ForPatients
by Roche

Primary IgA Nephropathy

A clinical trial to see how well RO7434656 (also called sefaxersen) works compared with placebo in people with primary IgA nephropathy who are at high risk of their kidney disease getting worse

A Study to Evaluate the Efficacy and Safety of Sefaxersen (RO7434656) in Participants With Primary Immunoglobulin A (IgA) Nephropathy at High Risk of Progression

Trial Status	Trial Runs In	Trial Identifier
Recruiting	21 Countries	NCT05797610 2022-502102-32-00 WA43966

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, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Sefaxersen, an Antisense Inhibitor of Complement Factor B, in Patients With Primary IgA Nephropathy at High Risk of Progression

Trial Summary:

The purpose of this study is to evaluate the efficacy, safety, and pharmacokinetics of sefaxersen (RO7434656), a novel Antisense Oligonucleotide (ASO) therapy in participants with primary IgA nephropathy (IgAN) who are at high risk of progressive kidney disease despite optimized supportive care.

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT05797610 2022-502102-32-00 WA43966
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the WA43966 clinical trial needed?

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Primary IgA nephropathy (IgAN) is a disease where the immune system attacks healthy cells in the kidneys by mistake. In healthy individuals, the kidneys have the function of filtering blood to remove waste and control the body's fluid levels. One of the roles of the immune system is to create antibodies to help destroy foreign objects (e.g. bacteria and viruses), protecting your body against infection. However, in primary IgAN, the body produces some incorrect antibodies that end up causing high blood pressure, inflammation and long-term kidney damage. Standard treatment for primary IgAN includes drugs to control blood pressure and may include drugs to lower the activity of the immune system. These can cause unacceptable side effects, and there is no cure for primary IgAN. If not treated, IgAN causes kidney failure - a kidney transplant or dialysis (when blood is cleaned, usually by a machine) is needed to live. A drug called sefaxersen (also known as RO7434656) may reduce the levels of inflammation and protect the kidneys from long-term damage in people with primary IgAN. Sefaxersen is an experimental drug, which means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved it yet for treating IgAN. This clinical trial aims to compare the effects, good or bad, of sefaxersen versus placebo in people with primary IgAN who are at high risk of their kidney disease getting worse.

2. How does the WA43966 clinical trial work?

This clinical trial is looking for people with primary IgAN. People can take part if there is a high risk of worsening kidney disease. People who take part in this clinical trial (participants) will be given the clinical trial treatment sefaxersen OR placebo for about 2 years. The clinical trial doctor will see them approximately every 2–12 weeks (typically every 12 weeks after the first 6 months). These hospital visits will include checks to see how the participant responds to the treatment and any side effects they may have. The total time in the clinical trial will be approximately 2 years, or longer if participants choose to continue treatment after 2 years (see section 5 below). After the last dose of clinical trial treatment, participants will be seen at a follow-up visit. Participants can stop trial treatment and leave the clinical trial at any time. Participants are encouraged to remain in the study for follow-up visits even if they stop the treatment.

3. What are the main results measured in the WA43966 clinical trial?

The main clinical trial endpoint (the main result measured in the trial to see if the drug has worked) is the level of protein found in urine at Week 37 compared with the start of the trial (which indicates the level of kidney damage). The other clinical trial endpoints include:

- How well the kidneys are working after 2 years of treatment
- How much time passes before kidney failure
- How tired participants feel at 2 years compared with the start of the trial
- The number and seriousness of any side effects
- How the body processes RO7434656

4. Who can take part in this clinical trial?

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People can take part in this trial if they are over 18 years old, have high amounts of protein in their urine and have received certain treatments for primary IgAN for at least 3 months before the trial.

People may not be able to take part in this trial if they have:

- Received certain treatments, such as steroids or herbal therapies, within 3 months before the trial
- Certain other medical conditions such as very low kidney function, severe kidney disease, heart disease, diabetes, certain infections, or if they are women who are pregnant or breastfeeding or are planning to become pregnant during the trial or within 3 months after the final dose of RO7434656
- Refused to get vaccinations against certain bacterial infections

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

Everyone will be given sefaxersen OR **placebo** as an injection under the skin on Weeks 1, 3 and 5, then every 4 weeks up to 2 years of treatment. Participants will have an equal chance of being placed in either group. This is a 'placebo-controlled' clinical trial, which means that one of the groups will be given a substance with no active ingredients (also known as a 'placebo'); it looks like the drug being tested but does not contain any real medicine. Comparing results from the different groups helps the researchers know whether any changes seen result from the drug or occur by chance. This is a double-blinded trial, which 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 approach 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. After 2 years of clinical trial treatment, participants may be eligible to switch to open label treatment, where the participant will be given sefaxersen. In this case, the participant and the doctor will know they are being given sefaxersen. Treatment may continue until the last participant to join the trial has finished it. Participants or caregivers may give the injections themselves at home. Participants will be given specific vaccinations for *Neisseria meningitidis, Streptococcus pneumoniae,* and *Haemophilus influenzae* according to local guidelines to protect them from these bacterial infections.

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

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

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study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

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, 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 sefaxersen (such as increased risk of infection) and **placebo**, and possible side effects based on human and laboratory studies or knowledge of similar drugs. Sefaxersen and **placebo** will be given as an injection under the skin (subcutaneous injection). Participants will be told about any known side effects of subcutaneous injection.

Inclusion Criteria:

- Primary IgAN, as evidenced by a kidney biopsy performed within 10 years prior to or during screening, without known secondary cause
- Treatment with maximum tolerated doses of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) for at least 90 days immediately prior to screening, and without an intent to modify the dose during the study, except for interruptions due to illness (not greater than 7 consecutive days), unless the potential participant is intolerant to these medications
- Urine Protein-to-Creatinine Ratio (UPCR) # 1 gram per gram (g/g) or urine protein excretion # 1 gram per day (g/day) (with UPCR # 0.8 g/g), all measured from a 24-hour urine collection during screening
- eGFR # 20 mL/min/1.73 m^2, as calculated by the 2021 CKD-EPI creatinine equation (Inker et al. 2021a)
- Vaccination against Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae according to national vaccination recommendations
- Female participants of childbearing potential must use adequate contraception

Exclusion Criteria:

- Pregnancy or breastfeeding, or intention of becoming pregnant during the study or within 12 weeks after the final dose of sefaxersen
- Histopathologic or other evidence of another autoimmune glomerular disease
- Presence of # 50% crescents on kidney biopsy, sustained doubling of serum creatinine within 3 months prior to screening, or rapidly progressive glomerulonephritis in the opinion of the investigator
- History of kidney transplantation
- Glycated Hemoglobin (HbA1c) # 6.5% or a clinical diagnosis of diabetes mellitus of any type
- Systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg from the average of two measurements performed at least 1 minute apart during screening
- Initiation of sodium-glucose cotransporter-2 (SGLT2) inhibitors within 16 weeks prior to screening or during screening
- Initiation of endothelin receptor antagonists within 90 days prior to screening or during screening
- Initiation of mineralocorticoid receptor antagonists or non-dihydropyridine calcium channel blockers within 90 days prior to screening or during screening
- Use of herbal therapies within 90 days prior to or during screening

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- Treatment with investigational therapy within 28 days prior to screening or 5.5 drug-elimination half-lives of that investigational product prior to screening
- Treatment with an investigational therapy planned during the treatment period
- Previous treatment with sefaxersen
- Treatment with oral or intravenous (IV) corticosteroids with a dose equivalent to # 7.5 milligrams per day (mg/day) of prednisone for 7 days or equivalent to # 5 mg/day of prednisone for 14 days within 90 days prior to screening
- Treatment with corticosteroids with systemic effects during screening
- Treatment with a systemic calcineurin inhibitor within 2 months prior to screening or during screening
- Treatment with anti-CD20 therapy within 9 months of screening or during screening
- Treatment with other systemic immunosuppressive agents within 6 months of randomization including, but not limited to, complement inhibitors, alkylating agents (e.g., cyclophosphamide or chlorambucil), azathioprine, or mycophenolate
- Planned major procedure or major surgery during screening or the study
- Substance abuse within 12 months prior to screening or during screening
- Any serious medical condition or abnormality in clinical laboratory tests that precludes an individual's safe participation in and completion of the study
- History of malignancy within < 5 years prior to screening, with the exception of malignancies with a negligible risk of metastasis or death
- Usage of Glucagon-like Peptide-1 (GLP-1)-based therapy (i.e., GLP-1 mono-agonists, GLP-1/GIP dual agonists, etc.) within 90 days prior to screening or during screening, or intent to initiate during the study period

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