Huntington Study Group (HSG) 2020 Annual Conference: HD in Focus - Day 2

The 2020 virtual HSG conference HD in Focus continues on Day 2 with a focus on clinical trials and drugs in development.

 

By Dr Leora Fox and Dr Rachel Harding | **November 01, 2020**

Edited by Dr Leora Fox

The second day of the HSG conference was another busy day of presentations from HD researchers and clinicians.

The day kicked off with a talk from Vaccinex who gave us an overview of their work on the SIGNAL clinical trial. Unfortunately, pepinemab, the medicine tested in this trial, did not influence HD symptoms and the SIGNAL study did not meet its key clinical goals. The SIGNAL trial scientists suggested that perhaps with different patient groups or treatment regimens, pepinemab might still hold promise for treating HD, but that remains to be seen. HDBuzz recently wrote an in-depth account of [the outcomes of the SIGNAL trial]https://en.hdbuzz.net/292.

Next up was a tag-team talk from Lori Quinn (Columbia University) and Shelley Knewstep-Watkins (University of Virginia) who discussed the use of physical and occupational therapy for Huntington's Disease patients. Whilst many of us know anecdotally that exercise and other forms of activity can help us feel better mentally and physically, the role of physical and occupational therapy in HD has not been well studied until relatively recently. Quinn and Knewstep-Watkins covered the findings of a recent systematic review for physical therapy which supports the use of physical therapy for HD patients from early through late stage disease. They also highlighted PACE-HD, a clinical trial investigating physical activity and exercise outcomes in Huntington's disease from which we hope to have detailed findings soon. Technology is also helping to monitor the physical activity of HD patients with the use of wearable devices expected to promote exercise uptake and telehealth services to manage patient care, when face-to-face meetings are not possible.

Nikolaus McFarland (University of Florida) gave the following talk on mild cognitive impairment (MCI) and dementia in HD patients who have physical or motor symptoms. McFarland and his team examined patient data from the ENROLL-HD study. They found that MCI and dementia are fairly common symptoms in HD patients who have begun to experience motor symptoms, and that MCI symptoms are usually worse in patients with

longer CAG repeats. Understanding what symptoms to expect in patients throughout all stages of the disease is helpful for clinicians so that they may prescribe the best possible care.

In the next talk, four health professionals with expertise in HD, including a social worker, psychologist, and two neurologists, gave an overview of the behavioral changes that are common in HD. These very early changes are important for physicians and family members to know and be able to identify so that they may effectively support their patient or loved one. This type of professional education is especially important for the many doctors who may only see a few HD patients per year.

The afternoon was devoted to a "clinical trial roundup," a series of brief presentations from pharmaceutical companies that are all testing or planning to test HD drugs in human trials.

- Michael Hayden (University of British Columbia) spoke about the PROOF-HD study which is being conducted by a new company called Prilenia. This trial will assess the potential use of pridopidine for treating HD patients. Earlier trials of pridopidine for HD [had disappointing results]https://en.hdbuzz.net/227. But because some patients may have shown improvements in their ability to function at work and at home, Prilenia is planning PROOF-HD, a larger trial of pridopidine. This Phase III PROOF-HD trial will involve more participants (nearly 500) at an earlier stage of disease, who will take the drug for more than a year, in hopes that better outcomes will be achieved.
- Wave Life Sciences has been conducting PRECISION-HD1 and PRECISION-HD2, two trials of ASO drugs that aim to lower harmful huntingtin while keeping the healthy kind intact. So far the drugs have been well tolerated, and after observing some promising reductions in huntingtin levels, Wave added a higher dose group to both trials. They also shared that they are planning a trial of a third, similar drug. Because of the special genetic requirements of these treatments, if successful they could be used in around 80% of people with HD.
- uniQure presented an update on the status of HD-GeneTRX-1, their study of AMT-130. This is a genetic therapy for HD that is delivered once via brain surgery and is designed to lower huntingtin levels in the brain. They are proceeding carefully with this trial because it is the first of its kind. The first two patients underwent the procedure in June 2020, and when no safety concerns arose, the next two patients were treated in October 2020. This is a very small study with around 26 people anticipated to be recruited from the USA.
- Annexon Biosciences is working on drugs to target the proteins that remove connections between neurons. This process, known as "synaptic pruning," is very important during brain development, but in diseases like HD it becomes overactive during adulthood. Their drug ANX005 is designed to slow down pruning during disease in order to preserve more cells in the nervous system. It has been successfully tested for safety in people with a nerve disease called Guillain-Barré syndrome. They are

currently conducting a small safety trial (24 patients) to test whether ANX005 is safe for HD patients, with the hope that it could be used in the future to preserve brain cells.

- Neurocrine Biosciences is running the KINECT-HD trial to test the effectiveness of a drug called valbenazine for chorea, the movement symptoms of HD. This drug is approved for patients with tardive dyskinesia who, like HD patients, experience unwanted movements of the face and limbs. KINECT-HD is a 14-week trial that will recruit about 120 patients aged 18 to 75. Those who complete the trial can join KINECT-HD2, an open-label extension study, in which all participants receive the study drug for an extended period.
- Roche gave a brief update on their ongoing Phase III trial GENERATION-HD1, which is testing a huntingtin-lowering drug called tominersen. The study is fully recruited, with nearly 800 participants at more than 100 sites across 18 countries. This large trial aims to study safety, dosing strategy, and most importantly whether tominersen can slow or stop the progression of HD. The results are expected in 2022. Roche also shared findings from their open-label extension study in which participants took tominersen every month or every other month for more than a year. They found that less frequent dosing was better tolerated and still significantly lowered huntingtin.
- Azevan Pharmaceuticals presented data and future plans for their drug SRX246. They are testing whether it can be used to treat HD patients who experience episodes of extreme irritability and aggression. Azevan conducted a Phase II trial called STAIR, which found that SRX246 was safe for HD patients and lessened the number of aggressive outbursts they experienced. They are now planning for a larger Phase III trial. This is the first drug to focus specifically on a behavioral symptom in HD patients.
- Novartis shared data on their drug branaplam and plans for testing it in HD patients. Branaplam was developed for a childhood genetic disease called spinal muscular atrophy, but was also found to lower huntingtin in children with SMA. Upon discovering this, Novartis began testing branaplam for huntingtin-lowering in HD mice and HD patient cells, and when this was successful, they began a small safety trial in healthy adults. So far, it has been safe and well tolerated, and Novartis plans to begin a Phase IIb trial in 2021, in HD patients aged 25-75 who have begun to experience early movement symptoms. Branaplam is delivered by mouth, and the potential for an oral huntingtin-lowering drug is exciting. HDBuzz discussed Novartis and branaplam in [a recent article about orphan drug designation.]https://en.hdbuzz.net/294

Next, Colorado based neurologist Dr. Lauren Seeberger spoke about a research initiative called HD-NET, which is a 2020 survey of the HD healthcare provider community in the United States. A team of doctors, researchers, and patient advocates designed the study to identify the ongoing difficulties in HD care and research. Through phone interviews with HD

experts and non-experts alike they are identifying new ways to overcome challenges for the HD community, like limited funding, inadequate physician education, and lack of long-term care solutions.

In a moving final presentation of the day, Dr. Ignacio Muñoz-Sanjuan, a neuroscientist working at CHDI Foundation, talked about his work as the President of FACTOR-H. This is an organization that is working to diminish the suffering of poverty-stricken communities in South America where many people are affected by HD. He shared poignant videos of families and individuals in Venezuela and Colombia, and talked about the social implications of HD in the context of extreme poverty. He emphasized that helping HD families involves a lot more than developing treatments. FACTOR-H works with local communities to provide basic necessities and medicines, and to build new generations of empowered and self-sufficient youth at risk for HD.

Thanks for following along with this year's scientific updates from HSG 2020: HD in Focus!

Dr. Rachel J. Harding declares no conflicts of interest. Dr. Leora Fox works for the Huntington's Disease Society of America. HDSA communicates with the companies mentioned in this article and has nondisclosure agreements with uniQure and Roche. For more information about our disclosure policy see our FAQ...

GLOSSARY

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

phase III The phase in the development of a new treatment where clinical trials are conducted using many patients, to determine whether the treatment is effective

neuron Brain cells that store and transmit information

chorea Involuntary, irregular 'fidgety' movements that are common in HD

ASOs A type of gene silencing treatment in which specially designed DNA molecules are used to switch off a gene