Supplementary Material

▶ Supplementary file no. 1

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<th>No.</th>
<th>Author</th>
<th>Reason</th>
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<td>Kashiwagi et al.</td>
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</tr>
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<td>5</td>
<td>Takeuchi et al.[1]</td>
<td>Single arm</td>
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<td>6</td>
<td>Smulders et al.</td>
<td>Conference abstract</td>
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<td>Kadokura et al.</td>
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<td>8</td>
<td>Ohki et al.[2]</td>
<td>Single arm</td>
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<td>Yamada et al.[3]</td>
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<td>13</td>
<td>Iizuka et al.[4]</td>
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<td>16</td>
<td>Kusama et al.[5]</td>
<td>abstract</td>
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<td>17</td>
<td>Mihaei et al.[6]</td>
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<td>18</td>
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<td>healthy patients</td>
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<td>Zhang et al.[8]</td>
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<td>24</td>
<td>Goto et al.[9]</td>
<td>poster</td>
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<td>25</td>
<td>Ohkura et al.[10]</td>
<td>review</td>
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<td>Non-English</td>
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<td>Yokote et al.</td>
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<td>34</td>
<td>Osaki et al.[11]</td>
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<td>35</td>
<td>Terauchi et al.[12]</td>
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<td>37</td>
<td>Berhan et al.[13]</td>
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▶ Supplementary file no. 2  Effect estimate of ipragliflozin efficacy as monotherapy and as add-on to other treatments in mean difference.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies, n</th>
<th>Participants, n</th>
<th>Effect Estimate [95% CI]</th>
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<tr>
<td>A. Efficacy of ipragliflozin as monotherapy</td>
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<td>1. Change in HbA1c (%)</td>
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<tr>
<td>12.5 mg</td>
<td>2</td>
<td>281</td>
<td>-0.55 [-0.72, -0.37]</td>
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<td>50 mg</td>
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<td>432</td>
<td>-0.79 [-1.11, -0.47]</td>
</tr>
<tr>
<td>100 mg</td>
<td>2</td>
<td>165</td>
<td>-0.92 [-1.70, -0.14]</td>
</tr>
<tr>
<td>150 mg</td>
<td>1</td>
<td>137</td>
<td>-0.73 [-0.98, -0.48]</td>
</tr>
<tr>
<td>300 mg</td>
<td>2</td>
<td>161</td>
<td>-0.76 [-0.97, -0.55]</td>
</tr>
<tr>
<td>2. Change in FPG (mg/dL)</td>
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<tr>
<td>12.5 mg</td>
<td>2</td>
<td>281</td>
<td>-21.79 [-33.97, -9.60]</td>
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<tr>
<td>50 mg</td>
<td>5</td>
<td>449</td>
<td>-32.89 [-57.73, -8.05]</td>
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<tr>
<td>100 mg</td>
<td>3</td>
<td>184</td>
<td>-47.63 [-64.44, -30.82]</td>
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<td>150 mg</td>
<td>1</td>
<td>137</td>
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<td>300 mg</td>
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<td>3. Change in FSI (μU/mL)</td>
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<td>50 mg</td>
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<td>148</td>
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<td>19</td>
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</table>
### Effect estimate of ipragliflozin efficacy as monotherapy and as add-on to other treatments in mean difference.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies, n</th>
<th>Participants, n</th>
<th>Effect Estimate [95% CI]</th>
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<tbody>
<tr>
<td>4. Change in Body Weight (Kg)</td>
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</tr>
<tr>
<td>12.5 mg</td>
<td>2</td>
<td>281</td>
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<tr>
<td>50 mg</td>
<td>5</td>
<td>449</td>
<td>-1.10 [-1.74, -0.47]</td>
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<td>100 mg</td>
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<td>184</td>
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<td>150 mg</td>
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<td>137</td>
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<td>300 mg</td>
<td>2</td>
<td>161</td>
<td>-1.67 [-2.43, -0.92]</td>
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<tr>
<td>5. Change in HOMA-β (%)</td>
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<td>50 mg</td>
<td>1</td>
<td>129</td>
<td>9.40 [3.83, 14.97]</td>
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</table>

### Efficacy of ipragliflozin as add-on therapy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies, n</th>
<th>Participants, n</th>
<th>Effect Estimate [95% CI]</th>
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<tbody>
<tr>
<td>1. Change in HbA1c (%)</td>
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<tr>
<td>Ipragliflozin + metformin</td>
<td>3</td>
<td>467</td>
<td>-0.69 [-1.26, -0.12]</td>
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<td>Ipragliflozin + insulin</td>
<td>1</td>
<td>255</td>
<td>-1.06 [-1.23, -0.89]</td>
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<tr>
<td>Ipragliflozin + sulfonylurea</td>
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<td>404</td>
<td>-0.70 [-1.58, 0.19]</td>
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<tr>
<td>Ipragliflozin + pioglitazone</td>
<td>1</td>
<td>151</td>
<td>-0.86 [-1.11, -0.61]</td>
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<tr>
<td>2. Change in FPG (mg/dL)</td>
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<td></td>
</tr>
<tr>
<td>Ipragliflozin + metformin</td>
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<td>469</td>
<td>-21.82 [-33.81, -9.82]</td>
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<tr>
<td>Ipragliflozin + insulin</td>
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<td>255</td>
<td>-39.70 [-49.93, -29.47]</td>
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<tr>
<td>Ipragliflozin + sulfonylurea</td>
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<td>-24.08 [-55.63, 7.47]</td>
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<td>Ipragliflozin + pioglitazone</td>
<td>1</td>
<td>151</td>
<td>-42.50 [-53.10, -31.90]</td>
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<tr>
<td>3. Change in FSI (μU/mL)</td>
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<tr>
<td>Ipragliflozin + metformin</td>
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<td>338</td>
<td>-1.17 [-2.01, -0.34]</td>
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<td>Ipragliflozin + pioglitazone</td>
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<td>151</td>
<td>-1.79 [-2.82, -0.76]</td>
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<tr>
<td>4. Change in Body Weight (Kg)</td>
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<td>Ipragliflozin + metformin</td>
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<td>469</td>
<td>-1.54 [-1.93, -1.15]</td>
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<td>Ipragliflozin + insulin</td>
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<td>255</td>
<td>-1.04 [-1.39, -0.69]</td>
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<td>Ipragliflozin + pioglitazone</td>
<td>1</td>
<td>151</td>
<td>-2.80 [-3.51, -2.09]</td>
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<tr>
<td>5. Change in HOMA-β (%)</td>
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<tr>
<td>Ipragliflozin + metformin</td>
<td>1</td>
<td>168</td>
<td>3.80 [0.37, 7.23]</td>
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<tr>
<td>Ipragliflozin + sulfonylurea</td>
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<td>240</td>
<td>9.20 [4.92, 13.48]</td>
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<td>Ipragliflozin + pioglitazone</td>
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<td>151</td>
<td>3.30 [-0.33, 6.93]</td>
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<td>6. Change in SBP (mmHg):</td>
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<td>469</td>
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<td>Ipragliflozin + insulin</td>
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<td>404</td>
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<td>7. Change in DBP (mmHg):</td>
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<td>469</td>
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<td>1</td>
<td>151</td>
<td>-5.80 [-9.12, -2.48]</td>
</tr>
</tbody>
</table>

HbA1c, glycated hemoglobin; FPG, fasting plasma glucose; FSI, fasting serum insulin; HOMA-β, homeostasis model assessment of β cell function; SBP, systolic blood pressure; DBP, diastolic blood pressure; CI, confidence interval.