

Adults with OTC Deficiency Needed to Participate in a Clinical Study of an Experimental Medicine Called 'ARCT-810'

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Arcturus Therapeutics is developing a messenger RNA (mRNA) treatment for ornithine transcarbamylase deficiency (OTCD). The therapy, called ARCT-810, may help the liver produce functional OTC enzyme that is essential to rid the body of ammonia. Arcturus is seeking participants ≥ 18 years of age with stable OTCD to take part in an ongoing clinical safety study of ARCT-810 at academic clinical research sites in the US and Canada.

What is mRNA and how does it work?

Messenger RNA is a set of instructions derived from a gene (DNA) that tells the body's cells how to make a specific protein. Proteins are essential for the body's structures (like muscles and skin) and proper function (like enzymes that control chemical processes in the body). If a gene has a 'mistake' or mutation in it, the mRNA that is derived from that gene also has the mistake and it may stop producing the protein or it may make a faulty protein. The result of a mistake in the OTC gene (and thus the OTC mRNA) is the absence or poor function of OTC, leading to an impaired ability to remove toxic ammonia from the body. The investigational ARCT-810 therapy contains mRNA with instructions to make fully functional OTC in the liver, with the potential to correct the urea cycle defect.

You may have heard about mRNA in the context of COVID-19 vaccines made by Moderna and Pfizer BioNTech, which have been given to hundreds of millions of people worldwide. In the case of mRNA vaccines, the mRNA instructs the cell to make a protein that is found in the virus' coat, so that the body can build an immune response to it and protect against the virus. In the case of a 'therapeutic' mRNA like ARCT-810, the mRNA instructs the cells to make a missing protein, like OTC. It is important to understand that people who receive an mRNA COVID-19 vaccine are still eligible to get ARCT-810 in the study, and people who receive ARCT-810 are still eligible to get an mRNA COVID-19 vaccine.

What is the difference between genes and mRNA?

An analogy may help. Genes are made from DNA, are contained in our chromosomes, and reside in the nucleus or 'command center' of the cell. Genes contain the 'blueprints' for making all of the proteins in our body. Just as an architect has a complete set of blueprints in a central location for constructing a new office building, mRNA is like the working drawings that architects send to the worksite so the construction (framing, plumbing, wiring, etc.) of the building is done according to the blueprints. The building components are like our body's proteins; if the blueprint (gene) has an error, the working drawings (mRNA) will transmit that

error to the workers and the building will have a defect in it. In this analogy, investigational ARCT-810 bypasses the mistake in the 'blueprints' (gene) and supplies accurate 'working drawings' that instruct the cells in the liver to make OTC enzyme correctly.

When mRNA is given as a therapy or a vaccine, it stays at the 'worksite' in the cell and does not enter the nucleus (command center). It also does not become a permanent part of one's genetic makeup. Rather it is broken down by the body fairly quickly and the resulting parts are recycled or eliminated.

For more information about the Phase Ib clinical trial of ARCT-810

Visit the study page on ClinicalTrials.gov:

<https://www.clinicaltrials.gov/ct2/show/NCT04442347?term=Arcturus&draw=2&rank=3>

If you have questions or need help contacting one of the participating academic sites, please contact the National Urea Cycle Disorders Foundation (NUCDF) at (626)578-0833 or via email at info@nucdf.org

If you are eligible to participate and do not live close to one of the study sites, Arcturus Therapeutics will cover the cost of transportation and lodging for you and a companion.