Cost-Effectiveness Analysis of Patiromer in Heart Failure Patients with Reduced Ejection Fraction for the Treatment of Hyperkalaemia: Analysis of the DIAMOND Clinical Trial

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INTRODUCTION

- Hyperkalaemia (HK) is seen frequently in patients with heart failure (HF), often with chronic kidney disease (CKD) as a comorbidity[1]
- HK in HF and/or CKD increases the risk of adverse clinical outcomes, including chest pain, arrythmia, hospitalisation and death[2]
- Renin-angiotensin-aldosterone-system inhibitor (RAASi) are often prescribed to alleviate cardiovascular and renal symptoms, however as they increase the risk of HK they are often down titrated or discontinued[3]
- A real-world evidence (RWE) study showed an association between suboptimal use of RAASi and increased risk of cardiorenal outcomes, including major adverse cardiac events (MACE) and mortality[4]
- The Spanish Society of Cardiology and Spanish Society of Internal Medicine consensus 2022 highlighted the use of potassium (K+) binders for HK management in patients with HF[5-6]
- Phase III clinical trials have demonstrated the safety and efficacy of patiromer, an oral K+ binder for the treatment of HK, in cardiorenal patients receiving RAASi[7-10]
- Results from the recent DIAMOND clinical trial demonstrated the ability of patiromer to simultaneously reduce the risk of HK and RAASi dose reduction over a 54-week long period[7]

OBJECTIVES

- To assess the cost-effectiveness of patiromer versus standard of care (SoC) treatment of HK in HF patients with CKD in Spain, utilising data from DIAMOND[7] and a real-world evidence (RWE) study[4]

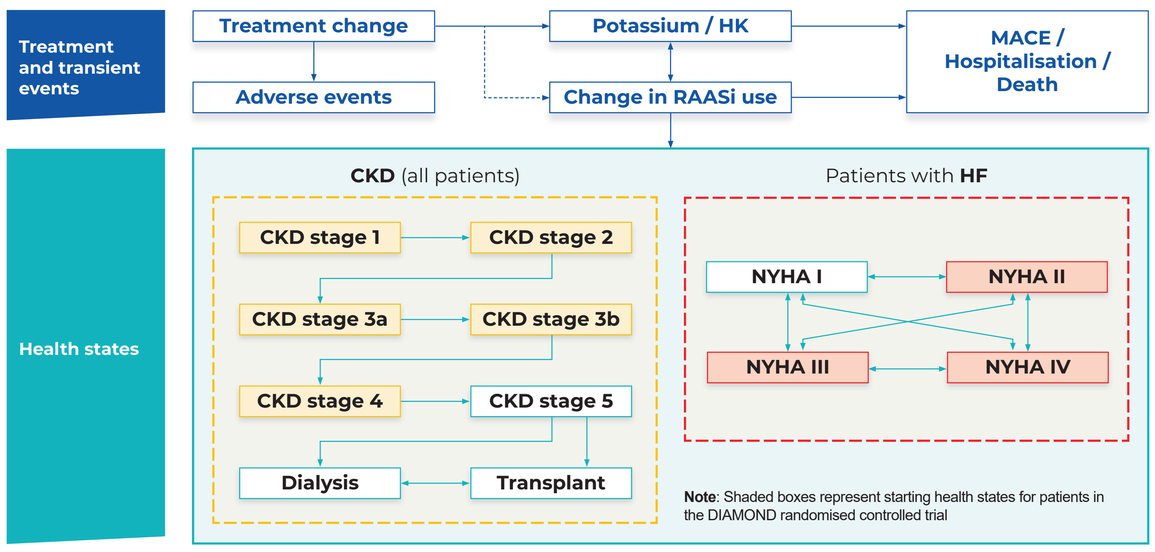
METHODS

Matching-adjusted indirect comparison (MAIC)

- K+ levels in the SoC arm of the DIAMOND trial was impacted by a legacy effect of patiromer treatment in the run-in period[4], resulting in lower mean K+ concentration when compared with patients from the real world
- Hence, data from RWE was sought to better represent SoC in the model[4]
- To account for the differing population characteristics between DIAMOND and the RWE study, an unanchored population-adjusted indirect treatment comparison (ITC), was undertaken
- Baseline patient characteristics from DIAMOND were matched to those from the real world[4]
- MAIC results provided serum K+ levels from 21,334 patients with HF in the UK
- Only those patients with HK (K+ values of ≥ 5.0 mmol/L) were used, to ensure alignment with the DIAMOND trial population

Cost-effectiveness analysis

Figure 1: Flow diagram of the patiromer cost-effectiveness Markov model[11-12] summarising health states and events



CKD: chronic kidney disease; HK: hyperkalaemia; MACE: major adverse cardiovascular event; NHYA: New York heart association classes; RAASi: Renin-angiotensin-aldosterone system inhibitors

Cohort state-transition Markov model	**Disease status**	New York Heart Association (NYHA) Class I-IV heart failure, CKD (stages 1–4), CKD stage 5, dialysis, transplant[13-14]
	Transient events	HK (defined as serum potassium of ≥ 5.0 mmol/L), MACE, hospitalisation and dialysis complication were derived from ITC and previously published literature[15-21]
	Clinical inputs	Derived from DIAMOND, RWE and other published data[4,7,22-26]
	Time horizon	Lifetime as HF and CKD are chronic and progressive diseases
	Costs and utilities	Event costs and utilities derived from Spanish-specific published literature, when available. Costs adjusted to 2022 currency units
	Discounting	An annual discount rate of 3% was applied

RESULTS

MAIC

- Adjustment of the DIAMOND trial population using an unanchored MAIC approach showed there was some overlap between the DIAMOND trial[7] and RWE study[4], with an effective sample size of 254
- Populations were well-matched on the adjusted variables
- The adjusted mean K+ concentration at baseline and after patiromer treatment, derived by MAIC are shown in **Table 1**
- To note, mean K+ concentration for SoC was derived by calculating weighted average, based on RWE data[4] (**Table 1**)

Table 1: Potassium levels used in cost-effectiveness model (CEM)

	Mean serum potassium level (mmol/L)
Baseline	**4.840†**
After patiromer treatment	**4.634†**
After SoC treatment	**5.239‡**

† Baseline and patiromer mean K+ concentrations were derived from MAIC analysis, utilising data from DIAMOND and RWE.[4,7] ‡ Patients in the SoC arm of the DIAMOND trial had lower mean potassium concentration levels compared with patients from the real world, thus mean potassium concentration value was calculated from weighted average of RWE data.[4]

Patiromer is cost-effective for the management of HK in HF patients with comorbid CKD

- Patiromer treatment was associated with an incremental cost-effectiveness ratio (ICER) of €23,251 per quality adjusted life year (QALY) gained and an incremental discounted total lifetime cost per patient of €37,428, driven mainly by treatment effect (**Table 2** and **Figure 2**)
- Use of patiromer was associated with an additional 2.05 discounted life years and an additional 1.61 discounted QALYs, compared to SoC (**Table 2**)
- Majority of QALY gains were attributable to the additional time spent in CKD stage 2–4 (**Figure 3**)

Table 2: Base case cost-effectiveness results

	Total costs	Total QALYs	Total LYs	NMB	ICER €/QALYG	ICER €/LYG
Patiromer	**€117,900**	**8.05**	**10.16**	**€123,661**	**—**	**—**
SoC	**€80,472**	**6.44**	**8.11**	**€112,797**	**—**	**—**
Incremental	**€37,428**	**1.61**	**2.05**	**€10,864**	**€23,251**	**€18,241**

ICER: incremental cost-effectiveness ratio; LY: life year; LYG: life years gained; SoC: standard of care; NMB: net monetary benefit; QALY: quality-adjusted life year

Figure 2: Incremental discounted cost breakdown

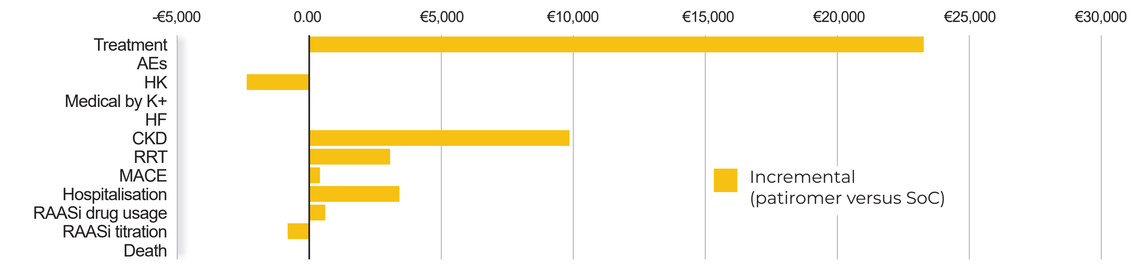
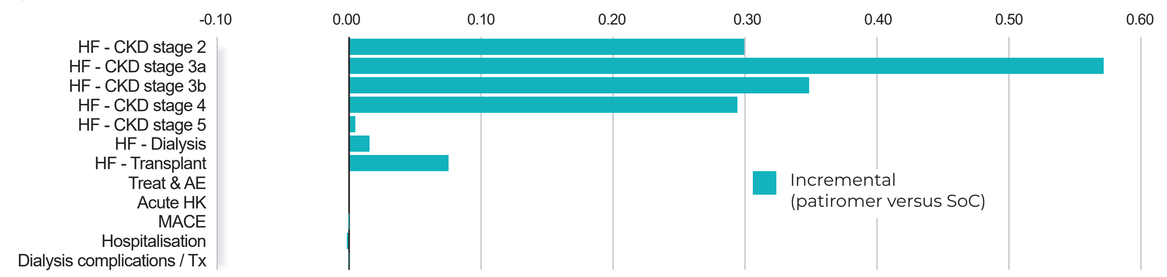


Figure 3: Incremental discounted QALY breakdown



AE: adverse event; CKD: chronic kidney disease; HF: heart failure; HK: hyperkalaemia; K+: potassium; MACE: major adverse cardiovascular event; RAASi: Renin-angiotensin-aldosterone system inhibitor; RRT: renal replacement therapy; Tx: transplant

Model was robust to sensitivity analyses

- The sensitivity analyses confirmed the robustness of results obtained in the base case (**Figure 4**)
- Probabilistic sensitivity analysis suggested a 68.5% probability that the ICER would fall below a willingness to pay threshold (WTP) of €30,000/QALY gained (**Figure 5**)

Figure 4: Deterministic sensitivity analysis (OWSA)

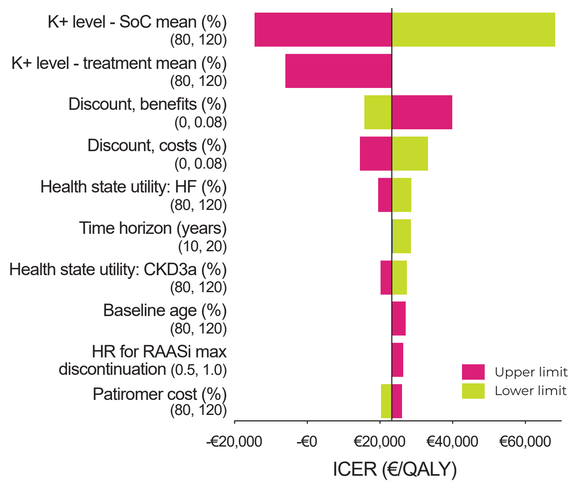
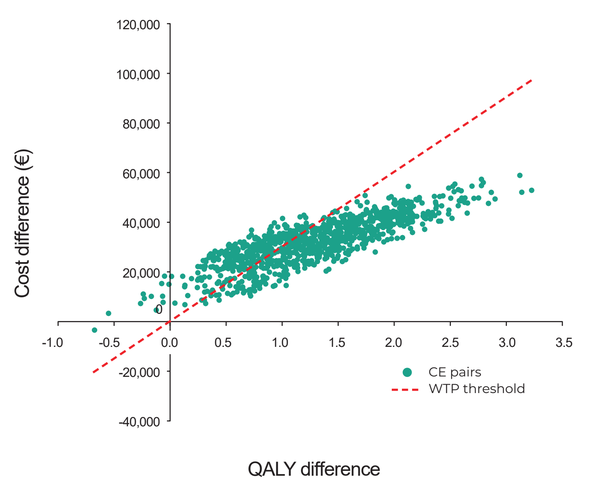


Figure 5: Cost-effectiveness plane (ICER scatter plot)



CE, cost effectiveness; CKD, chronic kidney disease; HF, heart failure; HR: hyperkalaemia related; ICER, incremental cost-effectiveness ratio; OWSA, one way sensitivity analysis; RAASi: Renin-angiotensin-aldosterone system inhibitors; QALY, quality-adjusted life year; SoC, standard of care; WTP, willingness-to-pay

CONCLUSION

- Patiromer is cost-effective compared to SoC for the management of HK in HF patients with comorbid CKD in Spain
- Management of HK results in increased survival and quality of life of patients treated with patiromer compared to SoC
- Patiromer reduces K+ levels and enables the continuation of RAASi therapy, which is required to further decrease the incidence of costly hospitalisation, MACE and end-stage kidney disease events
- Guidelines for HK management in Spain exist, however increased awareness among clinicians regarding the benefits associated with K+ lowering treatments, such as patiromer, could help optimise the use of these treatments and alleviate disease and healthcare system burdens

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DISCLOSURES

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