## Evidence Table D-62. Supplement intervention - composite outcomes categorical total symptom score (KQ2b)

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Arm</th>
<th>Instrument name</th>
<th>Baseline outcome</th>
<th>Time point(s)</th>
<th>Outcome at time point(s)</th>
<th>Within arm comparison</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziegler, 2011</td>
<td>Arm 2: placebo</td>
<td>TSS Total</td>
<td>N: 224, mean: 2.6, SD: 1.8</td>
<td>4 years</td>
<td>N:207, mean:NR, SD:NR</td>
<td>Mean change from baseline: -0.21, SD: 2.45</td>
<td></td>
</tr>
<tr>
<td>Ziegler, 2011</td>
<td>Arm 1: ALA</td>
<td>TSS Total</td>
<td>N: 230, mean: 2.4, SD: 1.9</td>
<td>4 years</td>
<td>N: 215, mean: NR, SD: NR</td>
<td>Mean change from baseline: -0.22, SD: 2.42</td>
<td>Mean change from baseline1 vs 2 p: NS</td>
</tr>
<tr>
<td>Ziegler, 2006</td>
<td>Arm 1: placebo</td>
<td>TSS Total</td>
<td>N: 43, mean: 9.27, SD: 1.56</td>
<td>5 weeks</td>
<td>N: NR, mean: NR, SD: NR</td>
<td>Mean change from baseline: -2.92, SD: 3.18</td>
<td>ALA600 vs placebo, p: &lt;0.05</td>
</tr>
<tr>
<td>Ziegler, 2006</td>
<td>Arm 2: ALA600</td>
<td>TSS Total</td>
<td>N: 45, mean: 9.44, SD: 1.86</td>
<td>5 weeks</td>
<td>N: NR, mean: NR, SD: NR</td>
<td>Mean change from baseline: -4.85, SD: 3.03</td>
<td>ALA1200 vs placebo, p: &lt;0.05</td>
</tr>
<tr>
<td>Ziegler, 2006</td>
<td>Arm 3: ALA1200</td>
<td>TSS Total</td>
<td>N: 47, mean: 9.4, SD: 1.64</td>
<td>5 weeks</td>
<td>N: NR, mean: NR, SD: NR</td>
<td>Mean change from baseline: -4.5, SD: 3.28</td>
<td>ALA1800 vs placebo, p: &lt;0.05</td>
</tr>
<tr>
<td>Ziegler, 2006</td>
<td>Arm 4: ALA1800</td>
<td>TSS Total</td>
<td>N: 46, mean: 9.02, SD: 1.61</td>
<td>5 weeks</td>
<td>N: NR, mean: NR, SD: NR</td>
<td>Mean change from baseline: -4.7, SD: 3.54</td>
<td></td>
</tr>
<tr>
<td>Ziegler, 1999</td>
<td>Arm 2: placebo</td>
<td>TSS Total</td>
<td>N: 165, mean: 8.4, SD: 3.2</td>
<td>19 days</td>
<td>N: 165, mean: NR, SD: NR</td>
<td>Median change from baseline: -3, SD: NR</td>
<td>ALA vs placebo, p:0.447 Median change from baseline - range reported: -12.3, 8. Post-hoc analysis with AUC - p=0.033</td>
</tr>
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<td>Author, year</td>
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<td>Outcome at time point(s)</td>
<td>Within arm comparison</td>
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<tr>
<td>Ziegler, 1999</td>
<td>Arm 1: ALA</td>
<td>TSS Total</td>
<td>N: 338, mean: NR, SD: NR</td>
<td>19 days</td>
<td>N: 338, mean: NR, SD: NR</td>
<td>Median change from baseline: -3.7, SD: NR</td>
<td>Note that in this study, Arm 1 and Arm 2 are used for the initial period, and then this is split into 3 arms for the longer-term study. Here we are reporting the initial period separately</td>
</tr>
<tr>
<td>Ziegler, 1999</td>
<td>Arm 1: A-A</td>
<td>TSS Total</td>
<td>N: 165, mean: 8.1, SD: 3</td>
<td>7 months</td>
<td>N: 165, mean: NR, SD: NR</td>
<td>Median change from baseline: -3.98, SD: NR</td>
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<tr>
<td>Ziegler, 1999</td>
<td>Arm 3: P-P</td>
<td>TSS Total</td>
<td>N: 165, mean: 8.4, SD: 3.2</td>
<td>7 months</td>
<td>N: 165, mean: NR, SD: NR</td>
<td>Median change from baseline: -3.98, SD: NR</td>
<td></td>
</tr>
<tr>
<td>Ziegler, 1996</td>
<td>Arm 4: placebo</td>
<td>TSS Total</td>
<td>N: 66, mean: NR, SD: NR</td>
<td>19 days</td>
<td>N: 66, mean: NR, SD: NR</td>
<td>Mean change from baseline: -2.5, SD: 3.2</td>
<td>Data taken from figure 1</td>
</tr>
<tr>
<td>Ziegler, 1996</td>
<td>Arm 3: ALA100</td>
<td>TSS Total</td>
<td>N: 66, mean: NR, SD: NR</td>
<td>19 days</td>
<td>N: 66, mean: NR, SD: NR</td>
<td>Mean change from baseline: -3.3, SD: 2.8</td>
<td>Data taken from figure 1</td>
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<td>Author, year</td>
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<tr>
<td>Ziegler, 1996</td>
<td>Arm 2: ALA600</td>
<td>TSS Total</td>
<td>N: 63, mean: NR, SD: NR</td>
<td>19 days</td>
<td>N: 63, mean: NR, SD: NR</td>
<td>Mean change from baseline: -4.9, SD: 4.1; p: &lt;0.05</td>
<td>Data taken from figure 1</td>
</tr>
<tr>
<td>Ziegler, 1996</td>
<td>Arm 1: ALA1200</td>
<td>TSS Total</td>
<td>N: 65, mean: NR, SD: NR</td>
<td>19 days</td>
<td>N: NR, mean: NR, SD: NR</td>
<td>Mean change from baseline: -4.4, SD: 3.7; p: &lt;0.05</td>
<td>Data taken from figure 1</td>
</tr>
<tr>
<td>Ruhnau, 1999</td>
<td>Arm 2: placebo</td>
<td>TSS Total-points</td>
<td>N: 11, mean: 8.18, SD: 0.89</td>
<td>Day 19</td>
<td>N: 11, mean: NR, SD: NR</td>
<td>Mean change from baseline: -1.94, SD: 1.5</td>
<td></td>
</tr>
<tr>
<td>Ruhnau, 1999</td>
<td>Arm 1: TA (COMPOSITE)</td>
<td>TSS Total-points</td>
<td>N: 11, mean: 7.99, SD: 0.97</td>
<td>Day 19</td>
<td>N: 11, mean: NR, SD: NR</td>
<td>Mean change from baseline: -3.75, SD: 1.88; Mean change from baseline placebo p: 0.021</td>
<td></td>
</tr>
<tr>
<td>Ametov, 2003</td>
<td>Arm 1: placebo</td>
<td>TSS-p</td>
<td>N: 60, mean: 8.2, SD: 1.06</td>
<td>3 weeks</td>
<td>N: 58, mean: 6.4, SD: 1.97</td>
<td>Mean change from baseline: -1.83, SD: 1.97</td>
<td>Data taken from figure 2</td>
</tr>
<tr>
<td>Ametov, 2003</td>
<td>Arm 2: ALA (COMPOSITE)</td>
<td>TSS-points</td>
<td>N: 60, mean: 8.8, SD: 1.02</td>
<td>3 weeks</td>
<td>N: 60, mean: 3, SD: 1.38</td>
<td>Mean change from baseline: -5.72, SD: 1.53; p: &lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

ALA = alpha-lipoic acid; N = sample size; NR = note reported; p = p-value; SD = standard deviation; TSS = Total Symptom Score