

## **CEREBROLYSIN IN VASCULAR DEMENTIA – IMPROVEMENT OF CLINICAL OUTCOME IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED MULTICENTRIC CLINICAL TRIAL**

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**Introduction:** Cerebrolysin is a peptide preparation acting like endogenous neurotrophic factors. Due to its pleiotropic effects, Cerebrolysin is regarded as potential therapeutic tool in complex diseases like stroke or dementia. The aim of this study was to compare Cerebrolysin with placebo in patients suffering from vascular dementia and to confirm and extend the findings of earlier clinical trials in a larger patient cohort.

**Methods:** The primary efficacy criterion was defined as the combined outcome of the two primary efficacy criteria ADAS-cog+ and CIBIC+. Primary endpoint for assessing efficacy is 168 days after the baseline assessment. Patients received a dose of 20 ml Cerebrolysin administered in two treatment-cycles as add-on therapy to basic treatment with acetylsalicylic acid.

**Results:** In this study 242 patients were randomized and a total of 217 (89.7 %) completed the study. The therapy with Cerebrolysin resulted in significant improvement of both primary parameters, the score change from baseline in ADAS-cog+ at week 24 and the CIBIC+ score at week 24. Cognition, as assessed by ADAS-cog+, improved by -10,628 points in the Cerebrolysin group at week 24 yielding a statistically significant treatment difference compared to placebo. In the CIBIC+, there was also a statistically significant treatment difference between Cerebrolysin and placebo at week 24. The rate of ADAS-cog+ responders, defined as having an improvement of  $\geq 4$  points from baseline, was higher in the Cerebrolysin group with 82.1 % compared to 52.2 % in the placebo group. The odds ratio for achieving a treatment response in the cognitive domain was 4.190 for Cerebrolysin versus placebo at week 24, indicating a 4.190-fold increased probability of achieving a clinically significant cognitive improvement during the study compared to placebo. In the CIBIC+, the rate of responders, defined as having a score of  $< 4$  at week 24, was also higher in the Cerebrolysin group with 75.2 % compared to 37.4 % in the placebo group. The odds ratio for achieving a favourable CIBIC+ response was 5.081 for Cerebrolysin versus placebo. Responder rates of the combined response in ADAS-cog+ and CIBIC+ were 67.5 % in the Cerebrolysin group compared to 27.0 % in the placebo group. The odds ratios were 5.633 for Cerebrolysin versus placebo at week 24. Also in the MMSE, measuring cognitive impairment, Cerebrolysin was significantly superior over placebo at week 24. Same applies in the activities of daily living as measured by the ADCS-ADL and in the executive function as measured by the Trail-making test and the Clock-drawing test. Results from the subgroup analysis of patients with more advanced cognitive impairment (MMSE  $\leq 20$ ) have demonstrated that Cerebrolysin exerts even slightly larger treatment effects.

**Discussion / Conclusion:** The study demonstrated that Cerebrolysin improves the clinical outcome of patients suffering from mild to moderately severe vascular dementia significantly by improving both the cognition and the overall clinical functioning and these benefits were shown to extend for at least 6 months. Furthermore Cerebrolysin was safe and well tolerated by patients suffering from mild to moderately severe VD in a dose of 20 ml. This study has confirmed previous findings in clinical studies with patients suffering from vascular dementia. Together with its efficacy in the treatment of Alzheimer's disease, Cerebrolysin is effective in the most common forms of dementia and represents a treatment approach, which might also be effective in the treatment of patients with mixed dementia, where vascular and Alzheimer's disease coexist.

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