The Integrated Results of the CANVAS (Canagliflozin Cardiovascular Assessment Study) Program

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The CANVAS Program

CV safety proved and marketing authorization achieved

UL 95% CI <1.8

Evaluate CV safety

UL 95% CI <1.3

CANVAS Program
N = 10,142

CANVAS Program
N = 4330

CANVAS-R
n = 5812

 Included Population

• T2DM ~14 years
• High CV risk
  – 2/3 with prior CV disease
  – 1/3 primary prevention
• High blood pressure
• Overweight
• Multiple comorbidities
Primary outcome
CV death, nonfatal myocardial infarction or stroke

Hazard ratio 0.86 (95% CI, 0.75-0.97)
p <0.0001 for noninferiority
p = 0.0158 for superiority

No. of patients
Placebo 4347 4153 2942 1240 1187 1120 789
Canagliflozin 5795 5566 4343 2555 2460 2363 1661

Intent-to-treat analysis
## Other vascular events and death

<table>
<thead>
<tr>
<th>Event</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death, nonfatal myocardial infarction, or nonfatal stroke</td>
<td>0.86 (0.75-0.97)</td>
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<tr>
<td>CV death</td>
<td>0.87 (0.72-1.06)</td>
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<tr>
<td>Nonfatal myocardial infarction</td>
<td>0.85 (0.69-1.05)</td>
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<tr>
<td>Nonfatal stroke</td>
<td>0.90 (0.71-1.15)</td>
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<tr>
<td>Hospitalization for heart failure</td>
<td>0.67 (0.52-0.87)</td>
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<tr>
<td>CV death or hospitalization for heart failure</td>
<td>0.78 (0.67-0.91)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.87 (0.74-1.01)</td>
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</tbody>
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**Intent-to-treat analysis**

- Favors Canagliflozin
- Favors Placebo
Composite of 40% Reduction in eGFR, End-stage Renal Disease, or Renal Death

Hazard ratio 0.60 (95% CI, 0.47-0.77)

Intent-to-treat analysis
Lower-extremity amputations

Hazard ratio 1.97 (95% CI, 1.41-2.75)

71% - toe or forefoot
29% - above ankle

No. at risk
Placebo 4344 4217 3037 1289 1247 1194 844
Canagliflozin 5790 5634 4420 2618 2536 2460 1765

Years since randomization

Patients with an event (%)
Benefits and risk

- **MACE:**
  - Placebo: 160 fewer patients per 1000 patients over 5 years
  - Canagliflozin: 23 fewer patients per 1000 patients over 5 years

- **Hospitalization for heart failure:**
  - Placebo: 17 fewer patients
  - Canagliflozin: 15 more patients

- **Renal composite Amputation:**
  - Placebo: 23 fewer patients per 1000 patients over 5 years
  - Canagliflozin: 16 fewer patients

- **Amputation:**
  - Placebo: 5 above ankle
  - Canagliflozin: 10 toe or forefoot
The CANVAS Program met its primary objective of demonstrating cardiovascular safety, and also showed efficacy of canagliflozin for the prevention of CV events.

Canagliflozin use was associated with an increased risk of amputation which should be taken into consideration when prescribing this agent.

These data suggest net overall benefit of canagliflozin for most patients with type 2 diabetes and high cardiovascular risk.
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