Serum VEGF levels are associated with cognition and functioning in AD: influence of the treatment with Cerebrolysin and donepezil
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BACKGROUND
Vascular endothelial growth factor (VEGF) is an angiogenic growth factor showing neuroprotective, neurotrophic and cognitive effects in experimental conditions that might be relevant for the treatment of Alzheimer’s disease (AD) patients, but changes in circulating VEGF and the interactions of VEGF with clinical responses after drug treatment have not been investigated in AD.

MATERIALS AND METHODS
Serum VEGF levels, cognitive and functional performance were evaluated in AD patients treated with Cerebrolysin (n=52), donepezil (n=52), or a combination of both drugs (n=53) in a 28-week double-blind, randomized clinical trial. VEGF levels were measured in serum samples by using specific ELISA kits for VEGF in serum samples obtained at baseline, at week-16 (end of active Cerebrolysin treatment) and at week-28 (endpoint).

RESULTS
Overall, there were no significant treatment effects on VEGF levels (Table 1).

Table 1. Effects of Cerebrolysin, donepezil and combined therapy on VEGF serum levels in AD patients

<table>
<thead>
<tr>
<th>Cerebrolysin</th>
<th>Donepezil</th>
<th>Combined Therapy</th>
<th>Analysis</th>
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</thead>
<tbody>
<tr>
<td>(n=52)</td>
<td>(n=52)</td>
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<tr>
<td>Baseline VEGF (pg/mL)</td>
<td>310.7±248.11</td>
<td>372.3±249.35</td>
<td>397.8±300.36</td>
</tr>
<tr>
<td>Week-16 VEGF (pg/mL)</td>
<td>204.2±136.35</td>
<td>268.9±167.71</td>
<td>249.2±146.45</td>
</tr>
<tr>
<td>Week-28 VEGF (pg/mL)</td>
<td>127.8±234.15</td>
<td>402.3±298.68</td>
<td>377.0±286.63</td>
</tr>
</tbody>
</table>

In moderately severe AD cases:

- The combination therapy reduced elevated VEGF levels significantly (p<0.05) at week-16 and week-28 as compared to donepezil alone (Figure 1).
- Higher baseline VEGF levels were associated to improvements in cognition (ADAS-cog) and functioning (ADCS-ADL) (Figure 2a,b,c).

CONCLUSIONS
Elevated baseline VEGF levels were associated with improved cognition-functioning in moderately-severe AD, but VEGF reductions at endpoint were found to be associated with treatment-induced cognitive-functional improvements particularly in APOE4 AD cases, and with better praxis and executive functions in advanced cases receiving Cerebrolysin plus donepezil. These findings are indicating the influence of VEGF on cognitive-functional performance and response to therapy in AD; and suggest that VEGF increases might represent a neuroprotective response in AD, especially in advanced and in APOE4 cases.