Supplementary Material for: Blood pressure lowering using transdermal glyceryl trinitrate in acute ischaemic stroke patients with carotid stenosis is safe

1. Efficacy of Nitric Oxide in Stroke (ENOS) trial steering and international advisory committees
2. ENOS carotid stenosis working practice document
3. Supplementary tables
1. **Efficacy of Nitric Oxide in Stroke (ENOS) trial steering and international advisory committees**

**Trial Steering Committee:**
D Thomas (Independent Chair to 2006, UK), G Venables (Independent Chair from 2006, UK), P Amarenco (Independent Physician, France), K Muir (Independent Physician, UK), P M W Bath (Chief Investigator, UK), N Sprigg (Deputy Chief Investigator, UK), E Berge (Norway), K R Lees (UK), S Pocock (Statistician from 2003, UK), A Shone (Sponsor’s Representative, UK), A Skene (Statistician to 2003, UK), J M Wardlaw (Neuroradiologist, UK), D Whynes (Health economist, UK).

**International Advisory Committee:**
P M W Bath (Chair, UK), E Berge (Norway), M Beridze (Georgia), C Bladin (Australia), V Caso (Italy), C Chen/H M Chang (Singapore), H Christensen (Denmark), R Collins (Eire), A Członkowska (Poland), E Díez-Tejedor (Spain), A El Etribi (Egypt), A R Ghani (Malaysia), J Gommans (New Zealand), A C Laska (Sweden), K R Lees (UK), J Navarro (Philippines), G Ntaios (Greece), S Ozturk (Turkey), S Phillips (Canada), K Prasad (India), H A de Silva (Sri Lanka), S Szatmari (Romania), L Wong (Hong Kong), Y-J Wang (China).
2. ENOS carotid stenosis working practice document

**ENOS TRIAL**

**INTERNAL CAROTID ARTERY STENOSIS (ICA)**

Completion of Hospital Event Information

<table>
<thead>
<tr>
<th>PEAK SYSTOLIC VELOCITY (PSV)</th>
<th>% DIAMETER REDUCTION</th>
<th>ENTER ON HOSPITAL EVENT FORM Equivalent mid-point</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-109</td>
<td>0-29</td>
<td>14</td>
</tr>
<tr>
<td>110-130</td>
<td>30-49</td>
<td>39</td>
</tr>
<tr>
<td>&gt;130</td>
<td>50-69</td>
<td>59</td>
</tr>
<tr>
<td>&gt;210</td>
<td>70-95</td>
<td>82</td>
</tr>
<tr>
<td>“STRING FLOW”</td>
<td>96-99</td>
<td>98</td>
</tr>
<tr>
<td>“NO FLOW”</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Both RIGHT and LEFT ICA needs entering

If the report states:

An exact percentage, then enter as reported

Between, or less than a certain percentage i.e. 0-29 or less than 29%, then enter the mid-point i.e. 14

If the report gives a velocity then find the equivalent mid-point percentage and enter this.
### Supplementary tables

#### Supplementary table 1: Secondary outcomes by degree of ipsilateral carotid stenosis

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>Stenosis &lt;30%</th>
<th>Stenosis 30-&lt;50%</th>
<th>Stenosis 50-&lt;70%</th>
<th>Stenosis ≥70%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%) / mean (SD)</td>
<td>OR/MD (95% CI)</td>
<td>p</td>
<td>n (%) / mean (SD)</td>
</tr>
<tr>
<td>Number of Participants</td>
<td>1431</td>
<td>224</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Day 7 (or discharge)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, by cause (%)</td>
<td>9 (0.6)</td>
<td>0 (0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Symptomatic recurrent stroke (%)</td>
<td>14 (1.0)</td>
<td>4 (1.8)</td>
<td>1.60 (0.50, 5.09)</td>
<td>0.43</td>
</tr>
<tr>
<td>Ischaemic</td>
<td>12 (0.8)</td>
<td>3 (1.3)</td>
<td>1.32 (0.36, 4.90)</td>
<td>0.68</td>
</tr>
<tr>
<td>NIH Stroke Scale (/42), calculated</td>
<td>6.8 (5.5)</td>
<td>7.5 (6.1)</td>
<td>-0.32 (0.65)</td>
<td>0.50</td>
</tr>
<tr>
<td>Clinical deterioration (%)</td>
<td>62 (4.3)</td>
<td>15 (6.7)</td>
<td>1.53 (0.84, 2.77)</td>
<td>0.16</td>
</tr>
<tr>
<td>Neurological deterioration (%)</td>
<td>59 (4.1)</td>
<td>9 (4.0)</td>
<td>0.97 (0.47, 2.02)</td>
<td>0.94</td>
</tr>
<tr>
<td>Headache (%)</td>
<td>192 (13.4)</td>
<td>20 (8.9)</td>
<td>0.80 (0.48, 1.32)</td>
<td>0.38</td>
</tr>
<tr>
<td>Hypotension (%)</td>
<td>21 (1.5)</td>
<td>3 (1.3)</td>
<td>0.89 (0.25, 3.10)</td>
<td>0.85</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>78 (5.5)</td>
<td>14 (6.3)</td>
<td>1.22 (0.66, 2.23)</td>
<td>0.53</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Death or discharge to institution (%)</td>
<td>356 (24.9)</td>
<td>50 (22.3)</td>
<td>0.81 (0.57, 1.15)</td>
<td>0.24</td>
</tr>
<tr>
<td>Day 90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barthel Index</td>
<td>77.0 (31.3)</td>
<td>72.8 (35.4)</td>
<td>-1.43 (-5.29, 2.43)</td>
<td>0.47</td>
</tr>
<tr>
<td>Zung Depression Scale (ZDS, /100)</td>
<td>52.3 (20.5)</td>
<td>57.2 (22.8)</td>
<td>3.57 (0.55, 6.58)</td>
<td>0.021</td>
</tr>
<tr>
<td>EQ-5D Health Utility Status (HUS, /1)</td>
<td>0.57 (0.38)</td>
<td>0.53 (0.37)</td>
<td>-0.01 (-0.06, 0.04)</td>
<td>0.63</td>
</tr>
<tr>
<td>EQ-Visual Analogue Scale (EQ-VAS, /100)</td>
<td>63.7 (26.0)</td>
<td>61.4 (29.8)</td>
<td>0.16 (-3.54, 3.87)</td>
<td>0.93</td>
</tr>
<tr>
<td>Verbal Fluency</td>
<td>11.7 (7.1)</td>
<td>10.7 (8.3)</td>
<td>-0.32 (-1.56, 0.91)</td>
<td>0.61</td>
</tr>
<tr>
<td>TICS-M</td>
<td>18.7 (8.8)</td>
<td>16.1 (10.0)</td>
<td>-1.49 (-3.05, 0.07)</td>
<td>0.06</td>
</tr>
<tr>
<td>MMSE</td>
<td>14.0 (5.8)</td>
<td>12.0 (6.9)</td>
<td>-1.17 (-2.21, -0.13)</td>
<td>0.028</td>
</tr>
</tbody>
</table>

Data are n (%), mean (SD), mean difference (MD) or odds ratio (OR) with 95% confidence intervals. Comparison using logistic or multiple regression with <30% stenosis as reference group. Adjusted for age, sex, baseline mRS, history of previous stroke, history of diabetes mellitus, TACS, nitrate use, baseline SSS, thrombolysis, feeding status, time to randomisation, baseline SBP, GTN/no GTN and continue/stop.
## Supplementary table 2: Secondary outcomes by GTN vs. no GTN by degree of ipsilateral carotid stenosis

<table>
<thead>
<tr>
<th>Number of Participants</th>
<th>Stenosis 30–&lt;50%</th>
<th>Stenosis 50–&lt;70%</th>
<th>Stenosis ≥70%</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTN No GTN (OR/MD)</td>
<td>OR/MD (95% CI)</td>
<td>OR/MD (95% CI)</td>
<td>OR/MD (95% CI)</td>
</tr>
<tr>
<td>111 192</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9.8 (17.5)</td>
<td>0.06 (0.02, 0.19)</td>
<td>0.05 (0.02, 0.15)</td>
<td>0.05 (0.02, 0.15)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SBP change day 0-1 (mmHg)*</th>
<th>0 (0)</th>
<th>-13.8 (19.8)</th>
<th>-10.9 (18.1)</th>
<th>-8.9 (17.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTN No GTN (OR/MD)</td>
<td>1 (1.3)</td>
<td>-11.0 (-15.7, -6.3)</td>
<td>-3.9 (-9.6, 18)</td>
<td>-6.5 (-11.0, -2.0)</td>
</tr>
<tr>
<td>OR/MD (95% CI)</td>
<td>0.09 (0.00, 11.08)</td>
<td>0.18 (0.00, 11.17)</td>
<td>0.18 (0.00, 11.17)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Day 7 (or discharge)</th>
<th>Death, by cause (%)</th>
<th>Symptomatic recurrent stroke (%)</th>
<th>Ischaemic</th>
<th>NIH Stroke Scale (/42), calculated</th>
<th>Clinical deterioration (%)</th>
<th>Neurological deterioration (%)</th>
<th>Headache (%)</th>
<th>Hypotension (%)</th>
<th>Hypertension (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTN No GTN (OR/MD)</td>
<td>3 (3.2)</td>
<td>0 (0)</td>
<td>6 (5.9)</td>
<td>7.6 (6.0)</td>
<td>4.6 (2.49)</td>
<td>1 (1.3)</td>
<td>3 (2.9)</td>
<td>20.3 (6.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>OR/MD (95% CI)</td>
<td>(1.7)</td>
<td>-</td>
<td>(0.19, 2.49)</td>
<td>(1.46, 0.64)</td>
<td>0.53 (0.06, 4.46)</td>
<td>(4.2)</td>
<td>(4.9)</td>
<td>(0.70, 5.94)</td>
<td>-</td>
</tr>
<tr>
<td>p</td>
<td>0.90</td>
<td>0.44</td>
<td>0.57</td>
<td>0.20</td>
<td>0.019</td>
<td>0.059</td>
<td>0.019</td>
<td>0.91</td>
<td>0.91</td>
</tr>
</tbody>
</table>

| Death, by cause (%) | 0 (0) | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) |
| Symptomatic recurrent stroke (%) | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) |
| Ischaemic | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) | 0 (0) | 3 (3.2) |
| NIH Stroke Scale (/42), calculated | 6 (6.3) | 6.6 (5.8) | 6.6 (5.8) | 6.6 (5.8) | 6.6 (5.8) | 6.6 (5.8) | 6.6 (5.8) | 6.6 (5.8) | 6.6 (5.8) |
| Clinical deterioration (%) | 1 (1.0) | 1 (1.4) | 1 (1.4) | 1 (1.4) | 1 (1.4) | 1 (1.4) | 1 (1.4) | 1 (1.4) | 1 (1.4) |
| Neurological deterioration (%) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Headache (%) | 12 (11.8) | 16 (20.8) | 19 (20.2) | 12 (11.8) | 16 (20.8) | 19 (20.2) | 12 (11.8) | 16 (20.8) | 19 (20.2) |
| Hypotension (%) | 3 (2.9) | 3 (3.9) | 3 (2.1) | 3 (2.9) | 3 (3.9) | 3 (2.1) | 3 (2.9) | 3 (2.9) | 3 (2.1) |
| Hypertension (%) | 6 (5.9) | 8 (6.6) | 6 (5.9) | 8 (6.6) | 6 (5.9) | 8 (6.6) | 6 (5.9) | 8 (6.6) | 6 (5.9) |

<p>| NIH Stroke Scale (/42), calculated | 7.3 (6.2) | 6.6 (6.0) | 6.6 (6.0) | 6.6 (6.0) | 6.6 (6.0) | 6.6 (6.0) | 6.6 (6.0) | 6.6 (6.0) | 6.6 (6.0) |
| Clinical deterioration (%) | 6 (5.9) | 9 (6.6) | 9 (6.6) | 9 (6.6) | 9 (6.6) | 9 (6.6) | 9 (6.6) | 9 (6.6) | 9 (6.6) |
| Neurological deterioration (%) | 3 (2.9) | 4 (4.9) | 4 (4.9) | 4 (4.9) | 4 (4.9) | 4 (4.9) | 4 (4.9) | 4 (4.9) | 4 (4.9) |
| Headache (%) | 12 (11.8) | 16 (20.8) | 19 (20.2) | 12 (11.8) | 16 (20.8) | 19 (20.2) | 12 (11.8) | 16 (20.8) | 19 (20.2) |
| Hypotension (%) | 3 (2.9) | 3 (3.9) | 3 (2.1) | 3 (2.9) | 3 (3.9) | 3 (2.1) | 3 (2.9) | 3 (2.9) | 3 (2.1) |
| Hypertension (%) | 6 (5.9) | 8 (6.6) | 6 (5.9) | 8 (6.6) | 6 (5.9) | 8 (6.6) | 6 (5.9) | 8 (6.6) | 6 (5.9) |</p>
<table>
<thead>
<tr>
<th>Death or discharge to institution (%)</th>
<th>22 (21.6)</th>
<th>28 (23.0)</th>
<th>0.84 (0.41, 1.75)</th>
<th>0.65</th>
<th>13 (16.9)</th>
<th>17 (23.9)</th>
<th>0.64 (0.25, 1.62)</th>
<th>0.34</th>
<th>27 (28.7)</th>
<th>45 (37.8)</th>
<th>0.51 (0.26, 1.00)</th>
<th>0.050</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Day 90</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Barthel Index</strong></td>
<td>75.2 (34.4)</td>
<td>70.8 (36.2)</td>
<td>5.78 (-2.37, 13.94)</td>
<td>0.16</td>
<td>74.9 (31.5)</td>
<td>69.7 (35.8)</td>
<td>7.86 (-2.24, 17.95)</td>
<td>0.13</td>
<td>65.7 (38.0)</td>
<td>57.9 (37.9)</td>
<td>-7.87 (-10.10, 16.74)</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Zung Depression Scale (ZDS, /100)</strong></td>
<td>56.5 (22.2)</td>
<td>57.8 (23.3)</td>
<td>-0.89 (-7.20, 5.43)</td>
<td>0.78</td>
<td>51.1 (19.2)</td>
<td>56.8 (24.6)</td>
<td>-7.33 (-14.93, 0.27)</td>
<td>0.059</td>
<td>59.7 (22.6)</td>
<td>62.1 (22.6)</td>
<td>-3.78 (-9.87, 2.32)</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EQ-5D Health Utility Status (HUS, /1)</strong></td>
<td>0.54 (0.38)</td>
<td>0.53 (0.36)</td>
<td>0.00 (-0.08, 0.09)</td>
<td>0.94</td>
<td>0.53 (0.39)</td>
<td>0.53 (0.40)</td>
<td>0.05 (-0.07, 0.17)</td>
<td>0.44</td>
<td>0.44 (0.39)</td>
<td>0.37 (0.40)</td>
<td>0.07 (-0.02, 0.17)</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EQ-Visual Analogue Scale (EQ-VAS, /100)</strong></td>
<td>62.4 (28.6)</td>
<td>60.5 (30.8)</td>
<td>2.12 (-5.81, 10.05)</td>
<td>0.60</td>
<td>62.6 (26.0)</td>
<td>59.7 (30.9)</td>
<td>5.57 (-3.96, 15.10)</td>
<td>0.25</td>
<td>54.3 (29.6)</td>
<td>47.4 (30.4)</td>
<td>-6.91 (-1.04, 14.85)</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Verbal Fluency</strong></td>
<td>11.3 (8.1)</td>
<td>10.2 (8.5)</td>
<td>0.78 (-1.97, 3.52)</td>
<td>0.58</td>
<td>10.6 (6.5)</td>
<td>9.8 (7.6)</td>
<td>0.96 (-1.54, 3.47)</td>
<td>0.45</td>
<td>9.5 (7.0)</td>
<td>9.7 (8.5)</td>
<td>0.23 (-2.48, 2.94)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TICS-M</strong></td>
<td>15.8 (9.2)</td>
<td>16.3 (10.6)</td>
<td>-0.88 (-4.16, 2.41)</td>
<td>0.60</td>
<td>18.4 (7.5)</td>
<td>13.3 (10.0)</td>
<td>4.92 (1.36, 8.49)</td>
<td>0.008</td>
<td>14.7 (9.8)</td>
<td>12.8 (9.6)</td>
<td>2.34 (-1.20, 5.88)</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MMSE</strong></td>
<td>12.2 (6.4)</td>
<td>11.9 (7.2)</td>
<td>0.26 (-1.94, 2.45)</td>
<td>0.82</td>
<td>14.0 (5.2)</td>
<td>10.1 (7.1)</td>
<td>4.11 (1.63, 6.59)</td>
<td>0.002</td>
<td>11.3 (4.0)</td>
<td>10.1 (7.4)</td>
<td>1.34 (-1.25, 3.94)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Data are n (%), mean (SD), mean difference (MD) or odds ratio (OR) with 95% confidence intervals. Comparison using logistic or multiple regression with <30% stenosis as reference group. Adjusted for age, sex, baseline mRS, history of previous stroke, history of diabetes mellitus, TACS, nitrate use, baseline SSS, thrombolysis, feeding status, time to randomisation, baseline SBP and continue/stop. *=adjusted for baseline SBP only
## Supplementary table 3: Secondary outcomes by stop vs. continue antihypertensives by degree of ipsilateral carotid stenosis

<table>
<thead>
<tr>
<th></th>
<th>Stenosis 30-&lt;50%</th>
<th></th>
<th>Stenosis 50-&lt;70%</th>
<th></th>
<th>Stenosis ≥70%</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cont  Stop</td>
<td>OR/MD (95% CI)</td>
<td>p</td>
<td>Cont  Stop</td>
<td>OR/MD (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Number of Participants</td>
<td>65   68</td>
<td>-</td>
<td>-</td>
<td>52   47</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SBP change day 0-1 (mmHg)*</td>
<td>-8.7  (17.3)</td>
<td>-6.0  (21.0)</td>
<td>-3.48  (-9.91, 2.96)</td>
<td>0.29</td>
<td>-8.4  (17.3)</td>
<td>-6.0  (18.0)</td>
</tr>
<tr>
<td>Day 7 (or discharge)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, by cause (%)</td>
<td>0 (0) 0 (0)</td>
<td>-</td>
<td>-</td>
<td>1 (1.9) 0 (0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Symptomatic recurrent stroke (%)</td>
<td>2 (3.1) 2 (2.9)</td>
<td>1.05  (0.05, 22.98)</td>
<td>0.97</td>
<td>0 (0) 1 (2.1)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ischaemic</td>
<td>2 (3.1) 1 (1.5)</td>
<td>5.13  (0.08, 338.19)</td>
<td>0.44</td>
<td>0 (0) 1 (2.1)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>NIH Stroke Scale (/42), calculated</td>
<td>7.6  (6.4)</td>
<td>8.0  (6.6)</td>
<td>0.63  (-0.98, 2.23)</td>
<td>0.44</td>
<td>7.3  (5.7)</td>
<td>6.7  (4.8)</td>
</tr>
<tr>
<td>Clinical deterioration (%)</td>
<td>6 (9.2) 5 (7.5)</td>
<td>1.95  (0.40, 9.51)</td>
<td>0.41</td>
<td>5 (9.8) 1 (2.1)</td>
<td>10.60  (0.63, 177.41)</td>
<td>0.10</td>
</tr>
<tr>
<td>Neurological deterioration (%)</td>
<td>4 (6.2) 2 (2.9)</td>
<td>-</td>
<td>-</td>
<td>2 (3.8) 0 (0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Headache (%)</td>
<td>4 (6.2) 7 (10.3)</td>
<td>0.53  (0.10, 2.77)</td>
<td>0.45</td>
<td>9 (17.3) 7 (14.9)</td>
<td>1.03  (0.29, 3.63)</td>
<td>0.96</td>
</tr>
<tr>
<td>Hypotension (%)</td>
<td>1 (1.5) 1 (1.5)</td>
<td>-</td>
<td>-</td>
<td>0 (0) 3 (6.4)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>2 (3.1) 6 (8.8)</td>
<td>0.38  (0.04, 3.35)</td>
<td>0.38</td>
<td>1 (1.9) 5 (10.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Day 90</td>
<td>Day 90</td>
<td>MD</td>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or discharge to institution (%)</td>
<td>17 (26.2)</td>
<td>17 (25.0)</td>
<td>1.37 (0.51, 3.65)</td>
<td>0.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (19.2)</td>
<td>8 (6.5)</td>
<td>2.47 (0.66, 9.18)</td>
<td>0.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>21 (36.8)</td>
<td>16 (28.1)</td>
<td>1.39 (0.54, 3.61)</td>
<td>0.50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Barthel Index**

<table>
<thead>
<tr>
<th></th>
<th>Day 90</th>
<th>Day 90</th>
<th>MD</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70.2 (38.3)</td>
<td>71.3 (36.3)</td>
<td>-2.48 (-14.27, 9.32)</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>67.5 (36.1)</td>
<td>74.9 (27.1)</td>
<td>-13.20 (-26.29, -0.11)</td>
<td>0.048</td>
</tr>
<tr>
<td></td>
<td>58.7 (37.8)</td>
<td>50.3 (42.5)</td>
<td>10.73 (-24.40, 2.94)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

**Zung Depression Scale (ZDS, /100)**

<table>
<thead>
<tr>
<th></th>
<th>Day 90</th>
<th>Day 90</th>
<th>MD</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>61.2 (24.6)</td>
<td>60.0 (22.1)</td>
<td>1.20 (-7.55, 9.96)</td>
<td>0.79</td>
</tr>
<tr>
<td></td>
<td>60.9 (23.3)</td>
<td>48.8 (17.8)</td>
<td>13.18 (3.80, 22.56)</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>67.6 (23.9)</td>
<td>61.6 (22.4)</td>
<td>10.21 (1.10, 19.33)</td>
<td>0.029</td>
</tr>
</tbody>
</table>

**EQ-5D Health Utility Status (HUS, /1)**

<table>
<thead>
<tr>
<th></th>
<th>Day 90</th>
<th>Day 90</th>
<th>MD</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.49 (0.41)</td>
<td>0.51 (0.36)</td>
<td>-0.03 (-0.15, 0.09)</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>0.48 (0.39)</td>
<td>0.56 (0.33)</td>
<td>-0.16 (-0.30, -0.01)</td>
<td>0.036</td>
</tr>
<tr>
<td></td>
<td>0.33 (0.43)</td>
<td>0.35 (0.39)</td>
<td>-0.06 (-0.20, 0.07)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

**EQ-Visual Analogue Scale (EQ-VAS, /100)**

<table>
<thead>
<tr>
<th></th>
<th>Day 90</th>
<th>Day 90</th>
<th>MD</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>57.0 (31.5)</td>
<td>59.5 (29.3)</td>
<td>-2.04 (-12.69, 8.62)</td>
<td>0.71</td>
</tr>
<tr>
<td></td>
<td>54.0 (32.3)</td>
<td>68.1 (20.4)</td>
<td>-17.20 (-29.41, -4.99)</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>44.1 (33.8)</td>
<td>48.3 (27.0)</td>
<td>-6.22 (-18.56, 6.13)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

**Verbal Fluency**

<table>
<thead>
<tr>
<th></th>
<th>Day 90</th>
<th>Day 90</th>
<th>MD</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.5 (7.5)</td>
<td>10.5 (7.7)</td>
<td>-2.08 (-5.71, 1.55)</td>
<td>0.26</td>
</tr>
<tr>
<td></td>
<td>7.6 (6.0)</td>
<td>11.3 (5.0)</td>
<td>-2.69 (-5.61, 0.22)</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>6.7 (6.2)</td>
<td>9.7 (8.6)</td>
<td>-3.11 (-6.84, 0.62)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

**TICS-M**

<table>
<thead>
<tr>
<th></th>
<th>Day 90</th>
<th>Day 90</th>
<th>MD</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12.9 (9.4)</td>
<td>15.8 (10.0)</td>
<td>-2.38 (-7.28, 2.52)</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>13.2 (9.9)</td>
<td>19.3 (7.8)</td>
<td>-5.66 (-10.40, -0.92)</td>
<td>0.021</td>
</tr>
<tr>
<td></td>
<td>11.1 (10.2)</td>
<td>13.1 (9.3)</td>
<td>-3.39 (-8.45, 1.67)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

**MMSE**

<table>
<thead>
<tr>
<th></th>
<th>Day 90</th>
<th>Day 90</th>
<th>MD</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10.1 (7.1)</td>
<td>11.7 (6.9)</td>
<td>-1.30 (-4.76, 2.16)</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>10.1 (7.4)</td>
<td>13.9 (5.1)</td>
<td>-2.71 (-6.57, 1.15)</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>8.3 (7.8)</td>
<td>10.4 (6.7)</td>
<td>-2.80 (-6.52, 0.92)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Data are n (%), mean (SD), mean difference (MD) or odds ratio (OR) with 95% confidence intervals. Comparison using logistic or multiple regression. Adjusted for age, sex, baseline mRS, history of previous stroke, history of diabetes mellitus, TACS, nitrate use, baseline SSS, thrombolysis, feeding status, time to randomisation, baseline SBP and GTN/no GTN. * = adjusted for baseline SBP only
## Supplementary table 4: Outcomes by degree of bilateral carotid stenosis

<table>
<thead>
<tr>
<th></th>
<th>Stenosis &lt;30%</th>
<th>Stenosis 30-&lt;50%</th>
<th>Stenosis ≥50%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%) / mean (SD)</td>
<td>OR/MD (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Number of Participants</td>
<td>1287</td>
<td>115</td>
<td>-</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>1282</td>
<td>115</td>
<td>-</td>
</tr>
<tr>
<td>mRS (/6)*</td>
<td>2 [3]</td>
<td>2 [3]</td>
<td>0.91 (0.65, 1.29)</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 7 (or Discharge)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, by cause (%)</td>
<td>9 (0.7)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td>Symptomatic recurrent stroke (%)</td>
<td>10 (0.8)</td>
<td>2 (1.7)</td>
<td>1.85 (0.38, 9.04)</td>
</tr>
<tr>
<td>Ischaemic</td>
<td>9 (0.7)</td>
<td>1 (0.9)</td>
<td>1.08 (0.13, 9.13)</td>
</tr>
<tr>
<td>NIH Stroke Scale (/42), calculated</td>
<td>6.8 (5.4)</td>
<td>6.9 (6.3)</td>
<td>-0.06 (-0.69, 0.58)</td>
</tr>
<tr>
<td>Clinical deterioration (%)</td>
<td>58 (4.5)</td>
<td>9 (7.9)</td>
<td>1.54 (0.72, 3.28)</td>
</tr>
<tr>
<td>Neurological deterioration (%)</td>
<td>52 (4.0)</td>
<td>6 (5.2)</td>
<td>1.20 (0.49, 2.92)</td>
</tr>
<tr>
<td>Headache (%)</td>
<td>179 (13.9)</td>
<td>11 (9.6)</td>
<td>0.82 (0.42, 1.61)</td>
</tr>
<tr>
<td>Hypotension (%)</td>
<td>20 (1.6)</td>
<td>1 (0.9)</td>
<td>0.52 (0.07, 4.10)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>73 (5.7)</td>
<td>8 (7.0)</td>
<td>1.32 (0.61, 2.88)</td>
</tr>
<tr>
<td>Death or discharge to institution (%)</td>
<td>327 (25.4)</td>
<td>28 (24.3)</td>
<td>0.85 (0.53, 1.37)</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------</td>
<td>-----------</td>
<td>------------------</td>
</tr>
<tr>
<td>Day 90</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death (%)</td>
<td>62 (4.8)</td>
<td>11 (9.6)</td>
<td>1.94 (0.93, 4.06)</td>
</tr>
<tr>
<td>Barthel Index</td>
<td>76.9 (31.6)</td>
<td>75.0 (35.8)</td>
<td>0.65 (-4.41, 5.71)</td>
</tr>
<tr>
<td>Zung Depression Scale (ZDS, /100)</td>
<td>52.4 (20.7)</td>
<td>57.2 (23.1)</td>
<td>3.91 (-0.10, 7.92)</td>
</tr>
<tr>
<td>EQ-5D Health Utility Status (HUS, /1)</td>
<td>0.56 (0.38)</td>
<td>0.56 (0.36)</td>
<td>0.01 (-0.05, 0.07)</td>
</tr>
<tr>
<td>EQ-Visual Analogue Scale (EQ-VAS, /100)</td>
<td>63.4 (26.2)</td>
<td>63.4 (30.2)</td>
<td>1.76 (-3.14, 6.66)</td>
</tr>
<tr>
<td>Verbal Fluency</td>
<td>11.8 (7.2)</td>
<td>11.2 (8.0)</td>
<td>0.18 (-1.39, 1.75)</td>
</tr>
<tr>
<td>TICS-M</td>
<td>18.7 (8.7)</td>
<td>16.7 (9.6)</td>
<td>-0.68 (-2.61, 1.26)</td>
</tr>
<tr>
<td>MMSE</td>
<td>13.9 (5.8)</td>
<td>12.5 (6.5)</td>
<td>-0.44 (-1.72, 0.84)</td>
</tr>
</tbody>
</table>

Data are n (%), mean (SD), median [interquartile range], mean difference (MD) or odds ratio (OR) with 95% confidence intervals. Comparison using logistic regression, multiple regression or ordinal regression. Adjusted for age, sex, baseline mRS, history of previous stroke, history of diabetes mellitus, TACS, nitrate use, baseline SSS, thrombolysis, feeding status, time to randomisation, baseline SBP, GTN/no GTN and continue/stop. *=ordinal logistic regression.
Supplementary table 5: Change in BP from baseline to day 1 and association with mRS at day 90 by degree of ipsilateral carotid stenosis and treatment allocation

<table>
<thead>
<tr>
<th>Carotid stenosis (%)</th>
<th>ΔSBP</th>
<th>Overall OR (95% CI)</th>
<th>p</th>
<th>Interaction p</th>
<th>GTN vs. no GTN OR (95% CI)</th>
<th>p</th>
<th>Interaction p</th>
<th>Stop vs. Continue OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>-8.0</td>
<td>0.95 (0.90, 1.00)</td>
<td>0.07</td>
<td>0.37</td>
<td>1.05 (0.87, 1.28)</td>
<td>0.61</td>
<td>0.88</td>
<td>0.96 (0.73, 1.26)</td>
<td>0.77</td>
</tr>
<tr>
<td>30-50</td>
<td>-8.1</td>
<td>0.93 (0.81, 1.07)</td>
<td>0.31</td>
<td>0.63</td>
<td>0.84 (0.50, 1.42)</td>
<td>0.52</td>
<td>0.94</td>
<td>0.91 (0.46, 1.80)</td>
<td>0.79</td>
</tr>
<tr>
<td>50-70</td>
<td>-8.3</td>
<td>0.80 (0.66, 0.97)</td>
<td>0.026</td>
<td>0.66</td>
<td>0.77 (0.41, 1.45)</td>
<td>0.41</td>
<td>0.44</td>
<td>1.93 (0.85, 4.41)</td>
<td>0.12</td>
</tr>
<tr>
<td>≥70</td>
<td>-5.7</td>
<td>1.05 (0.90, 1.22)</td>
<td>0.55</td>
<td>0.34</td>
<td>0.53 (0.32, 0.90)</td>
<td>0.019</td>
<td>0.98</td>
<td>1.44 (0.72, 2.91)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

ΔSBP = SBP day 0 - SBP day 1 (mmHg). Data are mean (SD) or odds ratio (OR) with 95% confidence intervals. Comparison using ordinal regression. Adjusted for age, sex, baseline mRS, history of previous stroke, history of diabetes mellitus, TACS, nitrate use, baseline SSS, thrombolysis, feeding status, time to randomisation, baseline SBP, stop/continue antihypertensives and GTN/no GTN. Overall ORs per 10mmHg reduction in BP.
Supplementary table 6: Change in BP from baseline to day 1 and association with mRS at day 90 by degree of bilateral carotid stenosis and treatment allocation

<table>
<thead>
<tr>
<th>Carotid stenosis (%)</th>
<th>ΔSBP</th>
<th>Overall OR (95% CI)</th>
<th>p</th>
<th>Interaction p</th>
<th>GTN vs. no GTN OR (95% CI)</th>
<th>p</th>
<th>Interaction p</th>
<th>Stop vs. Continue OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>-8.1 (18.4)</td>
<td>0.95 (0.90, 1.01)</td>
<td>0.09</td>
<td>0.10</td>
<td>1.02 (0.83, 1.26)</td>
<td>0.83</td>
<td>0.66</td>
<td>0.94 (0.70, 1.25)</td>
<td>0.66</td>
</tr>
<tr>
<td>30-50</td>
<td>-5.6 (19.4)</td>
<td>0.83 (0.67, 1.03)</td>
<td>0.09</td>
<td>0.22</td>
<td>1.27 (0.57, 2.83)</td>
<td>0.56</td>
<td>0.22</td>
<td>1.05 (0.37, 3.01)</td>
<td>0.92</td>
</tr>
<tr>
<td>≥50</td>
<td>-8.6 (19.5)</td>
<td>1.95 (0.74, 1.21)</td>
<td>0.65</td>
<td>0.21</td>
<td>1.01 (0.44, 2.32)</td>
<td>0.99</td>
<td>0.59</td>
<td>0.54 (0.16, 1.86)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

ΔSBP = SBP day 0 - SBP day 1 (mmHg). Data are n (%), mean (SD), median [interquartile range], mean difference (MD) or odds ratio (OR) with 95% confidence intervals. Comparison using ordinal regression. Adjusted for age, sex, baseline mRS, history of previous stroke, history of diabetes mellitus, TACS, nitrate use, baseline SSS, thrombolysis, feeding status, time to randomisation, baseline SBP, stop/continue antihypertensives and GTN/no GTN. Overall ORs per 10mmHg reduction in BP.