The cost-effectiveness of patiromer for the treatment of hyperkalaemia in patients with chronic kidney disease with and without heart failure in Ireland

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Introduction

- Hyperkalaemia (HK) refers to an elevation of serum potassium (K^+) concentration above 5.5 mmol/l and is considered a potentially life-threatening condition.[1]
- Common adverse clinical outcomes associated with HK include major adverse cardiac events (MACE) and increased hospitalisation and mortality.[2]
- Patients diagnosed with chronic kidney disease (CKD) with and without heart failure (HF) are predisposed to the risk of HK,[3] which is further exacerbated by the presence of older age, impaired renal function, concomitant medications, and comorbidities.
- Renin-angiotensin-aldosterone system inhibitors (RAASi) are major therapeutic strategies in HF with and without CKD,[4] but are often discontinued due to the increased risk of HK.[4] Consequently, a therapeutic balance between the beneficial use of RAASi and HK risk is required.
- Patiromer is a novel, once-daily, sodium-free potassium (k^+)-binder approved for treatment of hyperkalaemia in adults.[5]
- The OPAL-HK study[6] (evaluating the efficacy and safety of patiromer for the treatment of HK) demonstrated that patiromer was effective in treating high K^+ levels, preventing recurrent HK and enabling optimal use of RAASi in high-risk CKD patients with and without HF.

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 patients with CKD with and without HF from the perspective of the healthcare payers in Ireland.

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 classes.

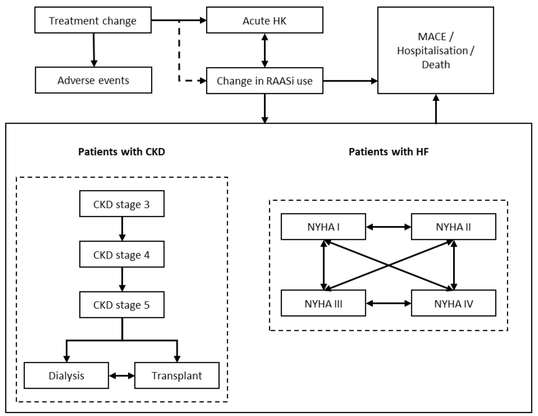

Figure 1: Flow diagram summarising the Patiromer model health states and events

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

- MACE, hospitalisation and mortality events, stratified by disease status, were informed by published event rates,[7-9] with K^+ levels and RAASi use impacting their incidence through the application of relevant hazard ratios (HRs) and odds ratios (ORs).[10-13]
- Optimal use of RAASi was defined as the recommended dose and suboptimal dose defined as 50% down-titration of RAASi dose.
- MACE was defined as hospitalisation for coronary heart disease, HF, ischemic stroke, and peripheral arterial disease. Hospitalisation was defined as any hospitalisation.
- Mortality risk was estimated from comorbidity, RAASi use and K+ levels using the Seattle Heart Failure Model.[14] Where all-cause mortality estimates from Irish-specific life tables exceeded this value, the greater mortality rate was assumed.
- RAASi use was dichotomised as any vs. none or optimal vs. sub-optimal vs. none, depending on data availability, with K^+ levels impacting on RAASi discontinuation and down-titration. Initially, RAASi use was modelled based on the observed trial data **(Table 1)**.[15] From month 4 onwards published RAASi discontinuation rates, stratified by K^+ level were used for the SoC arm; for the Patiromer arm, the HR for discontinuation estimated from trial data for months 2-3 was combined with the No patiromer rates **(Table 2)**.[16] Patients could return to optimal RAASi use independent of their K^+ level with a monthly probability of 3.51%.

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

- 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 to ≤ 5.5 and > 5.5, respectively, for months 4 onwards, based on observed trial data.[15]
- Patients discontinued patiromer at a constant monthly rate (10.33%) or if they initiated renal replacement therapy (RRT),[6] patients could repeat treatment if their K^+ levels reached a user-defined value prior to RRT.
- Healthcare costs (2019-2020 Euro) were sourced from the Healthcare Pricing Office ABF 2020 Admitted Patient Price List, NICE Clinical guidelines for CKD and other published literature and inflated to 2020/21 values if relevant,[17-24] utility values (EQ-5D), stratified by disease status, were sourced from published literature;[25-30] costs and benefits were discounted at an annual rate of 4.0%.
- Probabilistic and one-way sensitivity analysis, focusing on key parameters and those associated with RAASi use, was undertaken.

Results

- With patiromer treatment, discounted life years and quality adjusted life years (QALY) were predicted to increase from 6.72 to 6.78 (+0.06) and 5.02 to 5.07 (+0.05), respectively.
- Incremental discounted costs were predicted at €99 per patient, with an incremental cost-effectiveness ratio of €1,734 per QALY gained.
- Probabilistic analysis is presented in **Figure 2.** At a willingness-to-pay threshold of €45,000 in Ireland, treatment with patiromer was estimated to have a 99% chance of cost-effectiveness compared to SoC
- Probabilistic and one-way sensitivity analyses support the base case analysis, with results most sensitive to the magnitude of the impact of RAASi use on mortality and CKD progression, alongside treatment discontinuation and costs (**Figures 2 and 3**).

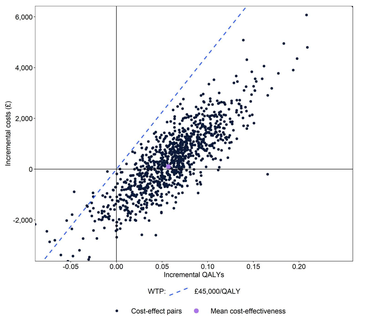

Figure 2: ICER scatterplot

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

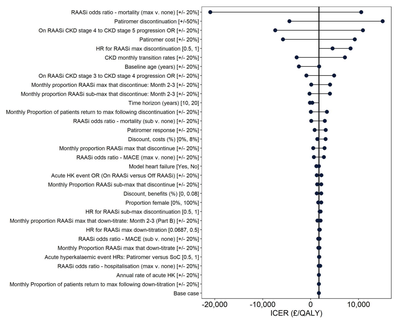

Figure 3: Impact of one-way sensitivity analyses on cost-effectiveness outcomes

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

Conclusions

- In patients with CKD with and without HF presenting with HK, patiromer is a cost-effective treatment strategy when compared to SoC in Ireland.
- The result is predominantly attributed to the ability of patiromer to enable the continuation of RAASi use and consequently slow down CKD progression, and was relatively stable across sensitivity analyses.

References

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