baseline (Day 1 of Week 0) and on Day 1 of Weeks 2, 24, 26, 50 and 52. At Week 76 participants who show an adequate response, as assessed by the investigator will continue to receive blinded placebo from Day 1 of Week 80 and every 6 months thereafter. Participants will also receive MMF, and corticosteroid (oral) as background therapy on multiple days starting from Day 1. The dose of MMF and corticosteroid may be adjusted at the investigator's discretion beginning at Week 80.

Open Label Treatment (OLT) Arm:
Participants with inadequate response after treatment with obinutuzumab or placebo at Week 76, will receive open-label treatment with obinutuzumab, 1000 mg, IV from Day 1 of Week 80 (Week 1 of OLT) followed by Day 1 of Weeks 2, 24, 26, 52 of the OLT period and every 6 months thereafter. Participants will also receive MMF and corticosteroid (oral) as background therapy on multiple days starting from Day 1. The dose of MMF and corticosteroid may be adjusted at the investigator's discretion beginning at Week 80 (Day 1 of OLT).

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Obinutuzumab

Primary outcome(s)
Percentage of participants with complete renal response (CRR) calculated programmatically based on central laboratory test results and investigator assessments at Week 76

Key secondary outcome(s))
1. Percentage of participants with proteinuric response calculated programmatically based on samples from 24-hour urine collection at Week 76
2. Percentage of participants with CRR with successful prednisone taper calculated programmatically based on central laboratory test results and investigator assessments at Week 76
3. Percentage of participants with overall renal response (ORR) calculated programmatically based on central laboratory test results and investigator assessments at Week 50
4. Percentage of participants who died or experienced renal-related events calculated programmatically based on central laboratory test results and investigator assessments from baseline up to Week 76
5. Mean change in eGFR estimated using the chronic kidney disease epidemiology collaboration (CKD-EPI) equation from baseline to Week 76
6. Change in anti-double-stranded deoxyribonucleic acid (anti-dsDNA) level determined using blood samples collected from baseline to Week 50
7. Change in complement 3 (C3) levels determined using blood samples collected from baseline up to Week 50
8. Change in systemic lupus erythematosus (SLE) disease assessed using systemic lupus erythematosus disease activity index 2000 (SLEDAI 2K) from baseline up to Week 76
9. Time to onset of CRR determined programmatically based on central laboratory test results and investigator assessments from baseline up to 76 weeks
10. Change in functional assessment of chronic illness therapy-fatigue (FACIT-F) scale used to assess treatment benefit of obinutuzumab in participants with SLE from baseline to Week 76
11. Percentage of participants with CRR according to serum creatinine criteria calculated programmatically based on central laboratory test results and investigators' assessment at Week 76

Completion date
31/08/2029

Eligibility

Key inclusion criteria
1. Participants with the diagnosis of active or active/chronic ISN/RPS 2003 Class III or IV proliferative LN by renal biopsy performed in the 6 months prior to screening or during screening.
2. Participants with the diagnosis of SLE according to the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria, which are met by the presence of Class III or IV LN and current or past positive antinuclear antibody (ANA).
3. Participants who have urinary protein to creatinine ratio (UPCR) ≥1 gram per gram (g/g) on a

24-hour collection at screening.
4. Receipt of at least one dose of pulse IV methylprednisolone (≥250 mg) or equivalent for treatment of the current episode of active LN during the 6 months prior to screening or during screening or on Day 1 prior to the first infusion.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Key exclusion criteria
1. Participants who have severe renal impairment, as defined by estimated glomerular filtration rate (eGFR) <30 milliliter per minute per 1.73-meter square (ml/min/1.73 m^2) (estimated using the CKD-EPI equation) or the need for dialysis or renal transplantation
2. Participants who have glomeruli sclerosis > 50% of on renal biopsy
3. Participants who have rapidly progressive glomerulonephritis
4. Participants with severe, active central nervous system SLE, including retinitis, poorly controlled seizure disorder, acute confusional state, myelitis, stroke, cerebellar ataxia, or dementia
5. Participants who have a history of progressive multifocal leukoencephalopathy (PML)
6. Participants who have human immunodeficiency virus (HIV) infection
7. Participants who have tuberculosis (TB) infection

Date of first enrolment
14/06/2022

Date of final enrolment
31/08/2024

Locations

Countries of recruitment
China

Study participating centre

General Hospital of Eastern Theater Command
China
210018

Study participating centre
West China Hospital - Sichuan University
China
610041

Study participating centre
Zhejiang Provincial People's Hospital
China
310014

Study participating centre
The First Affiliate Hospital of Guangxi Medical University
China
530021

Study participating centre
The First Affiliated Hospital of Zhengzhou University
China
450052

Study participating centre
General Hospital of Ningxia Medical University
China
750001

Study participating centre
Ruijin Hospital Shanghai Jiaotong University School of Medicine
China
200025

Study participating centre

Provincial People's Hospital
China
610072

Study participating centre
First Affiliated Hospital of Medical College of Xi'an Jiaotong University
China
710061

Study participating centre
Zhongshan Hospital Xiamen University
China
361004

Study participating centre
Sun Yat-sen Memorial Hospital
China
510120

Study participating centre
Tongji Hospital Tongji Medical College Huazhong University of Science and Technology
China
430010

Study participating centre
Peking Union Medical College Hospital
China
100730

Study participating centre
Peking University First Hospital
China
100034

Study participating centre

Huashan Hospital Affiliated to Fudan University
China
200040

Study participating centre
Fuyang People's Hospital
China
236004

Study participating centre
Renji Hospital Affiliated to Shanghai Jiaotong University
China
200127

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement.

IPD sharing plan summary
Not expected to be made available