Effects of Dapagliflozin on Symptoms, Function and Quality of Life in Patients with Heart Failure: The DAPA-HF Trial

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On Behalf of the DAPA-HF Investigators
Disclosures

• Research Grants:
  • AstraZeneca, Boehringer Ingelheim

• Consultant/Advisory Board:
  • Amarin, Applied Therapeutics, AstraZeneca, Amgen, Bayer, Boehringer Ingelheim, Eisai, Glytec, GSK, Intarcia, Janssen, Eli Lilly, Merck (Diabetes), Novartis, Novo Nordisk, Sanofi

• DAPA-HF Trial was sponsored by AstraZeneca
Goals of Care in Heart Failure

• Reduce death and hospitalizations

• Improve health status
  • Symptoms
  • Physical Limitations
  • Quality of Life
DAPA-HF Design

- Informed consent
- Inclusion/exclusion
- KCCQ evaluated at Randomization, 4 and 8 months

Enrolment Randomization

N=2371

N=2373

Placebo

Dapagliflozin 10 mg once daily

≥844 Primary endpoints
Composite of:
- CV death
- HF hospitalization
- Urgent HF visit

Visit 1 Visit 2 Visit 3 Visit 4 Visit 5 Visit 6 etc.

Day -14 Day 0 Day 14 Day 60 Day 120 Every 120 days
Kansas City Cardiomyopathy Questionnaire

• 23 items that measure 4 clinical domains
  • Symptoms: Frequency and Severity
  • Physical Limitation
  • Quality of Life
  • Social Limitation
• Represents the patient’s perspective of their HF
• Scores range 0-100, higher scores reflect better health status
• Established validity, reliability and responsiveness
  • Independently associated with death and hospitalization
• 5-point threshold established as clinically meaningful change
Mapping the KCCQ Scales

Disease ➔ Symptoms ➔ Functional Limitation ➔ Quality of Life

- Total Symptom Score (TSS)
- Physical Limitation Scale
- Quality of Life, Social Limitations Scales

KCCQ Clinical Summary Score

KCCQ Overall Summary Score
Statistical Analysis

- Patients divided based on baseline KCCQ-TSS tertiles
- Effects of dapagliflozin on clinical outcomes across the KCCQ tertiles evaluated using Cox proportional-hazards models
- Between-group differences in mean KCCQ-TSS, CSS and OSS at 4 and 8 months assessed by using mixed models for repeated measures, adjusted for baseline KCCQ
- Responder analyses examined proportions of patients with a deterioration, and clinically meaningful improvements in KCCQ at 8 months (≥5 point [at least small], ≥10 point [at least moderate], and ≥15 point [large] change)
## Baseline Characteristics

<table>
<thead>
<tr>
<th>KCCQ-TSS at Baseline</th>
<th>Tertile 1 (N=1,487)</th>
<th>Tertile 2 (N=1,564)</th>
<th>Tertile 3 (N=1,392)</th>
<th>Total (N=4,443)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.8</td>
<td>66.4</td>
<td>66.8</td>
<td>66.3</td>
<td>0.007</td>
</tr>
<tr>
<td>Male</td>
<td>72.2%</td>
<td>78.0%</td>
<td>83.3%</td>
<td>77.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White Race</td>
<td>79.0%</td>
<td>73.0%</td>
<td>62.1%</td>
<td>71.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NT-proBNP (pg/mL)</td>
<td>1716</td>
<td>1389</td>
<td>1292</td>
<td>1432</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA Class III/IV</td>
<td>49.9%</td>
<td>29.4%</td>
<td>18.2%</td>
<td>32.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T2DM</td>
<td>45.9%</td>
<td>39.5%</td>
<td>40.7%</td>
<td>42.0%</td>
<td>0.004</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>44.0%</td>
<td>36.8%</td>
<td>35.4%</td>
<td>38.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACE-I/ARB/ARNI</td>
<td>94.2%</td>
<td>94.8%</td>
<td>93.7%</td>
<td>94.3%</td>
<td>0.544</td>
</tr>
<tr>
<td>Diuretic</td>
<td>96.2%</td>
<td>94.0%</td>
<td>90.5%</td>
<td>93.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>96.3%</td>
<td>96.3%</td>
<td>96.0%</td>
<td>96.2%</td>
<td>0.653</td>
</tr>
<tr>
<td>MRA</td>
<td>73.8%</td>
<td>71.5%</td>
<td>67.0%</td>
<td>70.9%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Effects of Dapagliflozin on Primary Endpoint by KCCQ Tertiles

<table>
<thead>
<tr>
<th>Cardiovascular Death, Hospitalization for HF or Urgent HF Visit</th>
<th>Dapagliflozin</th>
<th>Placebo</th>
<th>HR (95% CI)</th>
<th>p-value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤65.6 (n=1487)</td>
<td>162/768</td>
<td>209/719</td>
<td>0.70 (0.57, 0.86)</td>
<td></td>
</tr>
<tr>
<td>65.7-87.5 (n=1564)</td>
<td>119/773</td>
<td>152/791</td>
<td>0.77 (0.61, 0.98)</td>
<td>0.52</td>
</tr>
<tr>
<td>&gt;87.5 (n=1392)</td>
<td>73/693</td>
<td>116/699</td>
<td>0.62 (0.46, 0.83)</td>
<td></td>
</tr>
</tbody>
</table>
## Effects of Dapagliflozin on Secondary Endpoints by KCCQ Tertiles

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dapagliflozin</th>
<th>Placebo</th>
<th>HR (95% CI)</th>
<th>p for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV Death or Hospitalization for HF</td>
<td></td>
<td></td>
<td></td>
<td>0.53</td>
</tr>
<tr>
<td>≤65.6 (n=1487)</td>
<td>160/768</td>
<td>205/719</td>
<td>0.71 (0.57, 0.87)</td>
<td></td>
</tr>
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<td>0.62 (0.46, 0.83)</td>
<td></td>
</tr>
<tr>
<td>Hospitalization for HF or Urgent HF Visit</td>
<td></td>
<td></td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>≤65.6 (n=1487)</td>
<td>99/768</td>
<td>134/719</td>
<td>0.67 (0.51, 0.86)</td>
<td></td>
</tr>
<tr>
<td>65.7-87.5 (n=1564)</td>
<td>78/773</td>
<td>101/791</td>
<td>0.76 (0.56, 1.02)</td>
<td></td>
</tr>
<tr>
<td>&gt;87.5 (n=1392)</td>
<td>43/693</td>
<td>78/699</td>
<td>0.54 (0.37, 0.78)</td>
<td></td>
</tr>
<tr>
<td>Hospitalization for HF</td>
<td></td>
<td></td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>≤65.6 (n=1487)</td>
<td>96/768</td>
<td>130/719</td>
<td>0.67 (0.51, 0.87)</td>
<td></td>
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<td>77/699</td>
<td>0.55 (0.38, 0.79)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular Death</td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
</tr>
<tr>
<td>≤65.6 (n=1487)</td>
<td>107/768</td>
<td>121/719</td>
<td>0.84 (0.64, 1.09)</td>
<td></td>
</tr>
<tr>
<td>65.7-87.5 (n=1564)</td>
<td>63/773</td>
<td>81/791</td>
<td>0.78 (0.56, 1.09)</td>
<td></td>
</tr>
<tr>
<td>&gt;87.5 (n=1392)</td>
<td>39/693</td>
<td>54/699</td>
<td>0.72 (0.48, 1.09)</td>
<td></td>
</tr>
<tr>
<td>Death from Any Cause</td>
<td></td>
<td></td>
<td></td>
<td>0.45</td>
</tr>
<tr>
<td>≤65.6 (n=1487)</td>
<td>134/768</td>
<td>142/719</td>
<td>0.89 (0.70, 1.13)</td>
<td></td>
</tr>
<tr>
<td>65.7-87.5 (n=1564)</td>
<td>76/773</td>
<td>99/791</td>
<td>0.77 (0.57, 1.04)</td>
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<td>&gt;87.5 (n=1392)</td>
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<td>0.68 (0.47, 0.99)</td>
<td></td>
</tr>
</tbody>
</table>
Effect of Dapagliflozin on KCCQ Total Symptom Score at 4 and 8 months

KCCQ Total Symptom Score

- Placebo
- Dapagliflozin

Adjusted Mean KCCQ Score

- Baseline
- 4 Months
- 8 Months

Δ 1.91 p<0.0001
Δ 2.76 p<0.0001
Effect of Dapagliflozin on KCCQ Clinical Summary Score and Overall Summary Score at 4 and 8 months
Clinically Meaningful Change in KCCQ: Dapagliflozin vs. Placebo

**KCCQ Total Symptom Score**

- **Deterioration**
  - ≥ 5 points: p<0.0001, 32.9% Placebo, 25.3% Dapagliflozin (NNT=14)
  - OR: 0.84 (95% CI: 0.78, 0.90)

- **Improvement**
  - ≥ 5 points: p<0.0001, 50.9% Placebo, 58.3% Dapagliflozin (NNT=15)
  - ≥ 10 points: p<0.0001, 47.6% Placebo, 54.5% Dapagliflozin (NNT=18)
  - ≥ 15 points: p<0.0001, 48.2% Placebo, 54.0% Dapagliflozin (NNT=18)
  - OR: 1.15 (95% CI: 1.08-1.23, 1.08-1.22, 1.07-1.22)
Clinically Meaningful Change in KCCQ: Dapagliflozin vs. Placebo

KCCQ Clinical Summary Score

- Placebo vs. Dapagliflozin
  - Deterioration: NNT=12
  - Improvement: NNT=17

KCCQ Overall Summary Score

- Placebo vs. Dapagliflozin
  - Deterioration: NNT=15
  - Improvement: NNT=13

**OR: 95% CI**

- Clinical Summary Score
  - Placebo: OR: 0.86 (0.81-0.92)
  - Dapagliflozin: OR: 1.14 (1.08-1.21)

- Overall Summary Score
  - Placebo: OR: 0.85 (0.80-0.91)
  - Dapagliflozin: OR: 1.17 (1.10-1.25)
Conclusions

• Dapagliflozin improved all key clinical outcomes, including CV death and worsening HF, to a similar extent across the entire range of KCCQ at baseline

• Dapagliflozin improved all major components of KCCQ - effects amplified over time

• Fewer dapagliflozin-treated patients had significant deterioration, and more experienced small, moderate and large clinically meaningful improvements across all key domains of KCCQ

• Effects were substantial, with NNT ranging between 12 and 18 when compared to placebo after just 8 months of treatment

• Dapagliflozin offers a new approach to improving symptoms, functional limitations and quality of life in patients with HFrEF
Effects of dapagliflozin on symptoms, function and quality of life in patients with heart failure and reduced ejection fraction: results from the DAPA-HF Trial

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