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'Tired of waiting,' Huntington's disease families engrossed in efforts to conduct clinical trials

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At Risk for Huntington's Disease

HD is a genetically caused brain disorder that causes uncontrollable bodily movements and robs people's ability to walk, talk, eat, and think. The final result is a slow, ugly death. Children of parents with HD have a 50-50 chance of inheriting the disease. There is no cure or treatment.

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WEDNESDAY, OCTOBER 30, 2013

'Tired of waiting,' Huntington's disease families engrossed in efforts to conduct clinical trials

The atmosphere in the packed San Diego Huntington's disease support group meeting room on the evening of October 28 was both somber and electric with anticipation.

Flanked by loved ones, HD-affected individuals struggled with involuntary movements and a hampered ability to communicate, providing stark evidence of the disease's unrelenting attack on minds and bodies.

For asymptomatic HD gene carriers like me, they represented our future if scientists don't soon find a way to stop the inevitable, devastating symptoms. I always leave these monthly meetings deeply unsettled and unable to sleep soundly.

At the front of the room, a key player in the effort to develop effective treatments, Jody Corey-Bloom, M.D., Ph.D., explained how the local firm Isis Pharmaceuticals, Inc., had successfully run the first ever safety test of its unique type of drug in patients suffering from a neurological disorder, in this case, amytrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease or motor neuron disease. The results were published in the May 2013 issue of the journal *Lancet Neurology*. Isis is developing an HD-gene-silencing drug in partnership with the pharmaceutical giant Roche.

"I realize you guys are just tired of waiting (for treatments)," Dr. Corey-Bloom told the audience of some 50 people. "But I think Isis is really in a good position right now (to get their HD drug into a clinical trial)…. They've got lots of money, with Roche's kind of support. I think that they're feeling comfortable about the fact that they were able to do this."

None of the ALS trial participants experienced adverse effects from the Isis drug, Dr. Corey-Bloom said.

Although Dr. Corey-Bloom pointed out that the very small dose of the Isis drug, an artificial form of DNA known as an antisense oligonucleotide (ASO), did not affect the ALS symptoms, the evidence from the trial of safety and patients' tolerance for the drug helped paved the way for additional tests to examine efficacy.

It also set the stage for the planned Isis-Roche HD clinical trial, tentatively scheduled to start sometime in the next 18 months. The project has the support of the CHDI Foundation, Inc., the non-profit virtual biotech firm dedicated to finding treatments for HD. (Click here to read more.)

Surveying the field

The San Diego support group had convened to hear Dr. Corey-Bloom's annual HD research update, usually the best attended meeting of the year.

HD Links

Huntington's Disease Society of America
International Huntington Association
Huntington's Disease Drug Works
Huntington's Disease Lighthouse
Hereditary Disease Foundation
Huntington's Disease Advocacy Center
Thomas Cellini Huntington's Foundation
HDSA Orange County (CA) Affiliate
HD Free with PGD!
Stanford HOPES
Earth Source CoQ10, Inc.

HD Blogs and Individuals

Chris Furbee: Huntingtons Dance
Angela F.: Surviving Huntington's?
Heather's Huntington's Disease Page

The diminutive but tireless neurologist dedicated the first half of her 85-minute presentation to HD research conducted locally, including projects at the unit she directs, the Huntington's Disease Society of America Center of Excellence for Family Services and Research at the University of California, San Diego. These studies have mainly focused on ways to measure the onset and progression of the disease – essential for gauging the efficacy of drugs tested in clinical trials. (Click here for an example.)

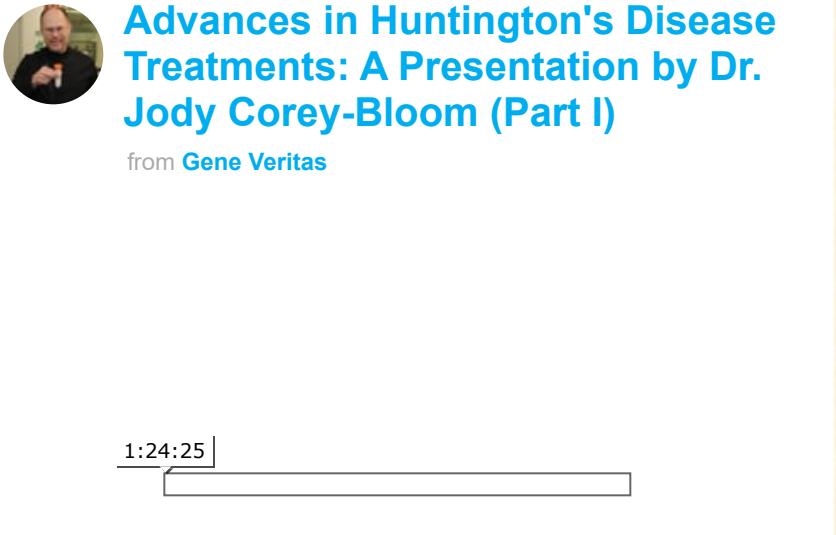
In addition, Dr. Corey-Bloom surveyed some of the clinical trials set to begin soon, including a phase II trial for a phosphodiesterase inhibitor (a kind of "Viagra for the brain") planned by Omeros Corporation.

Dr. Corey-Bloom also announced that she's seeking funding from the National Institutes of Health (NIH) to conduct a clinical trial in HD patients of an already widely used non-HD drug shown to increase BDNF (brain derived neurotrophic factor), a kind of "fertilizer" for the brain. HD patients have insufficient BDNF, which could cause cell death in the deep structures of the brain where the disease is thought to begin, she explained.

"I stumbled across it mainly because I was just reading some other things," said Dr. Corey-Bloom, who declined to identify the drug until funding is in place and the drug's manufacturer agrees to participate in the research. "I said, 'Ooh! Wow!' It's such a great story. It's been keeping me up at night thinking about it. We *will* get it going. First with animals, then with people."

Her project collaborator is Beth Thomas, Ph.D., of the Scripps Research Institute in San Diego.

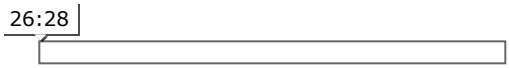
You can watch Dr. Corey-Bloom's presentation and the Q & A in the videos below.



Advances in Huntington's Disease Treatments: A Presentation by Dr. Jody Corey-Bloom (Part I) from Gene Veritas on Vimeo.

Advances in Huntington's Disease Treatments: A Presentation by Dr. Jody Corey-Bloom (Part II)

from **Gene Veritas**



Advances in Huntington's Disease Treatments: A Presentation by Dr. Jody Corey-Bloom (Part II) from Gene Veritas on Vimeo.

Comfort and risk versus efficacy

As potentially one of the best treatments for HD because of its genetic approach, the Isis ASOs for HD commanded the most attention from both Dr. Corey-Bloom and the audience.

As Isis and Roche move ever closer to the long-awaited trial – Isis had first hoped to start a Phase I several years ago – crucial questions of drug delivery and dosage have gained increasing attention.

Dr. Corey-Bloom's observations highlighted a delicate issue: the tensions between patient comfort/risk and drug efficacy.

She identified a key question: will enough of the ASO travel through the cerebral spinal fluid (CSF) from the patient's back, where Isis plans to introduce the drug via a spinal tap, all the way to the brain?

A certain amount of the CSF naturally travels up the spinal column and over the brain, Dr. Corey-Bloom explained, but some of the ASO medication could be lost along the way.

"I think one of the big issues is how to inject," she said. "I actually said the last time I was at Isis that they just need to put in an Ommaya reservoir and just inject it that way.... We do lots of chemotherapy for people that have brain cancer or brain infections. We put this little plastic disk into this space at the bottom of the brain [she indicated behind her ear], and then if people need to have anti-fungal medication ... or cancer chemotherapies, we inject right into that little bubble, and it goes right into the cerebral spinal fluid."

Dr. Corey-Bloom said that Isis scientists wanted to avoid the extra risk and cost of the Ommaya insertion, which, although done in just about 15 minutes and with minimal sedation, requires an operating room.

"It's so much easier to be doing it through a spinal tap in the back than to be doing 'brain surgery,' which is what they kept calling it," she continued, referring to the fact that the spinal tap doesn't require an operation.

However, she affirmed that opting for the "more involved" Ommaya reservoir could bring better trial results.

"At least we'll know that the medicine is getting in right up there, as opposed to way down here," she said, pointing to her back. "If it doesn't

work, or if it doesn't work as well as it should, we'll be kind of wondering if maybe should have put it in a lot closer to where we need it to go."

Proactive families

The support group/physician connection underscores the critical role of proactive patient and family participation in research and clinical trials.

The audience always follows up with questions that focus on the heart of the matter: when and how clinical trials and treatments will bring the promise of ameliorating HD.

Referring to Dr. Corey-Bloom's discussion of the critical use of MRI scans in HD research, one group member asked whether a similar magnetic force or some electronic structure could be used to "drive" the Isis ASO drug up to the brain.

That's "really kind of clever," she responded, noting that she would present the idea to Isis when she meets with company researchers on November 20 to discuss the clinical trial program, including the option of the Ommaya reservoir. Her job, she said, is to bring home the clinical reality of HD to scientists who spend most of their time in the lab.

Future benefits

Dr. Corey-Bloom also will urge Isis to go beyond the standard safety and tolerability measures of a Phase I trial to consider measuring efficacy, too, she added. "They're going to want to do a Phase I trial that is only safety and tolerability.... I think that misses your opportunity to do exploratory efficacy measures."

The Food and Drug Administration permits this type of exploratory work in Phase I, she noted.

Isis and Roche could not draw official conclusions from such exploratory data, she said, but it could give the scientists "some idea of what to use" in the potential Phases II and III of the trial and beyond.

Looking to the future could help broaden the application of the drug to people in different stages of HD – including presymptomatic gene carriers like me for whom an effective treatment would prevent onset and ultimately make HD a thing of the past.

Posted by Gene Veritas at 9:50 PM

Labels: ALS , antisense oligonucleotide , BDNF , CHDI , clinical trials , CSF , gene carrier , Huntington's disease , Isis , Jody Corey-Bloom , neurologist , Ommaya reservoir , risk , Roche , support group , symptoms , treatments

1 comment:

Anonymous said...

Why did the author leave out references to other promising clinical drug candidates for treatment of HD? The FDA, for example, just granted "Orphan Drug" status to OMS-824, a PDE-10 inhibitor that will soon undergo Phase II trials in patients (by YE 2013). Here is the story: http://investor.omeros.com/phoenix.zhtml?c=219263&p=irol-newsArticle_Print&ID=1859632&highlight=

12:32 PM, November 04, 2013

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