

Neurosearch Announces the Results of the American Huntexil (ACR-16) Trial: Encouraging but not Conclusive

Neurosearch has announced the results of its Phase IIB clinical trial of its dopamine stabilizer, Huntexil, originally named ACR16 when it was in preclinical development. The findings are consistent with the results of the earlier European Phase III trial reported in February 2010. The safety and tolerability profile again looks good and a trend was found towards motor improvement. At the higher dosage tested (45 mg twice daily), there was a trend toward improvement in the Modified Motor Score of the United Huntington's Disease Rating Scale, which was specified as the primary endpoint, and an even larger improvement in Total Motor Score. Balance, gait, eye movements, hand movements, dystonia, and chorea all showed improvements. However, the overall trend toward improvement did not reach statistical significance.

Had only the higher dose of Huntexil been tried and had the broader Total Motor Score been the pre-specified endpoint, then the results would have been successful instead of inconclusive. A clinical trial must be evaluated based on how it was originally set up; however, the results are encouraging and warrant further efforts. Determining the correct dosage for a new medicine is not easy to do and is especially difficult for drugs that affect the central nervous system (CNS). Most approved CNS drugs have required repeated Phase III trials.

Neurosearch's next step is to talk to the regulatory agencies, including the FDA here in the U.S. to see how they should proceed in their efforts to demonstrate the effectiveness of the drug. It is likely however, that they will have to conduct another Phase III trial.

- Marsha L. Miller, Ph.D., October 15, 2010

For more details read the press release below:

The HART study with Huntexil[®] shows significant effect on total motor function in patients with Huntington's disease although it did not meet the primary endpoint after 12 weeks of treatment

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- *The primary endpoint, the modified Motor Score, mMS, measuring voluntary motor function, showed an improvement of 1.2 points (p= 0.078)*
- *The secondary endpoint, the Total Motor Score, TMS, measuring all motor symptoms of the disease, showed an improvement of 2.8 points (p= 0.039)*
- *A statistically significant dose-response relationship was shown for Huntexil[®] on both the primary (mMS) and the secondary endpoint (TMS)*
- *The results support the good safety and tolerability profile of Huntexil[®]*
- *Results are consistent with the results from the MermaiHD study*

- ***NeuroSearch will consult with regulatory authorities to define the best strategy for obtaining marketing approval for Huntexil[®]***

Copenhagen, 14 October 2010 – Today, NeuroSearch A/S (NEUR) announced the first results from the 12-week randomised, double-blinded, placebo-controlled Phase II HART study with Huntexil[®] (pridopidine), a novel treatment for Huntington's disease.

The HART study was conducted in 28 centres across the United States and Canada and enrolled a total of 227 patients, who were randomised to treatment with three different doses of Huntexil[®] (10 mg, 22.5 mg or 45 mg – all twice daily) or placebo.

The primary endpoint of the HART study was the change from baseline at 12-weeks on the modified Motor Score, mMS, a subscale of the UHDRS (the Unified Huntington's Disease Rating Scale) Total Motor Score, TMS. For the Huntexil[®] 45 mg twice daily dose group, the effect versus placebo on the mMS did not reach significance, but on the secondary endpoint, the TMS, the change from baseline at week 12 was statistically significant. For both the mMS and the TMS, a statistically significant improvement in the change from baseline was seen with increasing dose, thus demonstrating an important dose-response relationship for Huntexil[®].

Importantly, the effect sizes for both the mMS and the TMS seen in the HART study are consistent with those seen in the MermaiHD study (see table):

Table: Huntexil[®] (45 mg twice daily) – effect on mMS and TMS (mean change versus placebo; p-value)

	The HART study*	The MermaiHD study at 12 weeks**	The MermaiHD study at 26 weeks***
mMS	-1.2 (<i>p</i> = 0.078)	-0.6 (<i>p</i> = 0.2)	-1.0 (<i>p</i> = 0.042)
TMS	-2.8 (<i>p</i> = 0.039)	-2.0 (<i>p</i> = 0.032)	-3.0 (<i>p</i> = 0.004)

* ANCOVA (ITT, LOCF) adjustment for baseline score, age, treatment

** MMRM (ITT, OC) adjustment for baseline score, neuroleptics (yes/no), gender, treatment, week and interaction between treatment and week

*** ANCOVA (ITT, LOCF) adjustment for baseline score, neuroleptics (yes/no), gender, treatment

In the HART study, Huntexil[®] 45 mg twice daily also showed significant effects on the patients' balance and gait as well as hand movements. For the TMS motor domains for eye movements, dystonia and chorea, positive trends were observed. In general, these results also show consistency with the observations in the MermaiHD study.

The endpoints for cognition, affective symptoms and generalised function/well-being did not show any statistically significant changes.

In the HART study, Huntexil[®] was found safe and well tolerated, and the most frequently reported adverse events across all treatment groups were falls, headache, diarrhoea and nausea with no apparent pattern related to active treatment. The adverse event findings were consistent with the observations in the MermaiHD study. Compliance with study medication was high across the study.

Treatment was discontinued due to adverse events for 7% of patients, and nine serious adverse events (recurrent breast cancer, suicidal ideation, depression, bipolar disorder, adjustment disorder, testicular torsion and three episodes of convulsions) were reported in six patients. No dose-dependent clinical patterns related to active treatment were observed.

Dr. Karl Kieburtz, University of Rochester Medical Center, Rochester, New York, the US, Primary Investigator on the HART study, commented:

"I find the results of the HART study encouraging as they provide additional support for the efficacy of pridopidine (Huntexil[®]) while helping also to demonstrate its benign safety profile in patients with Huntington's disease. Pridopidine is the first drug ever to target both the voluntary and involuntary motor features of this disease."

Patrik Dahlen, CEO of NeuroSearch, added:

"We are highly encouraged by the supportive HART study outcome and we look forward to taking the next steps towards our goal of establishing Huntexil[®] as a new and better treatment option for patients with Huntington's disease."

NeuroSearch is very encouraged by the strong trend in improvement on mMS, as well as the significant improvement on TMS and other secondary motor endpoints seen with Huntexil[®] in the HART study. This, together with the significant dose-response relationship on both endpoints provide strong support to previous clinical findings, demonstrating that the drug has beneficial and relevant effects on core motor functions in patients with Huntington's disease. Further, the efficacy of Huntexil has been shown to be associated with a good safety profile.

In the coming weeks, additional study analyses will be undertaken, including meta-analyses of data from both the HART and the MermaiHD studies. When the evaluation of all available clinical data is completed, NeuroSearch plans to engage in dialogue with regulatory authorities in North America and in Europe with a view to discussing the best way forward to obtaining marketing approvals for Huntexil[®] as a novel treatment for Huntington's disease.

NeuroSearch holds all commercial rights to Huntexil[®], and the company is on a continuous basis evaluating the best commercial options for the drug in North America, Europe and the rest of the world.

The HART results do not change the company's financial guidance for 2010 of a loss before financials and other shares of results of approximately DKK 350 million.

