How is AMT-260 administered?

AMT-260 is delivered directly into a deep part of the brain called the hippocampus. The hippocampus is responsible for the generation of seizures. Administration of AMT-260 is done by a trained neurosurgery team performing a surgical procedure. During the procedure the distribution of AMT-260 in the brain is monitored using magnetic resonance imaging (MRI) to help ensure that the hippocampus is sufficiently covered with AMT-260.

What are the potential risks of AMT-260?

This is the first time that AMT-260 is being administered to humans, so the safety profile is not known. Expected potential risks may include but are not limited to allergic reactions to AMT-260 and complications related to the administration of AMT-260 into the brain, which could include infection, bleeding, headaches and more serious conditions. AMT-260 treatment could lead to a worsening of your disease, for instance a worsening of seizure activity or cause problems with memory, concentration, language, decision making, and/or learning. There are risks associated with the stereotactic injection of AMT-260. The side effects most often seen after stereotactic surgery include bleeding; headache; nausea; pain; worsening of movements; vision loss; sleeplessness; infection; rash; constipation; depression; shakiness; anxiety; loss of sensation; high blood pressure; changes in neurological exam results.

What are we hoping to achieve in the AMT-260 clinical trial?

We hope to learn more about whether a single administration of AMT-260 is safe and well tolerated, and whether it may also lead to a reduction in the frequency of seizures.

For AMT-260 clinical trial information please visit:

https://clinicaltrials.gov/study/NCT06063850

Comments or Questions

Phone Number: 1-866-520-1257

Email: medinfo@uniqure.com

References

1. Boileau C, Deforges S, Peret A, et al. GluK2 Is a Target for Gene Therapy in Drug-Resistant Temporal Lobe Epilepsy. Ann Neurol. 2023 Oct;94(4):745-761. doi: 10.1002/ana.26723. Epub 2023 Jul 6. PMID: 37341588.
2. Asadi-Pooya AA, Stewart GR, Abrams DJ, Sharan A. Prevalence and incidence of drug-resistant mesial temporal lobe epilepsy in the United States. World Neurosurg. 2017;99:662-666.

AMT-260 is an investigational agent currently being studied in the treatment of TLE. Its safety and efficacy have not been established and it has not been approved by the United States Food and Drug Administration, European Medicines Agency, or any other regulatory body. There is no guarantee that investigational agents will receive health authority approval or become commercially available.

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AMT-260

An Investigational Agent Being Studied in Temporal Lobe Epilepsy

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What is TLE?

Temporal Lobe Epilepsy (TLE) is a chronic neurological disorder and is the most common type of focal epilepsy, affecting over 600,000 individuals in the United States.

The disease causes abnormal electrical activity in neurons of a part of the brain called the temporal lobe. This electrical activity leads to frequent seizures. A seizure is a sudden, uncontrolled burst of electrical activity. It can cause changes in behavior, movements, unwanted feelings, and change in levels of consciousness.

About 80% of all TLE cases are mesial, meaning the disease involves the inner part of the temporal lobe. This is why the condition is called mesial TLE, or MTLE. Many patients with MTLE do not respond well to anti-seizure medication, and patients do not reach seizure freedom. These cases are called drug refractory (refractory MTLE). Being refractory to medication limits the treatment options.

What should therapy for MTLE look like?

A therapy to treat refractory MTLE should be able to do the following:

- Provide substantial seizure reduction up to seizure freedom
- Be safe and well tolerated
- Have long lasting beneficial effects
- Improve quality of life
- Enable patients to regain a sense of normalcy, perform daily activities (driving, maintaining a job, etc.) and rely less on their caregivers
- Avoid cognitive impairments typically associated with surgical interventions of the affected brain structures
- Avoid the need for implantable devices, as patients often report feeling uncomfortable, and experiencing pain from electrical pulses generated by these devices (e.g., vagus nerve stimulation or VNS)

Introducing AMT-260

You may have heard about ways that scientists are trying to create gene therapies to treat various diseases. AMT-260 is an experimental (not approved by any health authority) gene therapy candidate that is being investigated to determine its potential to reduce seizure frequency in patients with MTLE. AMT-260 is intended to be a one-time treatment. While AMT-260 has been tested in animal models, this is the first time it is being tested in humans.

What is AMT-260?

AMT-260 is an investigational gene therapy candidate that is composed of a viral capsid (AAV9) that carries a genetic code. This code carries information (called micro-RNA) that is believed to be able to reduce the production of a particular receptor responsible for generating unwanted electric currents in the brain and causing seizures. The study will investigate if, when AMT-260 is delivered into the hippocampus, the micro-RNA can reduce or abort seizure generation in the treated area. The therapeutic goal is to sustainably lower the expression of a particular receptor type, which is believed to cause these seizures.

How is AMT-260 expected to work?

STEP 1: Administration into the brain

AMT-260 will be infused into the brain (hippocampus) via a very thin catheter. The viral capsid delivers genetic coding information directly to the brain.

STEP 2: Delivering the code to neurons

The delivered genetic information is a small DNA fragment. This fragment carries the code to produce two micro RNAs

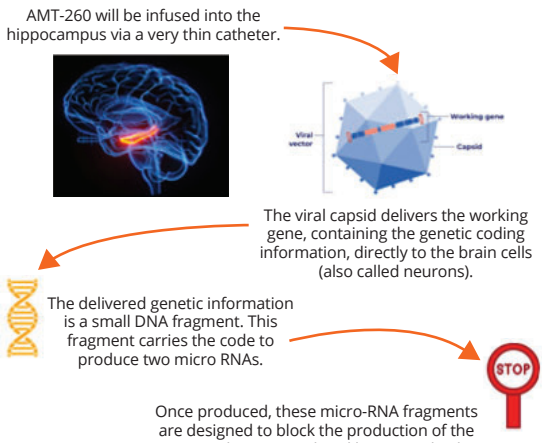
STEP 3: Production of the active compound by neurons

The code for the micro RNAs will be translated into two micro-RNA fragments. These fragments are designed to block the production of the receptor that is considered being involved in the generation of seizures.

STEP 4: Translation into a potential therapeutic effect

AMT-260 is designed to block the production of specific receptors which may result in preventing seizures from spreading across the affected brain areas and thus may potentially reduce the overall frequency of seizures.

AMT-260 is designed to block the production of specific receptors in order to stop seizures from spreading across the affected brain area and reduce seizure frequency or potentially prevent seizures.



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