Economic evaluation of patiromer for the treatment of hyperkalaemia in CKD patients with and without HF in Italy

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INTRODUCTION

- Hyperkalaemia (HK) (serum potassium concentration ≥ 5.5 mmol/L) is associated with adverse clinical outcomes, including major adverse cardiovascular events (MACE), hospitalisation and mortality.[1]
- Patients with chronic kidney disease (CKD) with and without heart failure (HF) are susceptible to HK.[2]
- Renin-angiotensin-aldosterone system inhibitors (RAASis) are major therapeutic strategies in HF and CKD, but are often discontinued in patients with HK as they exacerbate potassium (K^+) serum concentration.[3]
- Current standard of care (SoC) seeks a therapeutic balance between the beneficial use of RAASi and HK risk through down-titration/discontinuation, ultimately yielding detrimental outcomes.
- Patiromer is a once-daily, non-absorbed, cation-exchange polymer which decreases K^+ serum concentrations via the promotion of faecal K^+ excretion.[4]
- In the OPAL-HK trial patiromer therapy was shown to enable the maintenance of optimal RAASi treatment in high-risk CKD patients with and without HF. [5]

OBJECTIVES

The objective of this study was to evaluate the cost-effectiveness of patiromer compared with standard of care (SoC) for the treatment of HK in CKD patients with and without HF from the perspective of the National Health Service in Italy.

METHODS

- A lifetime, fixed time increment, Markov cohort model was developed (**Figure 1**). Patients were modelled from CKD stage III (55.1%) and CKD stage IV (44.9%) through dialysis and renal transplant; those who additionally had HF (41.9%) were modelled through New York Heart Association (NYHA) classes.
- MACE, hospitalisation and mortality events, stratified by disease status, were informed by published event rates[6,7], with K^+ levels and RAASi use impacting their incidence through the application of relevant hazard ratios (HRs).[8,9]
- Mortality risk was estimated from comorbidity, RAASi use and K^+ levels using the Seattle Heart Failure Model.[10] Where all cause mortality estimates from Italian specific life tables exceeded this value, the greater mortality rate was assumed.
- RAASi use was dichotomised as any versus none or optimal versus sub optimal (50% down-titration) versus none, depending on data availability, with K^+ levels impacting RAASi discontinuation and down titration. Initially, RAASi use was modelled based on the observed trial data (**Table 1**).[11] From month 4 onwards published RAASi discontinuation rates, stratified by K^+ levels were used for the SoC arm; for the patiromer arm, the HR for RAASi discontinuation was estimated from trial data for months 2 and 3 combined with rates for the SoC arm (**Table 2**).[9] Patients could return to optimal RAASi use independent of their K^+ level with a monthly probability of 3.51%.
- Patiromer was associated with a reduction in HK event incidence; whilst patients were receiving patiromer, a HR of 0.467 and 0.242 was applied to the likelihood of HK event incidence for K^+ levels of >5 mmol/L to ≤5.5 mmol/L and >5.5 mmol/L, respectively, for months 4 onwards, based on observed trial data.[11]
- Patients discontinued patiromer at a constant monthly rate (10.33%) or if they initiated renal replacement therapy (RRT)[1], patients could repeat treatment if their K^+ levels reached a user defined value prior to RRT.
- Resource utilisation and the costing of disease management and clinical events was primarily informed by published literature.[12-15] RAASi use was based on the OPAL-HK trial[7] and dose optimisation was aligned with technology appraisal guidance for sodium zirconium cyclosilicate in treating HK.[16] One-off event costs of MACE and hospitalisation were taken from Italian diagnostic-related-groups (DRGs)[17], and drug costs were primarily obtained from the list of class A medicines.[18] Costs expressed as 2020/21 Euros were discounted at 3%.
- Utility values (EQ 5D), stratified by disease status, were sourced from published literature[19-24], and discounted at 3%.
- Subgroup analysis was conducted in CKD patients with and without HF. Probabilistic sensitivity analysis was undertaken, focusing on key parameters and those associated with RAASi use.
- In sensitivity analysis, the influence of RAASi use on MACE and death were sourced from Italian studies reporting hazard ratios (HRs) of events for patients not receiving RAASi (non-adherent; threshold of proportion of days covered (PDC) >80%) versus receiving RAASi (adherent; PDC >80%).[25,26]

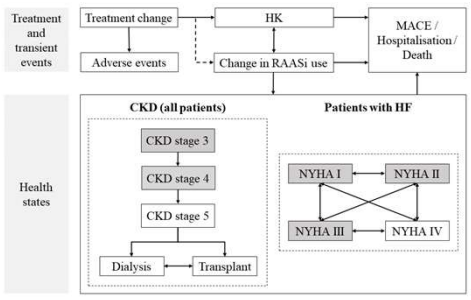

Figure 1: Flow diagram of the patiromer cost-effectiveness model summarising health states and events

HK: hyperkalaemia; RAASi: Renin-angiotensin-aldosterone system inhibitors; MACE: Major adverse cardiac event; CKD: Chronic kidney disease; NHYA: New York heart association classes

Table 1: Summary of trial-based RAASi use data

	Monthly probability (months 2-3)		HR
	Patiromer	SoC	(Patiromer versus SoC months 4+)
Optimal RAASi discontinuation[15]	3.34%	34.44%	0.069[a]
Optimal RAASi down-titration[15]	0.00%	35.55%	1.000[b]
Sub-optimal RAASi discontinuation	3.34%[c]	34.44%[c]	0.069[a]

HR: hazard ratio; RAASi: Renin-angiotensin-aldosterone system inhibitors; SoC: Standard of care; [a] Assumed based on ratio observed during trial period; [b] No data so no difference modelled; [c] Assumed to be the same as optimal RAASi discontinuation

Table 2: Summary of published RAASi use data

		Monthly probability (months 4+) – SoC			
		$K^+ \leq 5$	$K^+ > 5$ to ≤ 5.5	$K^+ > 5.5$ to ≤ 6	$K^+ > 6$
SoC	Optimal RAASi discontinuation[16]	2.60%	3.03%	4.55%	10.00%
	Optimal RAASi down-titration[16]	1.80%	2.62%	5.31%	8.90%
	Sub-optimal RAASi discontinuation[a]	2.60%	3.03%	4.55%	10.00%
Patiromer	Optimal RAASi discontinuation[b]	0.18%	0.21%	0.32%	0.72%
	Optimal RAASi down-titration[b]	1.80%	2.62%	5.31%	8.90%
	Sub-optimal RAASi discontinuation[b]	0.18%	0.21%	0.32%	0.72%

RAASi: renin-angiotensin-aldosterone system inhibitors; SoC: standard of care
[a] Assumed to be the same as optimal RAASi discontinuation; [b] After application of the HRs presented in Table 1

RESULTS

- Patiromer treatment was associated with incremental discounted costs of €3,618 and 0.167 quality adjusted life years (QALYs) gained per patient, with an incremental cost-effectiveness ratio (ICER) of €21,527 versus SoC (willingness-to-pay threshold €30,000/QALY).
- Patiromer use resulted in 286 HK events, 54 MACE and 247 RAASi discontinuation events being averted per 1,000 population (**Figure 2**).
- Sub-group analysis showed patiromer was more effective in reducing the number of clinical events in CKD patients with HF versus without HF; greater reduction of number of MACE (100 versus 21, respectively) and RAASi discontinuation was avoided with patiromer treatment (**Figure 2**).
- Total QALYs gained was less in CKD patients with HF versus without HF (0.062 versus 0.243 respectively). The incremental cost-effectiveness plane of each sub-group is shown in **Figure 3**.
- Probabilistic sensitivity analysis yielded outcomes in line with base-case analysis. In comparison to SoC, patiromer treatment yielded an incremental discounted costs of €4,004 and 0.176 QALYs gained, resulting in an ICER of €22,749.

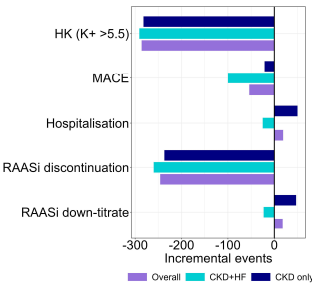

Figure 2: Incremental number of events per 1,000 patients (Patiromer vs SoC)

CKD: Chronic kidney disease; HK: hyperkalaemia; MACE: Major adverse cardiac event; RAASi: Renin-angiotensin-aldosterone system inhibitors

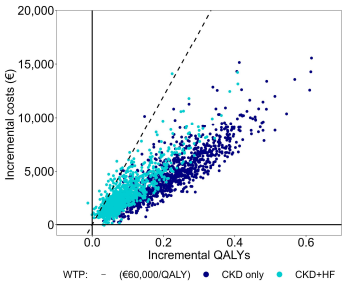

Figure 3: Cost-effectiveness scatterplot

QALYs: quality-adjusted life years; WTP: willingness-to-pay threshold

CONCLUSIONS

- This study demonstrates the helpful clinical and economic value of patiromer treatment for HK management in CKD patients with and without HF in Italy being the molecule cost-effective.
- Patiromer has the potential to avert MACE, through RAASi enablement, and improve patient QoL while being cost-effective when compared to SoC in Italy.

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