Introduction
Cerebrolysin (Cere) is a compound with neuroprotective activity which has been shown to be effective in the treatment of Alzheimer’s disease AD in earlier trials. The efficacy and safety of repeated treatments with Cere were investigated in a randomized, double-blind, placebo-controlled, parallel-group study.

Methods
The study was a 2-month, randomized, double-blind, placebo-controlled, parallel-group study conducted at nine investigational sites, hospitals and ambulances in Germany and Austria, with 149 patients being enrolled in two groups: Cere 30 ml (n=76) and placebo (n=73). Patients were screened for study entry within 14 days of the baseline visit, at which time eligible patients were randomized into the study. The selected demographic data and baseline disease characteristics are shown in Table 1. No significant group differences were observed at baseline.

Efficacy was evaluated based on the cognitive performance and the clinical global assessment of the patients. Primary efficacy measures were the Alzheimer’s Disease Assessment Scale cognitive subpart (ADAS-cog) and the Clinical Global Impression (CGI). In addition, a 7-point rating scale for global assessment of AD was used from 1 to 7, where 5 reflected no change from baseline, ratings of 3, 2, and 1 reflected increasing worsening from baseline. A rating of 1 was used if the patient could not be assessed. Secondary outcome measures included the Syndrome-Short-Test (SKT), the Montgomery-Asberg Depression Rating Scale (MADRS), the activities of daily living subscale of the Nuremberg Age Inventory (NAI) and the behavioral subpart of the ADAS, the ADAS-noncog.

Results
One hundred and forty-nine patients were randomized into two treatment groups. Forty-two patients were excluded due to violation of the inclusion criteria. Of these patients, 76 of Cere and 71 of placebo were included in the primary efficacy analysis. The analysis of the remaining secondary efficacy measures MADRS, CGI revealed no important effects.

The results of the secondary outcome parameter provided supportive evidence for the efficacy of Cere, most prominently in the activities of daily living and behavioral disturbances. In the activities of daily living NAI score treatment differences at the study endpoint favored the Cere group. Although not reaching statistical significance, there was a clear trend (P=0.071) in favor of Cere with a drug-placebo difference of 0.5 points (CI -1.2/0.2). Cere patients then started to deteriorate slowly in the washout phase from week 16 to the week 28, after which time they got back to their baseline levels, but still performed 1.4 points better than the placebo group (P=0.071). The presence of Cere over placebo was evident in the ADAS-noncog (Table 2). The analysis of the remaining secondary efficacy measures MADRS, CGI revealed no important effects.

Cere nonplacebo difference of 0.5 points at week 28 was confirmed in this subgroup, but drug-placebo differences were even more pronounced. This was largely due to the fact that the subgroup was defined as patients with a 1-point improvement on the ADAS-cog and the CGI score at the study endpoint. A similar significant superiority of Cere over placebo was evident for both primary parameters at the study endpoint (Table 3).

Conclusion
The neuroprotective compound Cerebrolysin is safe and effective for the treatment of patients with AD and leads to a statistically significant and clinically relevant improvement of cognitive performance and clinical global impressions. Most importantly, the therapeutic benefit is maintained in part for at least 3 months after drug withdrawal, suggesting a stabilization effect of Cere patients with AD. Long-term studies are warranted to further explore the possibility for Cere to slow the progression of AD. Issues such as the optimal therapy-free interval between successive treatments will need to be addressed.

References