ForPatients
by Roche

Childhood Nephrotic SyndromeChildhood Idiopathic Nephrotic Syndrome

A clinical trial to compare obinutuzumab with mycophenolate mofetil (MMF) in children and young adults with a kidney disorder called idiopathic nephrotic syndrome

A Study to Evaluate the Efficacy and Safety of Obinutuzumab Versus MMF in Participants With Childhood Onset Idiopathic Nephrotic Syndrome

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	9 Countries	NCT05627557 2022-000369-42 2023-505140-19-00 WA43380

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 III, International, Multicenter, Randomised Open Label Study to Evaluate the Efficacy and Safety of Obinutuzumab Versus MMF in Patients With Childhood Onset Idiopathic Nephrotic Syndrome

Trial Summary:

This open-label, randomized multicenter study is to assess the efficacy, safety, and pharmacokinetics (PK)/pharmacodynamics (PD) of obinutuzumab compared with mycophenolate mofetil (MMF) in children and young adults (aged >= 2-25 years) with frequently relapsing nephrotic syndrome (FRNS) or steroid-dependent nephrotic syndrome (SDNS).

Hoffmann-La Roche Sponsor	**Phase 3** Phase

NCT05627557 2022-000369-42 2023-505140-19-00 WA43380
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#2 Years & # 25 Years	No

1. Why is the INShore clinical trial needed?

Childhood-onset idiopathic nephrotic syndrome is a kidney disorder that starts in childhood and causes the body to pass too much protein in the urine. The condition causes swelling (also known as edema) especially in the face, legs, and feet, and changes in the person's urine. In most cases the cause is not known; this is called 'idiopathic'.

Current standard of care for childhood-onset idiopathic nephrotic syndrome is a combination of steroids and immunosuppressive drugs (such as a drug called mycophenolate mofetil [MMF]). However, in many people who receive these treatments, the protein in the urine keeps coming back. This is called 'relapsing'. Treatment with steroids is also linked to the risk of certain side effects. Researchers are looking for new treatments which are more effective and have better long-term health outcomes.

2. How does the INShore clinical trial work?

This clinical trial is recruiting children and young people between 2 and 25 years of age with idiopathic nephrotic syndrome that has started during childhood.

The purpose of this clinical trial is to compare the effects, good or bad, of obinutuzumab versus MMF in people with childhood-onset idiopathic nephrotic syndrome. People who take part in this clinical trial will receive either obinutuzumab or MMF.

During a '52 Week Treatment Period' participants will be given the clinical trial treatment (obinutuzumab or MMF) for 52 weeks (around 1 year), and will be seen regularly (at visits between 2 and 8 weeks apart) by the clinical trial doctor, for up to 12 visits. These clinic or home-nursing visits will include checks to see how the participant is responding to the treatment and any side effects they may be having.

After the '52 Week Treatment Period' participants may enter the 'Post Week-52 Extension Period'. They will be seen by the clinical trial doctor every 12 weeks until the last participant who joins the clinical trial reaches their Week 52 visit.

Participants will enter the 'Safety Follow-up Period' at either 1) time of early withdrawal, 2) at the time the last participant reaches their Week 52 visit, or 3) if the sponsor terminates the trial, and will continue to be seen by the clinical trial doctor approximately every 3 months. Participants who have not received obinutuzumab will return for a visit only once during the 'Safety Follow-up Period', 3 months after they have withdrawn or completed the trial. Participants who have received obinutuzumab will be monitored throughout the safety follow-up period until they have fulfilled both of the following criteria:

- Specific immune cells, known as peripheral B cells, have returned to pre-treatment levels (i.e. the same levels as before being given obinutuzumab treatment) or to within the normal range for this population, whichever is lower

- The last dose of obinutuzumab was at least 12 months ago

OR, until the last participant enrolled completes the safety follow-up requirements, up to a maximum of 18 months from the last dose of obinutuzumab, after which time the clinical trial will end.

Participants are free to stop trial treatment and leave the clinical trial at any time.

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

The main clinical trial endpoint (the main results that are measured in the trial to see if the treatment has worked) is: the effectiveness of obinutuzumab compared with MMF, as measured by the number of participants who are in ‘complete remission’ at 1 year. Complete remission is defined as undetectable protein in the urine, with no relapses during the treatment period that require the use of systemic corticosteroids or rescue medications.

The other clinical trial endpoints include the time to the first relapse, changes in how tired (fatigued) the participant is feeling, how well participants feel on a daily basis (general quality of life), evaluation of swelling in different parts of the body, and the number and seriousness of any side effects that occur whilst on treatment.

4. Who can take part in the INShore clinical trial?

People can take part in this trial if they are aged between 2 and 25 years, have been diagnosed with idiopathic nephrotic syndrome before18 years of age, have had at least one ‘relapse’ in the 6 months before the start of the trial, and are in ‘remission’ in the week before they start the trial (three daily tests in a row that show no protein in the urine, and no swelling in the face or body).

People may not be able to take part in this trial if they have a history of steroid resistant nephrotic syndrome, a history of genetic defects known to directly cause nephrotic syndrome, have had treatment with certain other immunosuppressive medications to prevent relapse within a specific time frame before potentially starting the trial, are pregnant or breastfeeding, or are planning to become pregnant.

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

Everyone who joins this clinical trial will be split into two groups randomly (like flipping a coin) and given either:

Group A: Obinutuzumab, given as an infusion into the vein on Days 1, 15, 168 (Week 24) and Day 182 (Week 26) during the '52 Week Treatment Period'

OR, **Group B**: MMF, given as either a tablet or liquid by mouth every day of the '52 Week Treatment Period'

After the '52 Week Treatment Period' participants may continue into the 'Post Week-52 Extension Period':

Participants in Group B will stop MMF treatment at Week 52 or it will be stopped gradually over 12 weeks (by Week 64)

If a participant in either Group A or B relapses before or during the 'Post Week-52 Extension Period' they may be treated with obinutuzumab, MMF, or another medication that their clinical trial doctor recommends

Participants will have an equal (1 in 2) chance of being placed in either group. This is an open-label trial, which means everyone involved, including the participants, parents, caregivers and trial doctors will know which group the participant is in.

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

The safety or effectiveness of the experimental treatment or use is not fully known at the time of the trial. Most trials involve some risks to the participant, although it may not be greater than the risks related to routine medical care or the natural progression of the health condition. Potential participants will be told about any potential 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. These will all be described in an informed consent document (a document that provides people with the information they need to make a decision to volunteer for a clinical trial). A potential participant should also discuss these with members of the research team and with their usual healthcare provider. Anyone interested in taking part in a clinical trial should know as much as possible about the trial and feel comfortable asking the research team any questions about the trial.

Risks associated with the clinical trial drugs

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 and even life-threatening and can vary from person to person.

Obinutuzumab

Potential participants will be told about the known side effects of obinutuzumab and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs. Obinutuzumab will be given by intravenous infusion (this means it is given directly into a vein). Participants will be told about any known side effects of intravenous infusion.

MMF

Potential participants will be told about the known side effects of MMF, and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs. MMF will be given by mouth (known as oral administration) either as a tablet or as a liquid. Participants will be told about any known side effects of oral administration.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial, but the information that is collected may help other people who have a similar medical condition in the future.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatients page or follow this link to ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT05627557

Inclusion Criteria:

- Diagnosis of frequently relapsing nephrotic syndrome (FRNS) or steroid dependent nephrotic syndrome (SDNS) before the age of 18 years
- Must be in complete remission defined by the absence of edema, UPCR <= 0.2 g/g at screening and have three consecutive daily urine dipstick readings of trace or negative for protein within the week prior to randomization
- Must have had at least one relapse in the 6 months prior to screening, after discontinuation of or while receiving oral corticosteroids and/or immunosuppressive therapy to prevent relapses
- Participants having received cyclophosphamide in the 6 months prior to randomization must have experienced at least 1 relapse subsequent to cyclophosphamide discontinuation
- Estimated glomerular filtration rate (eGFR) within normal range for age
- For females of childbearing potential: participants who agree to remain abstinent (refrain from heterosexual intercourse) or use highly effective contraception, during the treatment period and for 18 months after the final dose of obinutuzumab and for 6 weeks after the final dose of MMF

- For males: participants who agree to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods, and agree to refrain from donating sperm during the treatment period and for 90 days after the final dose of MMF

Exclusion Criteria:

- Secondary nephrotic syndrome
- History of steroid resistant nephrotic syndrome
- History of genetic defects known to directly cause nephrotic syndrome
- Treatment with other immunosuppressive medications to prevent relapse, other than MMF or oral corticosteroids within 2 months prior to randomization
- Pregnancy or breastfeeding or intending to become pregnant during the study or within 18 months after the final dose of obinutuzumab, or within 6 weeks after the final dose of MMF
- Females of childbearing potential, including those who have had a tubal ligation, must have a negative serum pregnancy test result within 28 days prior to initiation of study treatment and a negative urine pregnancy test at Day 1, prior to randomization
- History of organ or bone marrow transplant
- Participation in another therapeutic trial within 30 days of enrollment or 5 half-lives of the investigational drug
- Intolerance or contraindication to study therapies
- Participants demonstrating prior treatment failure to MMF as defined by two or more relapses in any 6-month period of time while receiving MMF for at least a 6-month duration
- Participants in the judgment of the investigator likely to require systemic corticosteroids for reasons other than idiopathic nephrotic syndrome during the study
- Active infection of any kind 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 human immunodeficiency virus (HIV) infection and other severe Immunodeficiency blood disorders
- History of progressive multifocal leukoencephalopathy
- History of or current cancer, including solid tumors, hematological malignancies, and carcinoma in situ within the past 5 years
- Major surgery requiring hospitalization during the 4 weeks prior to screening or during screening
- High risk for clinically significant bleeding or any condition requiring plasmapheresis, intravenous immunoglobulin, or acute blood product transfusions
- Evidence of any significant or uncontrolled concomitant disease that, in the investigator's judgment, would preclude participant's participation, including but not limited to nervous system, respiratory, cardiac, hepatic, endocrine, malignant, or gastrointestinal disorders
- Currently active alcohol or drug abuse or history of alcohol or drug abuse