ForPatients
by Roche

Lupus Nephritis

A clinical trial to look at how well obinutuzumab works, how safe it is and how the body processes obinutuzumab in young people with lupus nephritis compared with placebo

A Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Obinutuzumab in Adolescents With Active Class III or IV Lupus Nephritis and the Safety and PK of Obinutuzumab in Pediatric Participants

Trial Status	Trial Runs In	Trial Identifier
Recruiting	12 Countries	NCT05039619 2021-000097-29 2023-505825-15-00 WA42985

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A phase II, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy, safety, and pharmacokinetics of obinutuzumab in adolescent patients with active class III or IV lupus nephritis, including an evaluation of open label safety and PK in a cohort of pediatric patients (aged 5 to <12)

Trial Summary:

This phase II, randomized, double-blind, placebo-controlled study is designed to evaluate the safety, efficacy and pharmacokinetics (PK) of obinutuzumab in adolescent participants (AP) aged 12 to less than 18 with biopsy-confirmed proliferative lupus nephritis (LN). It will also evaluate open label safety and PK of obinutuzumab in pediatric participants (PP), aged 5 to <12 with LN.

Hoffmann-La Roche Sponsor	**Phase 2** Phase

NCT05039619 2021-000097-29 2023-505825-15-00 WA42985
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#5 Years & # 17 Years	No

1. Why is the POSTERITY clinical trial needed?

Systemic lupus erythematosus (SLE) is an autoimmune disease. Antibodies called ‘autoantibodies’ attack the body’s own tissues by mistake. Lupus nephritis (LN) is the most common symptom of SLE. LN affects how the kidneys work. Symptoms of LN flare up when LN is in an ‘active’ state. When LN is active, more autoantibodies are made, but symptoms reduce when LN is not active. Standard treatments include steroids, immunosuppressants (such as mycophenolate mofetil [MMF]) and antibody therapies. These treatments aim to reduce swelling and symptoms of LN, but some people have unacceptable side effects. For some people, their LN treatment may stop working. New treatments for LN are needed.

Obinutuzumab is a drug that lowers the number of antibodies made in people with SLE. Obinutuzumab has been approved by health authorities for treating certain blood cancers and has shown a positive effect in previous LN clinical trials in adults. Obinutuzumab has not yet been approved for treating LN in adults, young people aged 12 to less than 18 years, or children under 12 years old. This clinical trial aims to compare the effects, good or bad, of obinutuzumab against placebo in young people who are receiving MMF and steroids for LN. This clinical trial also aims to assess the effects, good or bad, of obinutuzumab in children that are receiving MMF and steroids for LN.

2. How does the POSTERITY clinical trial work?

This clinical trial is recruiting young people aged 12 to less than 18 years with active class III or IV LN. People who take part in this clinical trial (participants) will continue to receive steroids and MMF for LN and will be given either the clinical trial treatment obinutuzumab OR placebo. Treatment will be for up to 2 and a half years. At a later stage, children aged 5 to less than 12 years may be given obinutuzumab. The clinical trial doctor will see participants regularly while treatment is given and while they remain in the trial after stopping treatment. Some visits may take place in the participant’s home by a nurse if they agree to it. The visits with the clinical trial doctor or nurse will include checks to see how the participant responds to the treatment and any side effects they may have. Participants will also be seen every 6 months after the last dose of treatment for at least 1 year. Total time of participation in the clinical trial could be more than 3 and half years. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the POSTERITY clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see if the drug has worked) are:

- The number of young people who have no symptoms of LN on tests after 18 months of treatment
- The number and seriousness of side effects

The other clinical trial endpoints include:

- The number of participants who have:
    - no or reduced signs of LN on tests after 6 months, 12 months and 18 months of treatment
    - reduced the overall amount of steroids taken after starting the trial, with low or no steroid use from Month 15, and have no signs of LN on tests after 18 months of treatment
    - no improvement or change in their LN after 3 months of treatment
- Change in kidney function, the amount of protein within urine and the amount of specific proteins in the blood compared with the start of the trial
- The amount of time taken from the start of the trial for participants to have no symptoms of LN
- How quickly the body gets rid of obinutuzumab and how it affects the immune system
- The change in participants tiredness (fatigue), LN symptoms and quality of life throughout the trial
- Whether the participants' immune system tries to reject obinutuzumab and the effect this has on how safe obinutuzumab is, how well it works and how it moves around the body

4. Who can take part in this clinical trial?

People can take part in this trial if they are over 5 and under 18 years old and have active LN when they start the trial. People may not be able to take part in this trial if they:

- Have SLE in places other than their kidneys (such as the brain or spine)
- Have/had certain medical conditions such as infections, immune or blood disorders or cancer
- Have severe kidney scarring
- Have received or are taking certain treatments such as certain immunosuppressants
- Require a kidney transplant
- Are pregnant or breastfeeding or are planning to become pregnant during or within 18 months after the clinical trial

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be given:

- **Background treatment for LN**: MMF and steroids as tablets or liquids to be swallowed daily
- **Clinical trial treatment**: obinutuzumab OR placebo (placebo will only be given to young people aged 12 to less than 18) as a drip into the vein (infusion) on Day 1, and Weeks 2, 24, 26 and 52

Children and young people who show an improvement in their LN may continue to receive obinutuzumab OR placebo (young people only) treatment every 6 months for up to another year (2 years total). The part of the trial that young people will join is 'placebo-

controlled'. This means that they will join 1 of 2 groups randomly (like flipping a coin), and one group will be given a substance with no active ingredients (also known as a 'placebo'). A placebo looks like the drug being tested but does not contain any real medicine. The other group will be given obinutuzumab. Comparing results from the different groups helps the researchers know whether any changes seen result from the drug or occur by chance. Young people will have a 2 in 3 chance of being given obinutuzumab.

The part of the trial that young people will join is also 'double-blinded'. This means that neither the participant nor the clinical trial doctor can choose or know the group the participant is in, until the trial is over. This helps to prevent bias and expectations about what will happen. However, the participant's clinical trial doctor can find out which group the participant is in, if their safety is at risk. The later part of the trial that children aged 5 to less than 12 may join is 'open-label'. This means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the child has been given.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. Parents, caregivers and those who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly. Participants will be told about the known side effects of obinutuzumab and MMF, and possible side effects based on human and laboratory studies or knowledge of similar drugs. Participants will be told about any known side effects of infusions into the vein, swallowing tablets and swallowing liquids.

Potential benefits associated with the clinical trial Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Participants who are age 12 to <18 years at the time of randomization

- Participants who are age 5 to <12 years (younger participant cohort) at the time of randomization once recruitment is open. (Investigators will be notified by the Sponsor when recruitment is open to this younger population)
- International Society of Nephrology and the Renal Pathology Society (ISN/RPS) 2003 Class III or IV active LN demonstrated on renal biopsy performed in the 12 months prior to or during screening
- Class V disease may be present in addition to Class III or IV LN, but participants with isolated Class V disease are not eligible
- Diagnosis of SLE according to the Systemic Lupus International Collaborating Clinics (SLICC) 2012 criteria
- Significant proteinuria defined by a UPCR above > 0.5 based on a first-morning void (FMV) collection at screening
- During the 12 months prior to or during screening, all participants must have received at least one dose of pulse-range IV methylprednisolone (typically 30 mg/kg, maximum of 1000 mg per dose) or equivalent for the treatment of the current episode of active LN.

Exclusion Criteria:

- Severe, active central nervous system (CNS) SLE, including retinitis, poorly controlled seizure disorder, acute confusional state, myelitis, stroke, cerebellar ataxia, or dementia
- Sclerosis in >50% of glomeruli on renal biopsy
- Purely chronic Class III(c) or Class IV(c) disease on renal biopsy, defined as the absence of any active lesions
- Presence of rapidly progressive glomerulonephritis
- Pure Class V LN
- Intolerance or contraindication to study therapies
- Active infection of any kind (excluding fungal infection of nail beds) or any major episode of infection requiring hospitalization or treatment with IV anti-infective medications within 4 weeks prior to screening, or completion of oral anti-infectives within 2 weeks prior to randomization
- History of or currently active primary or secondary immunodeficiency, including known history of HIV infection and other severe Immunodeficiency blood disorders
- History of serious recurrent or chronic infection
- History of or current cancer, including solid tumors, hematological malignancies, and carcinoma in situ (except basal cell carcinoma and squamous cell carcinoma of the skin that have been excised and cured) within the past 5 years
- Significant or uncontrolled concomitant medical disease which, in the investigator's opinion, would preclude participant participation
- Currently active alcohol or drug abuse or history of alcohol or drug abuse