

Ethyl-EPA still in the pipeline

HDSA covered the ethyl-EPA trial results when they were announced last year, but now the medical journal article has been published in the Archives of Neurology and we can provide more in-depth coverage.

The Huntington Study Group conducted a double blind placebo controlled Phase III clinical trial of Amarin's Miraxion, a purified version of eicosapentaenoic acid, an Omega-3 fatty acid. The trial involved 316 patients and ran for six months. Those in the treatment group received one gram of ethyl-EPA twice a day while the control group received a placebo. The outcome measure was the score the fourth component of the Total Motor Score in the United Huntington's Disease Rating Scale.

This was a trial to determine whether Miraxion improved this set of motor symptoms rather than to determine whether Miraxion modifies the disease itself. With Phase III trials for HD currently requiring more than two years before significant differences can be detected in the slow progression of this disease, it makes sense for pharmaceutical companies to conduct shorter, symptomatic studies first.

At the end of the six months trial, no significant differences were found between the treatment group and the placebo group on the motor measures. The researchers also looked for possible differences in overall functioning or cognition and found none. The data was also analyzed to see if there were differences between those with CAG counts of 45 or more and those with counts below 45. This was done because an earlier twelve months study showed those with lower counts benefiting from ethyl-EPA. No differences were found in this study.

However, this was not the end of the story. The trial was followed by a six months open label study in which trial participants were offered Miraxion. 192 participants opted to continue. Their original assignments to either the treatment or the placebo approach were not disclosed to the participants nor to the investigators. At the end of the second six months, another assessment was done. At this point, significant differences were found between the original treatment group and the original placebo group in total chorea score, total motor score, and the original endpoint – total motor score 4. No other differences were found.

One should keep in mind that at this point all of the open label study participants were taking ethyl-EPA; the difference is that the original treatment group had been taking it for 12 months while the original placebo group had been taking it for six months. This suggests that ethyl-EPA's possible positive effect does not become significant until after six months of continuous use.

At this point, ethyl-EPA remains in the research pipeline as a potential treatment for movement symptoms. A conclusive determination would require an additional Phase III trial conducted for a longer period of time.

In a companion article, the HSG investigators detailed their efforts to communicate the trial results to participants in a timely fashion. Their efforts involved press releases, calls from site investigators to participants, and an interactive conference call with the sponsors, investigators and participants. More than four-fifths of the participants report satisfaction with the communication.

Currently, participants in clinical trials are not routinely informed of the results. Neither the federal government nor institutional review boards require investigators to do so.

“It is critical that we treat participants as partners in research,” said Dr. Ira Shoulson, chair of the Huntington Study Group. “It is our hope that the commitment that the investigators and sponsor made to communicate the results of the clinical trial in a timely and personalized manner to research participants will set the standard for future clinical trials.”

References

The Huntington Study Group TREND-HD Investigators. **“Randomized Controlled Trial of Ethyl-Eicosapentaenoic Acid in Huntington Disease: The TREND-HD Study.”** Archives of Neurology 2008 Dec:65(12)1582-89.

Dorsey ER, Beck, CA, Adams M, Chadwick G, de Bleeck EA, McCallum C, Briner, L, Deuel L, Clarke A., Stewart R, Shoulson I, and the Huntington Study Group TREND-HD Investigators. **“Communicating clinical trial results to research participants.”** Archives of Neurology 2008 Dec:65(12)1590-95.

- *Marsha L. Miller, Ph.D.*