ForPatients
by Roche

Angelman Syndrome

A 12-week study to investigate how the body handles alogabat once it is swallowed, how safe it is, and whether it could be effective in treating the symptoms of AS

A Study to Investigate the Pharmacokinetics (PK) and Safety and to Provide Proof of Mechanism of Alogabat in Children and Adolescents Aged 5-17 Years With Angelman Syndrome (AS) With Deletion Genotype.

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	6 Countries	NCT05630066 2022-501844-14-00 BP41315

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 IIa Multicenter, Open-label, 12-week Study to Investigate the Pharmacokinetics and Safety and to Provide Proof of Mechanism of Alogabat in Children and Adolescents Aged 5-17 Years With Angelman Syndrome (AS) With Deletion Genotype

Trial Summary:

This is a two-part, Phase IIa, multicenter, 12-week, open-label study. Up to 56 participants with deletion AS aged 5-17 years (inclusive) will be enrolled in the study.

Hoffmann-La Roche	Phase 2
Sponsor	Phase

NCT05630066 2022-501844-14-00 BP41315
Trial Identifiers

Eligibility Criteria:

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

1. WHY IS THIS STUDY NEEDED?

Angelman syndrome (AS) is a rare genetic disorder that affects all areas of a child's development, including thinking, language and movement. The disorder commonly also

affects sleep and behaviour and causes frequent seizures. Currently, there is no treatment that would address the core symptoms of AS.

This study is testing a medicine called alogabat. It is being developed to treat AS. Alogabat is an experimental medicine. This means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved alogabat for the treatment of AS.

The main cause of AS is a problem with a gene called UBE3A, but sometimes there can be issues with other genes too, including those coding proteins that are necessary to build the GABAA #5 receptor. This receptor plays a major role in the body e.g., in brain development, learning, sleep, and seizure control, among others. Such forms of AS are known as “deletion AS”.

Alogabat is designed to help the remaining receptors to perform their function and thus could potentially make up for their reduced number. This may improve various symptoms of AS.

The first part of the study aims to test how safe alogabat is in children at different doses, and to understand what happens to alogabat once it is in the body.

The second part of the study aims to test whether alogabat can improve abnormalities in brain activity that are typical for AS.

Both parts of the study aim to assess how safe alogabat is in children with AS.

2. WHO CAN TAKE PART IN THE STUDY?

People of 5-17 years of age with Angelman syndrome with the “deletion” subtype can take part in the study if:

- they have a genetic report confirming that they have deletion AS,
- can undergo blood draws, electrocardiograms and brain wave measurements (EEG), and
- have a stable caregiver (e.g., a parent) who accompanies them during the study.

People may not be able to take part in this study if

- they have any other type of Angelman syndrome other than deletion AS
- they need to take certain drugs that could interfere with alogabat, or if
- they have certain kinds of heart disease or a recent history of cancer.

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

3. HOW DOES THIS STUDY WORK?

Participants will be screened to check if they are able to participate in the study. The screening period will take place from 42 to 15 days before the start of treatment.

Everyone who joins this study will be given alogabat as a tablet every day for 12 weeks.

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.

During this study, the study doctor will see participants every 2-4 weeks. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have two follow-up visits 2 and 6 weeks after completing the study treatment, during which study doctor will check on the participant's well-being. Total time of participation in the study will be about 24 weeks. 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 results measured in the study are:

In Part 1: to assess the level of the drug in the blood at day 1, week 2 and week 12 of treatment.

In Part 2: to assess if the medicine has worked are the change in brain activity patterns from pre-baseline to week 2, week 4, and week 12.

Other key results measured in the study include the number of unwanted effects measured from baseline to week 12.

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 DRUG

Participants may have unwanted effects of the drug 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.

ALOGABAT

Participants will be told about the known unwanted effects of Alogabat, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines.

Alogabat will be given as an oral tablet (given by mouth).

The study medicine(s) 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:

- Clinical diagnosis of AS and a genetic subtype of deletion on chromosome 15q11q13 confirmed by a historical molecular diagnosis
- The participant's general health status, in the context of the disease under study, allows them to participate in a clinical trial in the opinion of the investigator
- The reliability of sexual abstinence for male and/or female enrollment eligibility needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or post-ovulation methods) and withdrawal are not acceptable methods of preventing drug exposure
- Female participants:

A female participant is eligible to participate if she is not pregnant, not breastfeeding, and non-childbearing or remain abstinent and/or Hormonal contraceptive methods must be supplemented

- Male participants: Male contraception is not required in this study because of the minimal seminal dose transmitted through sexual intercourse

Exclusion Criteria:

- A molecular diagnosis of AS with genotypic classification of any type besides the molecular diagnosis as specified in Inclusion Criterion
- Concurrent cardiovascular disease considered not well controlled by drug treatment, including participants with clinically significant hypertension, bradycardia and arrhythmias, myocardial infarction (MI) within 12 months of screening or uncompensated heart failure
- Confirmed clinically significant abnormality on 12-lead electrocardiogram (ECG), including:
- a QT corrected for heart rate using the Fridericia's correction factor (QTcF) of >/= 450 ms (based on the average of 3 consecutive measurements) for participants older than 10 years old
- a QT corrected for heart rate using Bazett's formula (QTcB) of >/= 450 ms (based on the average of 3 consecutive measurements) for participants up to, and including, the age of 10 years old

- Congenital heart diseases not treated and congenital QT corrected for heart rate (QTc) prolongation or family history of Long QT Syndrome
- Medical history of malignancy if not considered cured or if occurred within the last 5 years with the exception of fully excised non-melanoma skin cancers or in-situ carcinoma of the cervix that has been successfully treated
- Concomitant disease, condition, or treatment that would either interfere with the conduct of the study or pose an unacceptable risk to the participant in the opinion of the investigator
- Known active or uncontrolled bacterial, viral, or other infection (excluding fungal infections of nail beds) or any major episode of infection or hospitalization (relating to the completion of the course of antibiotics) within 6 weeks prior to the start of drug administration. Rescreening is allowed once the infection is cured and if the rescreening criteria are met
- Any concomitant condition that might interfere with the clinical evaluation of AS and that is not related to AS
- Known history of human immunodeficiency virus (HIV) or hepatitis B virus (HBV) or hepatitis C virus (HCV)
- Hospitalization for any major medical or surgical procedure involving general anesthesia within 12 weeks of Screening or planned during the study. Rescreening is allowed not earlier than 12 weeks after the surgery and if the rescreening criteria are met.
- Use of prohibited medications within 6 weeks or 5 half-lives (t1/2) prior to start of study medication on Day 1 (whichever is longer)
- Clinically significant loss of blood within 3 months prior to screening defined by participant age and weight per recommendations from Duke University (2012)
- Any prior or current treatment with an investigational study drug within 6 weeks or 5 times the t1/2 of the investigational molecule (whichever is longer) prior to baseline or prior or current use of an investigational medical device within 6 weeks prior to baseline or if the device is still active. Concurrent or planned concurrent participation in any clinical study (including observational and non-interventional studies) without approval of the Investigator.
- Previous participation in a cellular therapy, gene therapy, or gene editing clinical study
- Clinically significant vital sign or ECG abnormalities at Screening
- Confirmed clinically significant abnormality in hematological, chemistry or coagulation laboratory parameters
- Uncorrected hypokalemia or hypomagnesaemia
- Positive test result at screening for hepatitis B surface antigen (HBsAg), HCV (untreated), or HIV-1/2. Participants with HCV who have been successfully treated and who test negative for HCV ribonucleic acid (HCV RNA) may be considered eligible for entry into the study