Additional file 1: General trial details of PDE-5 inhibitors

<table>
<thead>
<tr>
<th>Sildenafil</th>
<th>Reference</th>
<th>Patients</th>
<th>Country</th>
<th>Treatment</th>
<th>Duration</th>
<th>GS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boole et al. 1996</td>
<td>History of ED &gt;6 months (mean 3.4 years) ED severity: no details Age:48 (36-63) years</td>
<td>UK</td>
<td>(1) sildenafil 25 mg (2) placebo x-over n=12</td>
<td>2x1 week</td>
<td>R1, D1, W1</td>
<td></td>
</tr>
<tr>
<td>Padma-Nathan et al. 1998 [103]</td>
<td>History of ED &gt;6 months (mean 5 yrs) ED severity: no details Age:90 (26-81) years Organic 59%, Psychogenic 15% Mixed 26%</td>
<td>USA</td>
<td>(1) sildenafil 25-100 mg, n=163 (2) placebo, n=166 As needed, approx one hour before intercourse, max one dose/day</td>
<td>12 weeks</td>
<td>R1, D2, W1</td>
<td></td>
</tr>
<tr>
<td>Goldstein et al. 1998 dose-escalation study</td>
<td>History of ED &gt;6 months (mean 3 years) ED severity: no details Age:58 (20-87) years</td>
<td>USA</td>
<td>(1) sildenafil 25 mg, n=102 (2) sildenafil 50 mg, n=107 (3) sildenafil 100 mg, n=107 (4) placebo, n=216 As needed, approx one hour before intercourse, max one dose/day</td>
<td>24 weeks</td>
<td>R1, D2, W1</td>
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</tr>
<tr>
<td>Boulton et al. 2001</td>
<td>History of ED due to spinal cord injury (T6-L5) &gt;6 months (mean 7 years), with grade 2 or more reflexogenic response to PVS ED severity: no details SC lesion: classified Age:33 (21-49) years</td>
<td>UK</td>
<td>(1) sildenafil 50 mg, n=12 (2) placebo, n=13 As needed, approx one hour before intercourse, max one dose/day</td>
<td>4 weeks</td>
<td>R1, D2, W1</td>
<td></td>
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<tr>
<td>Giuliano et al. 1999</td>
<td>ED due to spinal cord injury &gt;6 months (mean 10 years) ED severity: no details SC lesion: classified Age:38 (19-63) years</td>
<td>Europe, Australia</td>
<td>(1) sildenafil 25-100 mg, n=175 (2) placebo, n=174 (n=complete: 178 randomised) As needed, approx one hour before intercourse, max one dose/day</td>
<td>2x6 week x-over with 2 week washout</td>
<td>R2, D2, W1</td>
<td></td>
</tr>
<tr>
<td>Dinsmore et al. 1999</td>
<td>History of ED &gt;6 months (most &gt;3 years) ED severity: no details Age:56 (29-89) years Organic 20%, Psychogenic 40%, Mixed 38%, Other 2%</td>
<td>UK</td>
<td>(1) sildenafil 25-100 mg, n=57 (2) placebo, n=54 As needed, approx one hour before intercourse, max one dose/day</td>
<td>12 weeks</td>
<td>R2, D2, W1</td>
<td></td>
</tr>
<tr>
<td>Montorsi et al. 1999</td>
<td>History of ED &gt;6 months (most &gt;4 years) ED severity: no details Age:56 (19-78) years Organic 32%, Psychogenic 25%, Mixed 43%</td>
<td>Denmark, Ireland, Italy, Norway, Sweden, UK</td>
<td>(1) sildenafil 25 mg, n=128 (2) sildenafil 50 mg, n=132 (3) sildenafil 100 mg, n=127 (4) placebo, n=127 As needed, approx one hour before intercourse, max one dose/day</td>
<td>12 weeks</td>
<td>R2, D2, W1</td>
<td></td>
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<tr>
<td>Rendell et al. 1999</td>
<td>History of ED &gt;6 months (mean 5 years) and diabetes (mean 12 years) ED severity: no details Age:57 (27-79) years Organic 95%, Mixed 5%</td>
<td>USA</td>
<td>(1) sildenafil 25-100 mg, n=136 (2) placebo, n=132 As needed, approx one hour before intercourse, max one dose/day</td>
<td>12 weeks</td>
<td>R2, D2, W1</td>
<td></td>
</tr>
<tr>
<td>Tan et al. 2000</td>
<td>History of ED &gt;6 months (most &gt;3 years) ED severity: no details Age:52 (26-78) years Organic 63%. Psychogenic 13%, Mixed 24%</td>
<td>SE Asia (Malaysia, Singapore, Philippines)</td>
<td>(1) sildenafil 25-100 mg, n=127 (2) placebo, n=127 As needed, approx one hour before intercourse, max one dose/day</td>
<td>12 weeks</td>
<td>R2, D2, W0</td>
<td></td>
</tr>
<tr>
<td>Olsson et al. 2000</td>
<td>History of ED &gt;3 months (most &gt;4 years), not organic aetiology ED severity: no details, but had 1 or more g3/4 erection in prev 4 weeks Age: 53 (24-70) years Psychogenic 99%, Mixed 41% (2 pts organic)</td>
<td>UK, France, Sweden</td>
<td>(1) sildenafil 10 mg, n=90 (2) sildenafil 25 mg, n=85 (3) sildenafil 50 mg, n=81 (4) placebo, n=95 As needed, approx one hour before intercourse, max one dose/day</td>
<td>4 weeks</td>
<td>R1, D1, W1</td>
<td></td>
</tr>
<tr>
<td>Palmer et al. 2000</td>
<td>ED and spina bifida ED severity: no details SC lesions: region given, not classified Age: 19-35 years Neurogenic</td>
<td>USA</td>
<td>(1) sildenafil 25 mg (2) sildenafil 50 mg (3) placebo (4) placebo n=17 5 tablets per treatment, complete sets taken in random order As needed, approx one hour before intercourse</td>
<td>4 treatment x-over</td>
<td>R1, D1, W0</td>
<td></td>
</tr>
<tr>
<td>Chen et al. 2001</td>
<td>History of ED &gt;6 months (mean 4 years) ED severity: no details Age:60 (26-80) years Organic 82%, Psychogenic 8%, Mixed 10%</td>
<td>Taiwan</td>
<td>(1) sildenafil 25-100 mg, n=119 (2) placebo, n=117 As needed, approx one hour before intercourse, max one dose/day</td>
<td>12 weeks</td>
<td>R1, D2, W1</td>
<td></td>
</tr>
<tr>
<td>Hussein et al. 2001</td>
<td>History of ED (most &gt;4 years) and parkinsonism Age:61 (48-88) years for Parkinson's disease Age:54 (46-81) years for multiple system atrophy</td>
<td>USA</td>
<td>(1) sildenafil 25-100 mg, n=14 (2) placebo, n=16 As needed, approx one hour before intercourse, max one dose/day</td>
<td>2x10 week x-over</td>
<td>R1, D1, W1</td>
<td></td>
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<tr>
<td>Boulot et al. 2001</td>
<td>History of ED (mean &gt;3 years) and diabetes ED severity: no details Age:59 (38-80) years</td>
<td>Denmark, France, Germany, Sweden, UK</td>
<td>(1) sildenafil 25-100 mg, n=110 (2) placebo, n=109 As needed, approx one hour before intercourse, max one dose/day</td>
<td>12 weeks</td>
<td>R1, D2, W0</td>
<td></td>
</tr>
<tr>
<td>Meuleman et al. 2001 [363]</td>
<td>History of ED &gt;6 months (most &gt;4 years) ED severity: no details Age:55 (23-82) years Organic 29%, Psychogenic 32%, Mixed 37%, Other 2%</td>
<td>Belgium, France, Germany, Netherlands, UK</td>
<td>(1) sildenafil 25-100 mg, n=159 (2) placebo, n=158 As needed, approx one hour before intercourse, max one dose/day</td>
<td>26 weeks</td>
<td>R1, D2, W1</td>
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</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>ASSESS-2 (2001)</td>
<td>ED severity</td>
<td>Age (years)</td>
<td>ED treatment</td>
<td>Duration</td>
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<tr>
<td>Eardley et al. 2001</td>
<td>USA</td>
<td>History of ED &gt;6 months (mean 3 years)</td>
<td>mild to moderate, with 1 or more gd3/4 erections in previous 4 weeks</td>
<td>Age:53 (33-89)</td>
<td>UK</td>
<td>2x4 week x-over</td>
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<tr>
<td>Lewis et al. 2001</td>
<td>USA</td>
<td>History of ED &gt;6 months (most &gt;3 years)</td>
<td>ED severity: no details</td>
<td>Age:59 (36-81)</td>
<td>USA</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Seidman et al. 2001</td>
<td>USA</td>
<td>History of ED &gt;6 months (mean &gt;5 years) and depression (HAM-D21 &gt;12)</td>
<td>ED severity: no details</td>
<td>Age:56 ±11 years</td>
<td>USA</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Incrocci et al. 2001</td>
<td>Netherlands</td>
<td>ED following radiotherapy for PC</td>
<td>ED severity: no details</td>
<td>Age:68 (56-79) years</td>
<td>Netherlands</td>
<td>2x6 week x-over</td>
</tr>
<tr>
<td>Seibert et al. 2002</td>
<td>Brazil</td>
<td>ED and chronic renal failure (min 12 haemodialysis hrs/wk)</td>
<td>mild to severe (75% mild to mod, 13% severe)</td>
<td>Age:48 ±10 years</td>
<td>Brazil</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Blecher et al. 2002</td>
<td>Argentina, Chile, Peru, Uruguay</td>
<td>History of ED (most &gt;2 years)</td>
<td>mild to severe (75% mild to mod, 17% severe)</td>
<td>Age:57 ±11 years</td>
<td>Argentina, Chile, Peru, Uruguay</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Young et al. 2002</td>
<td>USA</td>
<td>History of ED &gt;6 months</td>
<td>mild to severe (60% mild to mod, 30% severe)</td>
<td>Age:54 (3-84) years</td>
<td>USA</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Glini et al. 2002</td>
<td>Mexico</td>
<td>History of ED &gt;6 months</td>
<td>ED severity: no details</td>
<td>Age:57 (27-85) years</td>
<td>Mexico</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Gomez et al. 2002</td>
<td>Columbia, Ecuador, Venezuela</td>
<td>History of ED &gt;6 months (most &gt;3 years)</td>
<td>ED severity: no details</td>
<td>Age:56 (22-77) years</td>
<td>Latin America</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Lindsey et al. 2002</td>
<td>UK</td>
<td>ED following rectal surgery for cancer and IBD</td>
<td>ED severity: 55% severe, 44% mild/mod</td>
<td>Age:59 (QDR 49-65)</td>
<td>UK</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Nurnberg et al. 2003</td>
<td>USA</td>
<td>ED (for &gt;4 weeks) due to antidepressant treatment for MDD (in remission) (&lt;10 on HAM-D and HAM-A)</td>
<td>ED severity: no details</td>
<td>Age:45±8 years</td>
<td>USA</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Padma-Nathan et al. 2003</td>
<td>USA</td>
<td>History of ED &gt;6 months (most &gt;6 years), and previous response to sildenafil</td>
<td>ED severity: 40% severe, 21% mild/mod</td>
<td>Age:52 (26-78) years</td>
<td>USA</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Kongkanand et al. 2003</td>
<td>Thailand</td>
<td>History of ED &gt;6 months (most &gt;2 years)</td>
<td>ED severity: 71% mod or severe, 17% mild/mod</td>
<td>Age:55 (26-77) years</td>
<td>Thailand</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Levinson et al. 2003</td>
<td>Egypt and S Africa</td>
<td>History of ED &gt;6 months (mean 4 years)</td>
<td>ED severity: no details</td>
<td>Age:52 (26-78) years</td>
<td>Egypt, S Africa</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Sluckey et al. 2003</td>
<td>Australia, Argentina, Brazil, Canada, Italy, Spain</td>
<td>History of ED &gt;6 months (mean 5 years) and type 1 diabetes</td>
<td>ED severity: no details</td>
<td>Age:47 (25-69) years</td>
<td>Australia, Argentina, Brazil, Canada, Italy, Spain</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Choi et al. 2003</td>
<td>Korea</td>
<td>History of ED &gt;6 months (mean 5 years)</td>
<td>ED severity: no details</td>
<td>Age:51 (28-78) years</td>
<td>Korea</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Tigran et al. 2004</td>
<td>Belgium, France, Germany, Italy, Spain</td>
<td>History of ED (mean 4 years) with MDD (in remission)</td>
<td>ED severity: no details</td>
<td>Age:53 ±10 years</td>
<td>Belgium, France, Germany, Italy, Spain</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Safarnejad et al. 2004</td>
<td>Iran</td>
<td>History of ED &gt;6 months (mean &gt;3 years) and diabetes (mean 11 years)</td>
<td>ED severity: no details</td>
<td>Age:46 (35-88) years</td>
<td>Iran</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>
DeBusk et al. 2004
History of ED (mean 5 years) with stable CHD
ED severity: no details
Age: 62 (39-82) years
Organic 47%, Psychogenic 5%, Mixed 48%
USA
12 weeks R2, D1, W1

Mahon et al. 2005
History of ED (0.5-7 years) and on peritoneal
dialysis (0.5-5 years).
ED severity: no details
Age: 53 (26-74) years
UK
24 week x-over R0, D1, W1

Fowler et al. 2005
History of ED >6 months (most >4 years) and
MS >1 year (mean 10 years)
ED severity: no details
Age: 46 (23-73) years
USA, Europe
12 weeks R2, D2, W1

Tadalafil

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patients</th>
<th>Country</th>
<th>Treatment</th>
<th>Duration</th>
<th>QS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Padma-Nathan et al. 2001</td>
<td>History of ED &gt;3 months,ESE: mild to severe (25% severe, 66% mild to mod/mod)</td>
<td>USA</td>
<td>Tadalafil 2 mg, n=36; tadalafil 5 mg, n=37; tadalafil 10 mg, n=36; placebo, n=35</td>
<td>3 weeks</td>
<td>R1, D1, W1</td>
</tr>
<tr>
<td></td>
<td>Age: 56 ±11 years Excl: prev unsuccessful use of PDE5 inhibitor</td>
<td></td>
<td>As needed, max one dose/day, 14 doses in total</td>
<td></td>
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<tr>
<td>Saenz de Tejada et al. 2002</td>
<td>Diabetes and history of ED &gt;3 months, ESE: mild to severe Age: 56±9 years</td>
<td>Spain</td>
<td>Tadalafil 10 mg, n=73; tadalafil 20 mg, n=72; placebo, n=71</td>
<td>12 weeks</td>
<td>R1, D1, W1</td>
</tr>
<tr>
<td></td>
<td>Age: 57 (22-87) years Organic 35%, Psychogenic 30%, Mixed 35%</td>
<td></td>
<td>As needed, max one dose/day, 2 attempts/4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Porst et al. 2003</td>
<td>History of ED &gt;3 months, ESE: severe (35%), mod 25% Age: 57 (22-87) years</td>
<td>Germany, Italy,</td>
<td>Tadalafil 20 mg, n=175; placebo, n=173</td>
<td>2 weeks</td>
<td>R2, D2, W1</td>
</tr>
<tr>
<td></td>
<td>Age: 55 (22-78) years Organic 35%, Psychogenic 30%, Mixed 35%</td>
<td>USA</td>
<td>2 attempts/4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eardley et al. 2004</td>
<td>History of ED &gt;3 months, ESE: mild to severe (severe 40%, mod 25%)</td>
<td>UK, Italy, USA</td>
<td>Tadalafil 20 mg, n=168; placebo, n=52</td>
<td>12 weeks</td>
<td>R1, D1, W1</td>
</tr>
<tr>
<td></td>
<td>Age: 53 (26-78) years Organic 35%, Psychogenic 29%, Mixed 38%</td>
<td>(Western European)</td>
<td>As needed, max one dose/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skoumal et al. 2004</td>
<td>History of ED &gt;3 months, ESE: severe (23%) mod 30% Age: 53 (26-78) years</td>
<td>Czech Republic,</td>
<td>Tadalafil 20 mg, n=301; placebo, n=102</td>
<td>12 weeks</td>
<td>R1, D1, W1</td>
</tr>
<tr>
<td></td>
<td>Age: 53 (26-78) years Organic 29%, Psychogenic 16%, Mixed 56% Excl due to prev unsuccessful use of sildenafil at disapproval of investigators</td>
<td>Poland, Slovakia, Israel, Hungary, Lebanon, Romania</td>
<td>As needed, max one dose/day</td>
<td></td>
<td></td>
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<tr>
<td>Sofitel et al. 2004</td>
<td>History of ED &gt;3 months, ESE: mild to severe (42% severe, 26% mod 29%)</td>
<td>USA, Puerto Rico</td>
<td>Tadalafil 20 mg, n=159; placebo, n=48</td>
<td>12 weeks</td>
<td>R2, D2, W1</td>
</tr>
<tr>
<td></td>
<td>Age: 59 ±10 years Organic 57%, Psychogenic 10%, Mixed 33% Excl: prev unsuccessful use of sildenafil</td>
<td>(70-100% white, 12% Hispanic)</td>
<td>As needed, max one dose/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montorsi et al. 2004</td>
<td>History of ED &gt;3 months, ESE: mild to severe (66% with postop penile tumescence)</td>
<td>Canada, Germany, Italy, Netherlands, Spain, UK, USA</td>
<td>Tadalafil 20 mg, n=201; placebo, n=102</td>
<td>12 weeks</td>
<td>R1, D1, W1</td>
</tr>
<tr>
<td></td>
<td>Age: 60 ±5 years Organic 35%, Psychogenic 1%, Mixed 64% Excl: prev unsuccessful use of sildenafil</td>
<td>&gt;60% white</td>
<td>As needed, max one dose/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carson et al. 2006</td>
<td>History of ED &gt;3 months, ESE: mild to severe (50% mod 17%) Age: 59 ±10 years</td>
<td>USA</td>
<td>Tadalafil 20 mg, n=146; placebo, n=49</td>
<td>12 weeks</td>
<td>R1, D1, W1</td>
</tr>
<tr>
<td></td>
<td>Organic 83%, Psychogenic 3%, Mixed 14% Excl: prev unsuccessful use of sildenafil</td>
<td>&gt;80% white, 15%非洲</td>
<td>As needed, max one dose/day</td>
<td></td>
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</tbody>
</table>

Vardenafil

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patients</th>
<th>Country</th>
<th>Treatment</th>
<th>Duration</th>
<th>QS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porst et al. 2001</td>
<td>History of ED &gt;6 months, most &gt;2 years, ESE: mild to severe (33% severe, 35% moderate)</td>
<td>Belgium, France, Germany, Netherlands, Poland, RSA, USA</td>
<td>Vardenafil 5 mg, n=146; vardenafil 10 mg, n=140; placebo, n=147</td>
<td>12 weeks</td>
<td>R1, D2, W1</td>
</tr>
<tr>
<td></td>
<td>Age: 52 years Organic 30%, Psychogenic 27%, Mixed 43% Excl: prev unsuccessful use of PDE5 inhibitor</td>
<td></td>
<td>(4) placebo, n=147</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hellstrom et al. 2002</td>
<td>History of ED &gt;6 months, most &gt;3 years, ESE: mild to severe (38% mod 30%) Age: 57 years</td>
<td>USA, Canada</td>
<td>Vardenafil 5 mg, n=205; vardenafil 10 mg, n=206; vardenafil 20 mg, n=197</td>
<td>26 weeks</td>
<td>R2, D1, W1</td>
</tr>
<tr>
<td></td>
<td>Organic 58%, Psychogenic 7%, Mixed 35% Excl: prev unsuccessful use of PDE5 inhibitor</td>
<td></td>
<td>(4) placebo, n=197</td>
<td></td>
<td></td>
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<tr>
<td>Study</td>
<td>Duration</td>
<td>Severity</td>
<td>Age (years)</td>
<td>Main Findings</td>
<td>Country, Country, Country</td>
</tr>
<tr>
<td>-----------------</td>
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</tr>
<tr>
<td>Goldstein et al. 2003</td>
<td>History of ED &gt;6 months, and diabetes</td>
<td>ED severity: mild to severe (75%, mod 25%)</td>
<td>57</td>
<td>USA, Canada</td>
<td>(1) vardenafil 10 mg, n=149 (2) vardenafil 20 mg, n=141 (3) placebo, n=143 [ITT]</td>
</tr>
<tr>
<td>Brock et al. 2003</td>
<td>History of ED following NSRRP &gt;6 months</td>
<td>ED severity: mild to severe (70%, mod 17%)</td>
<td>60</td>
<td>USA, Canada</td>
<td>(1) vardenafil 10 mg, n=139 (2) vardenafil 20 mg, n=147 (3) placebo, n=137 [ITT]</td>
</tr>
<tr>
<td>Hatzichristou et al. 2004</td>
<td>ED (most &gt;2 years)</td>
<td>ED severity: no details</td>
<td>54</td>
<td>Austria, France, Germany, Greece, Italy, Netherlands, Spain, Switzerland, UK</td>
<td>(1) vardenafil 5-20 mg, n=155 (2) placebo, n=154 [ITT]</td>
</tr>
<tr>
<td>Carson et al. 2004</td>
<td>ED (most &gt;4 years), previously unresponsive to sildenafil</td>
<td>ED severity: moderate to severe (74%, mod 26%)</td>
<td>60</td>
<td>Many ?USA, UK, Canada, Greece, Australia, Denmark, Brazil</td>
<td>(1) vardenafil 5-20 mg, n=220 (2) placebo, n=225 [ITT]</td>
</tr>
<tr>
<td>Nagao et al. 2004</td>
<td>History of ED &gt;6 months</td>
<td>ED severity: mild to severe (72%, mod 28%)</td>
<td>51</td>
<td>Japan</td>
<td>(1) vardenafil 5 mg, n=67 (2) vardenafil 10 mg, n=75 (3) vardenafil 20 mg, n=66 (4) placebo, n=71 [ITT]</td>
</tr>
</tbody>
</table>