A COST-EFFECTIVENESS ANALYSIS OF PATIROMER FOR THE TREATMENT OF HYPERKALEMIA IN SPAIN

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INTRODUCTION AND OBJECTIVE

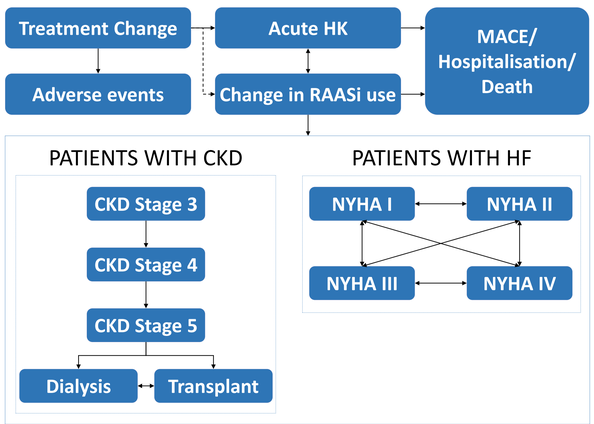
- Chronic kidney disease (CKD) is considered a major public health concern and is one of the leading causes of mortality due to the ageing of the population[1]. The prevalence of CKD is estimated to be 15.1% in Spain[2].
- Optimal renin-angiotensin-aldosterone system inhibitors (RAASi) therapy has demonstrated to delay progression of CKD, heart failure (HF) and hypertension[3]. However, its use is associated with an increased risk of hyperkalaemia (HK)[4], which may lead to discontinuation or dose reduction and shorten its potential cardio-renal benefits.
- Over the past decades, sodium polystyrene sulfonate (SPS) has been the most commonly used treatment to address HK, but it is associated with several drawbacks (serious gastrointestinal adverse events, risk of hypokalaemia, poor tolerability, etc.)[5,6,7].
- Patiromer is a novel therapy that has proven to decrease serum potassium levels and the recurrence of HK[5]. Thus, patiromer has demonstrated to maintain normokaelemia and enables to maintain RAASi therapy[8]. In Spain, patiromer is currently reimbursed in patients with advanced CKD and class III-IV HF and mild to moderate HK (5.5-6.4 mmol/L), who are receiving RAASi and with failure or intolerance to ion exchange resins.
- **The aim of the study was to assess the cost-effectiveness of patiromer versus no patiromer for the management of HK in patients with CKD with and without HF from the Spanish National Health Service (NHS) perspective.**

METHODS

Model Structure

- A Markov model was developed to predict the natural history of the disease for patients with CKD stage 3-4 with and without HF treated with RAASi, and evaluate the cost-effectiveness of patiromer versus no patiromer for the control and maintenance of normokalemia over a lifetime horizon.
- The model consisted on mutually exclusive health states, including acute HK, adverse events (AEs), major adverse cardiac events (MACE), hospitalisation, changes in RAASi use, mortality, and CKD and HF progression (Figure 1). The model also included an option to simulate re-treatment in patients who discontinue patiromer.

Figure 1. Model Structure



CKD: chronic kidney disease; HF: heart failure; HK: hyperkalemia; MACE: major adverse cardiac events; NYHA: New York Heart Association; RAASi: renin-angiotensin-aldosterone system inhibitors. Cycle length: 1 month.

Inputs, assumptions & outcomes

- Initial demographic characteristics of patients (Table 1), and clinical efficacy were derived from the OPAL-HK trial[8].

Table 1. Baseline demographic and clinical characteristics

Characteristics	Value
Age (SE) (years)	65.3 (0.9)
CKD	**100%**
Stage 3	55.1%
Stage 4	44.9%
HF	**42.0%**
NHYA I	18.6%
NHYA II	64.7%
NHYA III	16.7%
NHYA IV	0%
K+ levels (mmol/L)	
>5.5 to ≤6	81.4%
>6	18.6%
RAASi medication	
ACE inhibitor	67.6%
ARB	39.1%

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blockers; CKD: chronic kidney disease; HF: heart failure; HK: hyperkalemia; NYHA: New York Heart Association; RAASi: renin-angiotensin-aldosterone system inhibitors; SE: Standard error.

- The costs included were drug acquisition, CKD management, acute HK, MACE and hospitalization events (Table 2). No AEs-associated costs were included. Utility values were obtained from published literature[9,10,11].
- Model outcomes included total direct costs (expressed in €, 2021), quality-adjusted life years (QALYs), life years gained (LYG) and incremental cost-effectiveness ratio (ICER). An annual discount rate of 3% was applied to costs and health outcomes.
- Deterministic and probabilistic sensitivity analysis were performed to assess the robustness of the results.

Table 2. Costs for healthcare resources

Parameter	Cost (€ 2021)
Daily drug acquisition cost (retail price*)	
Patiromer 8.4 g[12]	€ 7.34
Patiromer 16.8 g[12]	€ 9.89
RAASi therapy	
ACE inhibitors[12]	€ 0.09
ARB[12]	€ 0.40
MRA[12]	€ 0.58
Health states & events	
CKD management	
CKD 3 (annual cost)[13]	€ 4,842
CKD 4 (annual cost)[14]	€ 8,180
CKD 5 (annual cost) [14]	€ 13,866
Dialysis (annual cost)[15]	€ 49,189
Transplant procedure (one-off cost)[16]	€ 35,318
Transplant maintenance (annual cost)[17]	€ 7,393
RAASi dose change**	
RAASi discontinuation[12,16,18]	€ 194.01
RAASi down-titration[12,16,18]	€ 388.01
Return to maximum RAASi use[12,16,18]	€ 58.50
MACE[18]	€ 4,369
Hospitalisation[18]	€ 3,698
Acute HK	
K+ >5.5 to ≤6 mmol/L[12,16,18]	€ 150.14
K+ >6 mmol/L[12,16,18]	€ 2,948.46

*The deductions described in Royal Decree Law (RDL) 8/2010 were applied. **The costs were applied in the month of change.
ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blockers; CKD: chronic kidney disease; HK: hyperkalaemia; MACE: major adverse cardiac events; MRA: mineralocorticoid receptor agonist; RAASi: renin-angiotensin-aldosterone system inhibitors.

RESULTS

Base case

- Patiromer was more effective than no patiromer (5.51 vs 5.43 QALYs; 7.33 vs 7.25 LYG), but resulted in an incremental cost of € 548, yielding an ICUR of €7,219/QALY gained and an ICER of €6,744/LYG (Table 3).

Table 3. Base case analysis

	Patiromer	No patiromer	Incremental
Costs			
Total costs (per patient)	**€ 110,442**	**€ 109,898**	**€ 548**
Acquisition of drugs	€ 1,509	€ 0	€ 1,509
Acute HK management	€ 993	€ 1,174	€ -181
CKD management	€ 43,638	€ 42,990	€ 648
RRT management	€ 37,526	€ 38,750	€ -1,224
MACE	€ 6,023	€ 6,150	€ -127
Hospitalization for HK	€ 19,594	€ 19,655	€ -61
RAASi change dose	€ 1,158	€ 1,174	€ -16
Effectiveness			
QALY	**5.51**	**5.43**	**0.08**
LYG	**7.33**	**7.25**	**0.08**
Results			
ICUR			**€ 7,219/QALY**
ICER			**€ 6,744/LYG**

CKD: chronic kidney disease; HK: hyperkalemia; ICER: Incremental cost-effectiveness ratio; ICUR: Incremental cost-utility ratio; LYG: life year gained; MACE: major adverse cardiac events; QALY: quality-adjusted life year; RAASi: renin-angiotensin-aldosterone system inhibitors; RRT: renal replacement therapy.

Sensitivity Analyses

- Deterministic analyses showed that the results were robust to changes in input parameters. The most influential parameter was the probability of patiromer treatment discontinuation. At a willingness-to-pay threshold of €30,000/QALY, patiromer resulted in a cost-effectiveness therapy in 85.6% of the simulations, compared to no patiromer.

CONCLUSIONS

- **Patiromer resulted to be a cost-effective intervention for the treatment of HK and maintenance of RAASi therapy in patients with CKD stage 3-4 with and without HF in Spain.**
- **This analysis confirms the cost-effectiveness of patiromer in CKD with and without HF, a larger patient group than current reimbursed visa conditions in Spain.**
- **Even though patiromer treatment was associated with additional costs, renal replacement therapy management costs were lower, and survival and quality of life improved.**

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