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COST-EFFECTIVENESS OF DAPAGLIFLOZIN IN THE TREATMENT OF HEART FAILURE WITH REDUCED EJECTION FRACTION (POOLED ANALYSIS FROM PARADIGM AND DAPA HF TRIALS)

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ABSTRACT

Bakground: The Dapagliflozin was associated with a reduction in cardiovascular mortality, all-cause mortality, and hospitalizations in patients with heart failure and reduced ejection fraction. **Objective:** To estimate the cost-effectiveness of Dapagliflozin in Gaza. **Design, Setting, and Participants:** Quality of life was based on trial EQ-5D scores. Hospital costs combined Medicare and private insurance reimbursement rates; medication costs included the wholesale acquisition cost for sacubitril/valsartan and Dapagliflozin. were performed on key inputs including: hospital costs, mortality benefit, hazard ratio for hospitalization reduction, drug costs, and quality-of-life estimates. **Main Outcomes and Measures**: Hospitalizations, quality-adjusted life-years (QALYs), costs, and incremental costs per QALY gained. **Results:** In DAPA HF trial: in patient with DM, the strategy of using dapagliflozin has an of $ 17287 per QALY gained and in patient without DM, the strategy of using dapagliflozin has an of $ 45192 per QALY gained. Indirect comparison between patients with dapagliflozin but without DM the strategy of using sacubitril/ valsartan has an ICER of $ 66000 per QALY gained and in patient with DM, ICER of 94 000 $ per QALY gained. **Conclusions:** For eligible patients with HF and reduced ejection fraction, Dapagliflozin was cost effective than the sacubitril/valsartan in Gaza.

INTRODUCTION

In DAPA HF trial, In this phase 3, placebo-controlled trial, we randomly assigned 4744 patients with New York Heart Association class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either dapagliflozin (at a dose of 10 mg once daily) or placebo, in addition to recommended therapy.

The primary outcome was a composite of worsening heart failure (hospitalization or an urgent visit resulting in intravenous therapy for heart failure) or cardiovascular death. Over a median of 18.2 months, the primary outcome occurred in 386 of 2373 patients (16.3%) in the dapagliflozin group and in 502 of 2371 patients (21.2%) in the placebo group (hazard ratio, 0.74; 95% confidence interval [CI], 0.65 to 0.85; P<0.001).

A first worsening heart failure event occurred in 237 patients (10.0%) in the dapagliflozin group and in 326 patients (13.7%) in the placebo group (hazard ratio, 0.70; 95% CI, 0.59 to 0.83).

Death from cardiovascular causes occurred in 227 patients (9.6%) in the dapagliflozin group and in 273 patients (11.5%) in the placebo group (hazard ratio, 0.82; 95% CI, 0.69 to 0.98); 276 patients (11.6%) and 329 patients (13.9%), respectively, died from any cause (hazard ratio, 0.83; 95% CI, 0.71 to 0.97).[1]

In PARADIGM trial, this double-blind trial, we randomly assigned 8442 patients with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either LCZ696 (at a dose of 200 mg twice daily) or enalapril (at a dose of 10 mg twice daily), in addition to recommended therapy. The primary outcome was a composite of death from cardiovascular causes or hospitalization for heart failure, but the trial was designed to detect a difference in the rates of death from cardiovascular causes.

The trial was stopped early, according to prespecified rules, after a median follow up of 27 months, because the boundary for an overwhelming benefit with LCZ696 had been crossed. At the time of study closure, the primary outcome had occurred in 914 patients (21.8%) in the LCZ696 group and 1117 patients (26.5%) in the enalapril group (hazard ratio in the LCZ696 group, 0.80; 95% confidence interval [CI], 0.73 to 0.87; P<0.001). A total of 711 patients (17.0%) receiving LCZ696 and 835 patients (19.8%) receiving enalapril died (hazard ratio for death from any cause, 0.84; 95% CI, 0.76 to 0.93; P<0.001); of these patients, 558 (13.3%) and 693

(16.5%), respectively, died from cardiovascular causes (hazard ratio, 0.80; 95% CI, 0.71 to 0.89; P<0.001).[2]

Study population

In DAPA HF trial, we randomly assigned 4744 patients (mean age 66.2± 11.0 years) with New York Heart Association class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either dapagliflozin (at a dose of 10 mg once daily) or placebo, in addition to recommended therapy. (Table 1).

Table 1: Model Inputs.

Dapagliflozin, HR (95% CI)	
Mortality	0.82 (0.69-0.98)
Hospitalization of Heart failure	0.70 (0.59-0.83)
Costs, median (range), $ Hospitalization Heart failure	1250 $
Annual treatment	600 $
Sacubitril/valsartan, HR (95% CI)	
Mortality	0.80 (0.71–0.89)
Hospitalization of Heart failure	0.79 (0.71-0.89)
Costs, median (range), $ Hospitalization Heart failure	1250 $
Annual treatment Sacubitril/valsartan	2052 $

Intervention Effects and Model Assumptions

Separate hazard ratios (HRs) for all-cause mortality, HF hospitalizations, non-HF hospitalizations, and absolute risk of dying.

In DAPA trial: For the primary composite outcome of CV death, HF hospitalization or an urgent HF visit the hazard ratio (HR) was 0.74 (0.65-0.85, *P* = .00001.) Within the components of the primary outcome, for a worsening HF event, the HR was 0.70 (0.59-0.83, *P* = .00003). For CV death, the HR was 0.82 (0.69-0.98, *P* =. 029).

In PARADIGM HF, A total of 558 deaths (13.3%) in the LCZ696 group and 693 (16.5%) in the enalapril group were due to cardiovascular causes (hazard ratio, 0.80; 95% CI, 0.71 to 0.89; P<0.001) Of the patients receiving LCZ696, 537 (12.8%) were hospitalized for heart failure, as compared with 658 patients (15.6%) receiving enalapril (hazard ratio, 0.79; 95% CI, 0.71 to 0.89; P<0.001).

Costs and Utilities

Medication costs were based on the wholesale acquisition cost for sacubitril/valsartan (trade name Entresto) and dapagliflozin (trade name Forxiga). The monthly cost for sacubitril/ valsartan was 171 $ and 50 $ for dapagliflozin. The mean cost of hospitalizations for HF was 1250 $.

Base-Case Cost-effectiveness Analysis

Incremental cost-effectiveness ratios (ICERs) were calculated per conventional cost-effectiveness analysis guidelines.[4]

We applied commonly accepted cost effectiveness thresholds of $50000 per QALY, $100000 per QALY, and $150000 per QALY to determine the optimal strategy in base-case and sensitivity analyses.[5]

RESULTS

Model Validation and Clinical Results

in DAPA HF trial: with mean follow-up 18 months, A total of 276 patients (11.6%) in the dapagliflozin group and 329 patients (13.9%) in the placebo group died from any cause (hazard ratio, 0.83; 95% CI, 0.71 to 0.97).

Cost-effectiveness Analysis

In DAPA HF trial

Patients with DM: In a given year, 1000 patients with DM and receiving Dapa cost approximately 600000 $ more in differential drug costs. In the same year, the reductions in hospitalizations would lead to a savings of 36250 $ compared with patients receiving placebo and the reduction of the cost of one antidiabetic drug would lead to saving of 348000 $ compared with patient receiving placebo. The cost per patient over the average life expectancy would be approximately **$13484** for each patient treated with dapagliflozin. After adjustments for quality of life, the difference in health effects is 0.78 QALYs. the strategy of using dapagliflozin has an of **$ 17287** per QALY gained.

Patients without DM: In a given year, 1000 patients with DM and receiving dapagliflozin cost approximately 600000 $ more in differential drug costs. In the same year, the reductions in hospitalizations would lead to a savings of 36250 $ compared with patients receiving placebo. The cost per patient over the average life expectancy would be approximately **$35250** for each patient treated with dapagliflozin. After adjustments for

quality of life, the difference in health effects is 0.78 QALYs. the strategy of using dapagliflozin has an of **$ 45192** per QALY gained.

In PARADIGM trial: In a given year, 1000 patients receiving sacubitril/valsartan would cost approximately $ 2 million more in differential drug costs. In the same year, the reductions in hospitalizations would lead to a savings of 15000 compared with patients receiving enalapril. The cost per patient over the average life expectancy would be approximately **$70 000** per patient treated with the enalapril and $**156 692** for each patient treated with sacubitril/valsartan. After adjustments for quality of life, the difference in health effects is 0.78 QALYs. Compared with enalapril, the strategy of using sacubitril/ valsartan has an ICER of **$ 111 143** per QALY gained.

Indirect comparison between dapagliflozin and sacubitril/ valsartan

Compared with dapagliflozin, in patient without DM the strategy of using sacubitril/ valsartan has an ICER of $ 66000 per QALY gained and in patient with DM, ICER of 94 000 $ per QALY gained.

DISCUSSION

Our model-based analyses suggest that the health benefits associated with the use of sacubitril/valsartan in patients with New York Heart Association class II through IV HF with reduced ejection fraction is cost-effective when compared with the use of enalapril at commonly not accepted willingness-to-pay thresholds of $ 111000 per QALY gained.

At same time we suggested that thee health benefits associated with the use of dapagliflozin in patients with New York Heart Association class II through IV HF with reduced ejection fraction is cost-effective when compared with the use of placebo at commonly accepted willingness-to-pay thresholds of $ 17000-45000 per QALY gained.

This study only evaluated the cost-effectiveness of dapagliflozin and sacubitril/ valsartan in the Gaza. Although the HRs for reductions in hospitalizations and mortality were trial wide. Further costs for hospitalizations are different in each country so that individual analyses need to be conducted in other countries.

REFERENCES

1. Eri T. Kato Michael G. Silverman Ofri Mosenzon, et al Effect of Dapagliflozin on Heart Failure and Mortality in Type 2 Diabetes Mellitus Circulation, 2019; 139: 2528–2536.
2. McMurray JJ, Packer M, Desai AS, et al; PARADIGM-HF Investigators and Committees. Angiotensin-neprilysin inhibition vs enalapril in heart failure. N Engl J Med., 2014; 371(11): 993-1004.
3. Hunink MM, Weinstein MC, Wittenberg E, et al. Decision Making in Health and Medicine: Integrating Evidence and Values. 2nd ed. Cambridge, United Kingdom: Cambridge University Press, 2014.
4. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness—the curious resilience of the $50 000-per-QALY threshold. N Engl J Med., 2014; 371(9): 796-797.