uniQure gets the green light to resume testing HD gene therapy

Following a 3-month pause in enrollment due to concerns about side effects, uniQure shared the good news that their trial of the HD gene therapy AMT-130 will continue as planned, with new safety measures in place.

By Dr Leora Fox | November 03, 2022 | Edited by Dr Rachel Harding

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In August 2022, uniQure announced a pause in new recruitment for their trial of AMT-130, an HD gene therapy delivered via brain surgery. The decision was made after 3 out of 14 participants who had received a high dose of the drug experienced serious side effects after the procedure. The trial's Data Safety Monitoring Board (DSMB), an independent panel of experts who track the safety of the drug during the trial, have been carefully reviewing the safety data since August. They recently determined that new high dose surgeries can continue, with some additional monitoring for participants. Let's talk about this news and what it means for AMT-130 going forward.

What is AMT-130?

AMT-130 is the first gene therapy designed for Huntington's disease. Gene therapies use man-made genetic material to diminish the harm caused by a faulty or a missing gene. AMT-130 is a "one-shot" therapy, meaning that it only need to be administered once, and the effects are permanent.

This hopeful news from uniQure shows that a roadblock in clinical research is not always the end of the road for that drug or therapy

Image credit: TaraPatta

In the case of AMT-130, instructions to block the huntingtin genetic message are packaged inside of a harmless virus. This virus is delivered to different parts of the brain via surgery using ultra-thin needles, so that the drug is spread throughout the brain.

The result is that many brain cells produce less huntingtin protein, with the goal of slowing the progression of Huntington's disease. AMT-130 can successfully lower huntingtin in animals, and there is an ongoing trial in people.

A recap of what we know about the trial

Since the middle of 2020, uniQure has been conducting a safety trial, known as a Phase I/II study, of AMT-130. This is a very small trial, involving 26 people in the USA, and another 15 in Europe.

The U.S. arm of the trial involves a placebo, meaning that 10 of those undergoing the surgery will have a "sham" procedure, where they don't receive AMT-130. Of the 16 who do receive AMT-130, 6 people will receive a low dose, and 10 a high dose. In the European arm of the trial, there is no placebo, and 6 people will receive a low dose, and 9 a high dose of AMT-130.

In June 2022, uniQure shared a positive update about the first year of data from the U.S. trial's low dose group. The low dose of AMT-130 seemed safe with limited side effects, and there were early signs of huntingtin lowering in a few participants for whom data was available.

Then, in August, more difficult news arrived: in the high dose group, 3 people experienced serious neurological problems following surgery. At the recommendation of the Data Safety Monitoring Board, uniQure paused new high dose surgeries. At that time, 24 out of the 26 planned U.S. trial participants had already undergone surgery, and 10 out of 15 in Europe. They announced that a decision about next steps would come later in the fall, to give the DSMB a chance to review the data more thoroughly.

What we learned from the recent update

Since August, the DSMB has been conducting a more thorough review of the data. On November 2nd, uniQure shared a press release as well as a statement directed to HD families. First, they shared that the serious side effects have now gone away in those three high-dose participants. Second, they let the community know that the remaining high-dose surgeries will proceed as planned. The 2 remaining U.S. participants have already been enrolled in the trial, and uniQure hopes to enroll the final 5 European participants by the first half of 2023.

Finally, uniQure shared what the DSMB recommended for the remaining surgeries: after the procedure, participants will be monitored more closely for 2 weeks, including an in-person

visit on day 7 after the procedure. This will help the study doctors decide whether to prescribe drugs to help control any immune reaction in the weeks after the surgery. This is likely what caused the serious side effects, like swelling, confusion, and headaches.

Moving forward and awaiting more news

The overall message for the HD community is that uniQure's study of AMT-130 will proceed as planned. What this means is that uniQure is still on track to announce the latest data from the U.S. study in the second quarter of 2023. With more data, we're likely to gain a better sense of whether AMT-130 could be safely tested in a larger trial for HD, one that would test its effectiveness at slowing HD symptoms.

The way this study pause was implemented and lifted demonstrates the importance of independent data monitoring, which is built into every clinical trial. In this case, the pause allowed the DSMB to investigate further and to recommend changes that would keep participants safer. That's absolutely paramount for all of us who benefit from medical research, especially the brave folks who are the first to receive an unprecedented experimental therapy.

Most of all, this news brings renewed hope, and illustrates that a roadblock in clinical research is not always the end of the road!

Dr. Leora Fox works at the Huntington's Disease Society of America, which has relationships and non-disclosure agreements with pharmaceutical companies, including uniQure. Dr. Rachel Harding has no conflicts to declare. For more information about our disclosure policy see our FAQ...

GLOSSARY

huntingtin protein The protein produced by the HD gene.

clinical trial Very carefully planned experiments designed to answer specific questions about how a drug affects human beings

placebo A placebo is a dummy medicine containing no active ingredients. The placebo effect is a psychological effect that causes people to feel better even if they're taking a pill that doesn't work.