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With more Huntington's disease clinical trials, volunteers need help with comparison shopping

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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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TUESDAY, NOVEMBER 24, 2015

With more Huntington's disease clinical trials, volunteers need help with comparison shopping

After learning last month that some researchers believe the drug under study in the SIGNAL clinical trial might slow the progression of Huntington's disease, I was excited about the possibility of participating.

SIGNAL is open to asymptomatic carriers of the HD gene like me. I tested positive in 1999, and my mother succumbed to the disease in 2006.

This is a huge decision, so I have been weighing the risks and benefits with my wife and members of the HD community.

After posting an article about SIGNAL on November 1, I started to waver about whether I should take part in the trial of VX15/2503, a monoclonal antibody made by the small Rochester, NY-based biotech company Vaccinex.

I wondered: how safe is the drug? Why hadn't I heard about SIGNAL before? With the trial based on just one recent paper about a test of the drug in transgenic HD mice, and with other trials typically based on more tests, I wanted to know more about the science behind it.

I contacted a number of people in the HD research community. Privately I received assurances about the safety of VX15/2503 and its potential for alleviating HD – but also recommendations against participation. One obvious major concern is that the compound is non-HD-specific, in contrast with the one currently under study in the historic Isis Pharmaceuticals, Inc., gene-silencing trial.

In a future article, I hope to interview Vaccinex scientists about why they think their compound can help HD patients and presymptomatic individuals like me.

Learning the background of clinical trials and deciding on participation can be challenging. In addition to consulting with physicians and clinical trial administrators, HD people and their families could benefit from better information about clinical trials. In this article I explore these issues and one (albeit partial) solution: the idea of a patient/caregiver advisory council to provide information and advice about HD trials.

No ranking system

Each year, more HD trials take place, each with unique drug mechanisms and participant selection criteria. Each volunteer must ask: which is best for me?

It's possible that a good drug could be left out of the race because of the increase in the number of trials: the patient pool might be too small to furnish enough volunteers for every trial.

Huntington's Disease Society of America
International Huntington Association
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Huntington's Disease Lighthouse
Hereditary Disease Foundation
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HD Blogs and Individuals

Chris Furbee: Huntingtons Dance
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The Huntington's Disease Society of America (HDSA), the leading patient organization in the U.S., recently launched an online search tool, HDTrialfinder. It's a "clinical trial matching service" that provides information similar to that found on at Clinicaltrials.gov, but in a somewhat clearer format. It has HD-specific search tools and provides the opportunity to receive updates via email. It lists current HD trials.

However, it does not rank or recommend trials.

"HDSA does not endorse any interventional HD drug studies, but we do encourage individuals to talk with their physicians about the opportunities to participate in all types of clinical research that can help lead to treatments for HD," said George Yohrling, Ph.D., HDSA's Director of Medical & Scientific Affairs. "Additionally, we strongly recommend that patients do their own due diligence to better understand exactly what their involvement in a study would mean to them and their families."

HDBuzz.net, podcasts such as Help4HD's "The HD View," and other online sources also provide easy-to-understand information about HD research and HD clinical trials, but don't offer recommendations or rankings.

Cautions about new experimental drugs

To get a broader understanding of clinical trial planning and HD families' part in the process, I conducted a 90-minute phone interview with LaVonne Goodman, M.D., on November 16. The founder of Huntington's Disease Drug Works and physician to many HD patients, Dr. Goodman has provided the HD community with a constructively critical view of the process and its many related issues.

Dr. Goodman began with some general observations about clinical trials and volunteering for them.

"In general, I have problems with giving an experimental drug with unknown risks to individuals who have minor or no symptoms of HD," she said. "Though it may sound maternalistic, it is my bias that, if you have a clinical trial for this group of people who aren't very sick at all clinically, then a new experimental drug should not be tried in them first. The risks are unknown, and that's different than giving the drug to a symptomatic individual who is already sick, because they have more at stake and are willing to take a greater risk."

LaVonne Goodman, M.D. (photo by Gene Veritas)

Two key questions about trials

"We trust our beloved doctors," Dr. Goodman continued. "When they do a clinical trial, we may assume incorrectly that they know all the background. But they aren't given all the (scientific) background."

Dr. Goodman referred to an article she posted in March about the drug laquinimod, currently under study in a clinical trial sponsored by the Israel-based pharmaceutical firm Teva. (Laquinimod has already undergone testing for multiple sclerosis and shown various benefits for the brain, making it a good compound, with fairly well known risks, for an HD trial.)

In the article, she noted that prominent cancer researcher and author Siddhartha Mukherjee, M.D., Ph.D., has suggested that patients ask two "vital" questions about clinical trials: "Why is the trial being done?[...] What were the data that led to the clinical trial in the first place?"

"This is particularly important as our clinical trials become more complicated, and several are recruiting concurrently," Dr. Goodman wrote. "This information should be provided to the community in a format that is easily assessable and in language that potential participants can understand for every new trial."

She warned: "Can sponsors or investigators expect participants to sign up when the rationale for testing the drug isn't more available?"

A clinical trial rating scale

Dr. Goodman proposed that a rating scale – done with feedback from HD families – could help patients select trials and assure that the most important trials secure enough volunteers.

"I think there are some broad recommendations that could be done with a rating scale," she said, adding that it could be created with an

"independent" group made of patient advocates and representatives from the Huntington Study Group (administrator of SIGNAL and other HD trials), HDSA, and other organizations.

"Patients' families are not part of the discussion when it comes to HD clinical trials," Dr. Goodman said. "There are groups like cystic fibrosis and breast cancer where there is precedent for this. I think it would be helpful to our particularly vulnerable community."

Dr. Goodman believes the establishment of such a council may be a "moral obligation" to HD families.

Indeed, behind the scenes, some HD researchers, advocates, and others in the community have begun discussing the formation of a patient/caregiver advisory council to furnish input to HSG and other groups involved in clinical trials regarding clinical trial design and selection. Such an initiative could include a rating scale.

However, a rating scale must be built in a positive and efficient way that would "not push drug company sponsors away," Dr. Goodman added.

Dr. Goodman pointed out that drug companies may trial a new drug in HD that was originally developed for another disease. This is true for drugs in the LEGATO (laquinimod), Amaryllis, and SIGNAL trials. It remains to be seen whether this is a good approach for HD, she said.

Furthermore, HDSA Centers of Excellence and other HD clinics need greater funding to increase access to care and therefore the number of people potentially interested in clinical trials, she said. At best, just a quarter of individuals with HD are seen by research center neurologists. High costs prevent more HD people from seeing these neurologists, a situation unlikely if the U.S. had a national healthcare system, she noted.

The FDA and momentum for a council

Momentum for patient/caregiver advisory councils for HD and other diseases is building in the wake of the recent and historic set of "patient-focused drug development" hearings held by the U.S. Food and Drug Administration (FDA), including the September 22 meeting on Huntington's (click here to read more).

In the words of one informed observer, the FDA is "not just doing this for show." The agency will likely start requiring drug companies to include patients' perspective in clinical trial design.

Despite its duty to safeguard the public, the FDA itself also does not rate or recommend drugs, although it does carefully examine the outcome of a clinical trial before approving a drug for the market.

Likewise, the FDA is concerned primarily about toxicity when allowing a company to go forward with a Phase I or II clinical trial (when safety is the primary concern). For instance, the agency does not look at whether a drug for HD actually gets into the brain, Dr. Goodman said.

"Their primary objective is to not let something that appears too unsafe get into a clinical trial," she observed. "They don't discourage drug companies from testing drugs. On the contrary, they want drugs to be tested."

Comparing trials

We can imagine the idea of an HD clinical trial rating scale overseen by a patient/caregiver advisory council as giving us the same power people have when doing comparison shopping at sites such as Consumer Reports or CNET.com.

We need information that is succinct but relevant, scientifically rigorous but understandable.

We also need the capability to compare the different trials. For those council members who ask, the trial sponsors could furnish full scientific data.

In effect, the HD community has often acted as its own clinical trial guide.

The decision to participate in a clinical trial is ultimately a personal one best made in consultation with a physician.

Having the additional assistance of a rating scale can facilitate the process and potentially speed the search for effective treatments.

Posted by Gene Veritas at 3:49 PM

Labels: clinical trial rating scale , clinical trials , HDSA , HDTrialfinder , Huntington's disease , LaVonne Goodman , patient/caregiver advisory council , presymptomatic , SIGNAL , symptoms , treatments , Vaccinex , VX15/2503

4 comments:

Jimmy Pollard said...

Ken,

Yours is an important voice!

Jimmy

5:41 PM, November 24, 2015

Unknown said...

I would welcome the opportunity to be on a caregiver advisory board. Lou Alworth

2:31 AM, November 25, 2015

Anonymous said...

Ken, my sister, who is pre-manifest, was turned down for Signal because she doesn't have chorea. This was surprising to her and our family. What do you know about requirements for this clinical trial?

7:05 AM, December 05, 2015

Anonymous said...

Thanks for the informative article and your hard work keeping us abreast of all things HD.

11:57 PM, December 07, 2015

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