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Original research (includes database studies and QI projects)

Title: Dapagliflozin versus sacubitril-valsartan for heart failure with mildly reduced or preserved ejection fraction

Dapagliflozin versus sacubitril-valsartan for heart failure with mildly reduced or preserved ejection fraction

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Background: Heart failure with preserved ejection fraction (HFpEF) is associated with increased risk of heart failure hospitalizations (hHF) and cardiovascular death (CVD). Both dapagliflozin and sacubitril-valsartan have shown convincing reduction in combined risk of CVD and hHF in patients with mildly reduced ejection fraction (HFmrEF) or HFpEF. We aimed to investigate the cost-per-outcome implications of dapagliflozin vs. sacubitril-valsartan in treatment of HFmrEF or HFpEF patients, based on a comparison of randomized control trials.

Methods: We compared the annualized Cost Needed to Treat (CNT) to prevent the composite outcome of total hHF and CVD with dapagliflozin or sacubitril-valsartan. The CNT was estimated by multiplying the annualized Number Needed-to-Treat (aNNT) by the annual cost of therapy. The aNNTs were calculated based on data from the DELIVER and pooled analysis of PARAGLIDE-HF and PARAGON-HF trials for dapagliflozin and sacubitril-valsartan, respectively. Costs were based on 2022 US prices. Scenario analyses were performed to attenuate the differences in the studies' populations.

Results: The aNNT with dapagliflozin in DELIVER was 30 (95% confidence interval [CI]: 21-62) vs. 44 (CI: 25-311) with sacubitril-valsartan in pooled analysis of PARAGLIDE-HF and PARAGON-HF, with an annual cost of \$4,951 vs. \$5,576, respectively. The corresponding CNTs were therefore \$148,547 (95% CI: \$103,989 - \$306,997) for dapagliflozin and \$245,346 (95% CI: \$139,401 – 1,734,155) for sacubitril-valsartan (Table 1).

Conclusion: Dapagliflozin provides better monetary value than sacubitril-valsartan in preventing composite outcome of total hHF and CVD among patients with HFmrEF or HFpEF.

Table1. Step by step calculations of the number and cost needed to treat

<u>Parameter</u>	<u>Dapagliflozin</u>	<u>Sacubitril/valsartan</u>
Number of patients in control arm	3132	2622
Follow-up	2.3	2.8
Patient years of therapy in control arm	7203.6	7341.6
Number of events in control arm	1057	1181
Annualized Event Rate in Control Arm	14.67%	16.09%
Number of patients in intervention arm	3131	2640
Patient years of therapy in intervention arm	7201.3	7392
Number of events in the intervention arm (95% CI)	814 (708-941)	1016
Annualized Event Rate in the Intervention arm (95% CI)	11.30% (9.83%-13.06%)	13.83% (12.06%-15.76%)
Annualized Absolute Event Rate Reduction (95% CI)	3.37% (1.61%-4.84%)	2.25% (0.32%-4.02%)
Annualized Number Needed to Treat (95% CI)	30 (21-62)	44 (25-311)
Annual drug cost (US)	\$ 4,951.57	\$ 5,576.06
Cost Needed to Treat to prevent one event (95% CI)	\$ 148,547.13 (\$ 103,983-\$ 306,997.39)	\$ 245,346.77 (\$ 139,401.58-\$ 1,734,155.60)
<u>Secondary Outcome analysis</u>		
Cardiovascular death (95% CI)	\$1,138,861.29 (\$524,866.51 - ∞)	\$2,542,684.79 (\$775,072.76 - ∞)
All-cause Mortality (95% CI)	\$1,128,958.15 (\$401,077.24 - ∞)	\$2,185,816.71 (\$607,790.87 - ∞)