ForPatients
by Roche

LGI1 Autoimmune EncephalitisAutoimmune EncephalitisNMDAR Autoimmune Encephalitis

A clinical trial to compare satralizumab with placebo in people with autoimmune encephalitis

A Study to Evaluate the Efficacy, Safety, Pharmacokinetics (PK), and Pharmacodynamics (PD) of Satralizumab in Participants With Anti-N-methyl-D-aspartic Acid Receptor (NMDAR) or Anti-leucine-rich Glioma-inactivated 1 (LGI1) Encephalitis

Trial Status	Trial Runs In	Trial Identifier
Recruiting	16 Countries	NCT05503264 2021-002395-39 2023-504226-18-00 WN43174

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, Double-blind, Placebo-controlled, Multicenter Basket Study to Evaluate the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Satralizumab in Patients With Anti-N-methyl-D-aspartic Acid Receptor (NMDAR) or Anti-leucine-rich Glioma-inactivated 1 (LGI1) Encephalitis

Trial Summary:

The purpose of this study is to assess the efficacy, safety, PK, and PD of satralizumab in participants with NMDAR and LGI1 encephalitis.

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

NCT05503264 2021-002395-39 2023-504226-18-00 WN43174
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#12 Years	No

1. Why is the Cielo clinical trial needed?

Acute encephalitis is a rare and debilitating disease of the brain caused by inflammation. Autoimmune encephalitis (AIE) includes disorders that are associated with an identifiable

cause, such as autoantibodies. Autoantibodies are antibodies (a type of immune protein) that mistakenly attack healthy tissues and proteins. NMDAR AIE and LGI1 AIE are two of the most common types of AIE and are caused by the production of autoantibodies against NMDAR and LGI1 proteins, respectively.

There are currently no approved therapies for NMDAR AIE or LGI1 AIE, highlighting a significant need for further research into treatment for these specific types of AIE.

The purpose of this clinical trial is to assess the effectiveness and safety of satralizumab in patients with NMDAR AIE or LGI1 AIE.

2. How does the Cielo clinical trial work?

This clinical trial is recruiting people who have a health condition called NMDAR AIE or LGI1 AIE. People can take part if they are at least 12 years old and have been diagnosed with NMDAR AIE, or at least 18 years old and have been diagnosed with LGI1 AIE.

The purpose of this clinical trial is to compare the effects, good or bad, of satralizumab against placebo in people with NMDAR AIE or LGI1 AIE. People who take part in this clinical trial will receive either satralizumab or placebo.

Participants will be given the clinical trial treatment satralizumab OR placebo for 52 weeks. Participants will be seen by the clinical trial doctor every four weeks to be given their clinical trial treatment. These hospital visits will include checks to see how the participant is responding to the treatment and any side effects they may be having. Depending on whether participants choose to take part in an optional extension period of the trial (which will last for at least two years), their total time in the clinical trial may last for up to five years (including follow-up appointments). Participants are free to stop trial treatment and leave the clinical trial at any time.

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

The main clinical trial endpoint (the main result that is measured in the trial to see if the medicine has worked) is the proportion of participants who show an improvement in their degree of disability or dependence when performing daily activities, after 24 weeks of treatment.

The other clinical trial endpoints include the number and severity of adverse events (any unexpected medical problems that occur while receiving the treatment), and the time for participants to achieve seizure freedom (no seizures for at least six weeks).

4. Who can take part in this clinical trial?

People can take part in this trial if they have been diagnosed with NMDAR AIE or LGI1 AIE, with symptoms that started no longer than nine months ago.

People may not be able to take part in this trial if they have a history of cancer or certain other medical conditions, or if they have been treated with particular medications. People who are pregnant or breastfeeding will not be able to take part in this clinical trial.

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

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

Satralizumab as a subcutaneous injection (involves inserting a needle under the skin of the abdomen or leg) at Weeks 0, 2 and 4, and then every four weeks until Week 52

OR placebo as a subcutaneous injection at Weeks 0, 2 and 4, and then every four weeks until Week 52.

Participants will have a 50% chance of being placed in either the satralizumab or placebo 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. Comparing results from the different groups helps the researchers know whether any changes seen are a result of the drug or occurring by chance.

This is also a double-blind 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 based on 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. If participants choose to enter the extension period of the clinical trial, they can choose to either continue with the original double-blinded treatment they were assigned to, receive satralizumab, or stop clinical trial treatment altogether but continue to attend clinical trial assessments.

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, 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 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.

Satralizumab

Potential participants will be told about the known side effects of satralizumab, and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs.

Satralizumab and placebo will be given by subcutaneous injection. Participants will be told about any known side effects of subcutaneous injections.

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/NCT05503264

Inclusion Criteria:

- Reasonable exclusion of tumor or malignancy before baseline visit (randomization)
- Onset of AIE symptoms # 9 months before randomization
- Meet the definition of "New Onset" or "Incomplete Responder" AIE
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use adequate contraception during the treatment period and for at least 3 months after the final dose of satralizumab or placebo
- For participants enrolled in the extended China enrollment phase at China's sites: participants who are current residents of mainland China, Hong Kong, or Taiwan, and of Chinese ancestry

NMDAR AIE Cohort:

- Age # 12 years
- Diagnosis of probable or definite NMDAR encephalitis

LGI1 AIE Cohort

- Age # 18 years
- Diagnosis of LGI1 encephalitis

Exclusion Criteria:

- Any untreated teratoma or thymoma at baseline visit (randomization)
- History of carcinoma or malignancy, unless deemed cured by adequate treatment with no evidence of recurrence for # 5 years before screening
- For participants with NMDAR AIE, history of negative anti-NMDAR antibody in cerebrospinal fluid (CSF) using a cell-based assay within 9 months of symptom onset
- Historically known positivity to an intracellular antigen with high cancer association or glutamate decarboxylase 65 (GAD-65)
- Historically known positivity to any cell surface neuronal antibodies other than NMDAR and LGI1, in the absence of NMDAR and LGI1 antibody positivity
- Confirmed paraneoplastic encephalitis
- Confirmed central or peripheral nervous system demyelinating disease
- Alternative causes of associated symptoms
- History of herpes simplex virus encephalitis in the previous 24 weeks
- Any previous/concurrent treatment with interleukin-6 (IL-6) inhibitory therapy (e.g., tocilizumab), alemtuzumab, total body irradiation, or bone marrow transplantation
- Any previous treatment with anti-cluster of differentiation 19 antibody (CD19 antibody), complement inhibitors, neonatal Fc receptor antagonists, anti-B-lymphocyte stimulator monoclonal antibody
- Any previous treatment with T-cell depleting therapies, cladribine, or mitoxantrone
- Treatment with oral cyclophosphamide within 1 year prior to baseline
- Treatment with any investigational drug (including bortezomib) within 24 weeks prior to screening
- Concurrent use of more than one immunosuppressive therapy (IST) as background therapy
- Contraindication to all of the following rescue treatments: rituximab, intravenous immunoglobulin (IVIG), high-dose corticosteroids, or intravenous (IV) cyclophosphamide
- Any surgical procedure, except laparoscopic surgery or minor surgeries within 4 weeks prior to baseline, excluding surgery for thymoma or teratoma removal
- Planned surgical procedure during the study
- Evidence of progressive multifocal leukoencephalopathy
- Evidence of serious uncontrolled concomitant diseases
- Congenital or acquired immunodeficiency, including human immunodeficiency virus (HIV) infection
- Active or presence of recurrent bacterial, viral, fungal, mycobacterial infection, or other infection

- Infection requiring hospitalization or treatment with IV anti-infective agents within 4 weeks prior to baseline visit
- Positive hepatitis B (HBV) and hepatitis C (HCV) test at screening
- Evidence of latent or active tuberculosis (TB)
- History of drug or alcohol abuse within 1 year prior to baseline
- History of diverticulitis or concurrent severe gastrointestinal (GI) disorders that, in the investigator's opinion, may lead to increased risk of complications such as GI perforation
- Receipt of live or live-attenuated vaccine within 6 weeks prior to baseline visit
- History of blood donation (1 unit or more), plasma donation or platelet donation within 90 days prior to screening
- History of severe allergic reaction to a biologic agent
- History of suicide attempt within 3 years prior to screening except if this is clearly associated with and occurs during the acute phase of LGI-1 or NMDAR encephalitis
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes safe participation in and completion of the study
- Pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after the final dose of study drug