ForPatients
by Roche

Membranous NephropathyPrimary Membranous Nephropathy

A study to compare the effects of obinutuzumab with tacrolimus in people with a kidney disease called primary membranous nephropathy

A Study Evaluating the Efficacy and Safety of Obinutuzumab in Participants With Primary Membranous Nephropathy

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	11 Countries	NCT04629248 2020-003233-38 2023-506525-11-00 WA41937

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 Randomized, Open-Label Active Comparator-Controlled Multicenter Study to Evaluate Efficacy and Safety of Obinutuzumab in Patients With Primary Membranous Nephropathy

Trial Summary:

This study will evaluate the efficacy, safety, pharmacodynamics, and pharmacokinetics (PK) of obinutuzumab compared with tacrolimus in participants with primary membranous nephropathy (pMN).

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

NCT04629248 2020-003233-38 2023-506525-11-00 WA41937
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years & # 75 Years	No

1. Why is this study needed?

Membranous nephropathy (MN) is a kidney disease where the body's immune system mistakenly attacks the small filters in the kidneys (called glomeruli). This damage allows

protein to leak into the urine. In some cases, if the disease gets worse over time, the kidneys may stop working, and a kidney transplant or frequent dialysis (a treatment that cleans the blood when the kidneys can't, using a machine outside the body) could be needed.

MN can be primary (with no clear cause) or secondary (caused by other health problems, such as infections, cancer, or certain medicines). Currently, there are no approved treatments for primary MN (pMN), and there is still a need for effective treatment options.

This study is testing a medicine called obinutuzumab. It is being developed to treat pMN.

Obinutuzumab is an experimental medicine. This means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved obinutuzumab for the treatment of pMN. However, obinutuzumab is an approved medicine for some types of blood cancer.

This study aims to compare the effects of obinutuzumab versus tacrolimus in people with pMN. It will also look at how obinutuzumab gets to different parts of the body and how the body gets rid of it.

2. Who can take part in the study?

People (males / females) of 18 to 75 years of age with pMN can take part in the study if they have high amounts of protein in their urine despite already receiving certain treatments.

People may not be able to take part in this study if they have secondary MN, diabetes, or uncontrolled blood pressure. They also cannot take part if they are on dialysis, have had a kidney transplant, have an active infection or are known not to respond to tacrolimus.

People who are pregnant, planning to get pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

People will be screened to check if they are able to participate in the study. The screening period will take place from 28 days before the start of treatment.

Participants in this study will be randomly put to **one of** 2 groups (like flipping a coin) and given either:

- Obinutuzumab, as a drip into a vein (intravenous infusion) at the first day of the study and 3 more times at weeks 2, 24 and 26 OR

- Tacrolimus, as a capsule to be swallowed, twice a day, every 12 hours for up to 14 months.

Participants will have an equal chance of being placed in either group.

This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

If participants do not respond to treatment, or if they get better initially but then worsen again, participants in the obinutuzumab group will receive additional obinutuzumab as determined by the study doctor whereas participants in the tacrolimus group can newly receive obinutuzumab.

During this study, the study doctor will see participants on a regular basis, initially every 2 weeks and later every 3 months. They will see how well the treatment is working and record any unwanted effects participants may have. Participants in the tacrolimus group will have 1 follow-up visit, while those who receive obinutuzumab will have follow-up visits every 6 months after completing the study treatment. During these visits, the study doctor will check on the participant's well being. Total time of participation in the study will be about 4 -5 years. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main result measured in the study to assess if the medicine has worked is the number of participants with no signs of disease at week 104. Other key results measured in the study include:

- The number of participants whose disease got better (either fully or partly) at week 104
- The number of participants with no signs of disease at week 76
- The time it takes for a participant's kidney function (measured by estimate Glomerular Filtration Rate, calculated by the blood test results) to drop by 30% or more from the start of the study
- The time it takes for the treatment to stop working, for the participant to need a new treatment, or for the disease to come back after getting better
- How participants' energy levels and overall physical health changed at week 104
- The time between when a participant has no signs of disease and when the disease returns.
- Change in the levels of a protein called 'anti-PLA2R' (which is known to cause the kidney problems in most patients with pMN) at week 52

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.

It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study medicines Participants may have unwanted effects of the medicines used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Participants will be told about the known unwanted effects of obinutuzumab and tacrolimus, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects of obinutuzumab include a reaction to the infusion, a low number of white blood cells, not having energy or strength and a weakened immune system. Known unwanted effects of tacrolimus include high blood sugar, loose, watery [and more frequent] stools, difficulty falling asleep, high blood pressure, kidney problems, pain or discomfort in the head, and high levels of potassium in blood.

Obinutuzumab will be given as a drip into a vein (infusion). Known unwanted effects during or shortly after the drip into the vein include throwing up, wanting to throw up, a feeling of coldness that makes the body shiver, low or high blood pressure, fever, pain or discomfort in the head, frequent watery stools, and shortness of breath.

The study medicines may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

Inclusion Criteria:

- Diagnosis of primary membranous nephropathy (pMN) according to renal biopsy prior to or during screening
- Screening urinary protein-to-creatinine ratio (UPCR) >= 5 g/g from 24-hour urine collection after best supportive care for >= 3 months prior to screening or screening UPCR >= 4 g/g after best supportive care for >= 6 months prior to screening
- eGFR >= 40 mL/min/1.73m^2 or qualified endogenous creatinine clearance >= 40 mL/min/1.73m^2 based on 24-hour urine collection during screening
- Other inclusion criteria may apply

Exclusion Criteria:

- Participants with a secondary cause of MN
- Pregnancy or breastfeeding
- Evidence of >= 50% reduction in proteinuria during the previous 6 months prior to randomization
- Severe renal impairment, including the need for dialysis or renal replacement therapy
- Type 1 or 2 diabetes mellitus
- Receipt of an excluded therapy, including any anti-CD20 therapy less than 9 months prior to or during screening; or cyclophosphamide, tacrolimus, or cyclosporin less than 6 months prior to or during screening
- Significant or uncontrolled medical disease which, in the investigator's opinion, would preclude participant participation
- Known active infection of any kind or recent major episode of infection
- Major surgery requiring hospitalization within the 4 weeks prior to screening
- Current active alcohol or drug abuse or history of alcohol or drug abuse within 12 months prior to screening
- Intolerance or contraindication to study therapies
- Other exclusion criteria may apply