Update on the PTC Therapeutics PIVOT-HD Trial

Last week, PTC Therapeutics released a statement sharing that recruitment of participants into the US arm of the PIVOT-HD trial has been paused. In this article, we will lay out exactly what is known and what this announcement means.


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Recruitment of participants into the US arm of the PTC Therapeutics PIVOT-HD trial has been paused. Since this announcement, there have been a lot of different (and confusing!) headlines about the pause in recruitment. In this article, we will lay out what is going on and what this announcement means.

What is the aim of the PIVOT-HD trial?

The PIVOT-HD trial, run by PTC Therapeutics, aims to test how the drug PTC518 might be beneficial in HD patients, by lowering levels of huntingtin protein. PTC518 can be taken in pill form, and is a type of drug called a splice modulator. This type of drug can change how genetic messages are processed which can affect the levels of the protein molecules they encode.

In the case of PTC518, the drug affects how our bodies process the genetic message made by the Huntington's gene, resulting in lowered huntingtin protein levels. PTC518 does not discriminate between the unexpanded or the expanded forms of the huntingtin genetic message, so both the regular and toxic forms of the huntingtin protein are lowered. You can find more about this drug from a piece we wrote earlier this year about how PTC518 works.

PIVOT-HD is a Phase 2 study which will test two different doses of PTC518, with the option for a third dose depending on the results, in addition to a placebo control. The study will run for a total of 12 months, with a 3-month dose-finding period at the beginning, followed by a 9-month period in which blood, spinal fluid and other measurements will be taken of the participants, to see how they are responding to the drug.

What did the update say?

On the 18th of October, PTC released an announcement which confirmed that enrollment for the trial is active and ongoing. The announcement also confirmed that the study has

approval from both European and Australian agencies to proceed as planned.

However, although enrollment for the trial had already started in the US, this has now paused. PTC reiterated in their statement that this is not due to any bad side effects seen with the drug. The reason for this pause is because the main drug regulation agency in the US, the FDA, has requested that PTC provide additional data in order for the study to continue as planned in the US.

More details on the US recruitment pause

In a November 2nd webinar hosted by the Huntington's Disease Society of America, PTC's Chief Operating Officer Dr. Matthew Klein elaborated on the reasons for the yellow light from the FDA. First he explained that the length of time that a drug can be tested in people usually needs to match what was tested in animals. Typically, if a company wants to test a drug for 9 months or more in humans, they must have tested the drug for at least 9 months in animals, and at doses that will match the human study.

When PTC launched the PIVOT-HD trial, they had 3 months of promising data in animals, allowing them to begin a 3 month study in humans. In the meantime, they knew they would be getting the results of their 9-month study in animals, so they could apply to extend the study up to 1-year in people. When they got the results of those longer animal studies, the safety and dosing data remained encouraging, so they applied to regulatory agencies, like the FDA in the US, and the EMA in Europe, to lengthen the study in humans.

Whereas agencies in several countries (for example, Australia, the UK, Germany, the Netherlands) approved the longer study, the FDA in the US said that they would like to see more data in animals before extending the study in people. Exactly what data has been requested is not public information at this stage. At this time, PTC is working with the FDA to move things forward in the US, while focusing their efforts on enrolling the study at active sites in other countries.

What does this mean for the PIVOT-HD clinical trial?

For the study sites outside of the US, everything will continue as planned for PIVOT-HD. As far as we know, once PTC meets the new criteria set out by the FDA, the study will also continue as planned in the US.

You may have seen that some blogs and pharma news sites have written different ideas about what this means for the future of PTC518 as a treatment for HD. Unfortunately, some of these articles are not based on facts but are instead, very speculative.

It's important to remember that the job of the FDA is to ensure that clinical trials are safe, ethical and scientifically sound. It is not uncommon for additional data to be requested by the FDA prior to trials proceeding, their remit is to work in the best interests of the

participants in the trial.

When will we know more?

The next planned update from PTC Therapeutics about this trial will be in the first half of 2023, when we will hear what they have found in the first 12 week portion of the trial. We also anticipate PTC Therapeutics will probably update the community once recruitment in the US begins again.

Whenever there is an update, HDBuzz will write again to keep the HD community informed.

The authors have 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

therapeutics treatments

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.
