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

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Introduction

- Hyperkalaemia (HK) is associated with adverse clinical outcomes, including major adverse cardiovascular events (MACE), hospitalisation and mortality.[1]
- Patients with chronic kidney disease (CKD) and heart failure (HF) are particularly susceptible to HK.[2]
- Renin-angiotensin-aldosterone system inhibitors (RAASi) are major therapeutic strategies in HF and CKD and are often discontinued in patients presenting with HK as they exacerbate K^+ serum concentration.[4] Consequently, a therapeutic balance between the beneficial use of RAASi and HK risk is required.
- Patiromer is a non-absorbed, cation-exchange polymer which normalises K^+ serum concentrations via the promotion of faecal K^+ excretion.[5]
- The OPAL-HK study[6] showed that therapeutic intervention with patiromer in HK patients enables the maintenance of RAASi in high-risk CKD patients with and without HF patients.

Objectives

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

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 end-stage renal disease and renal replacement therapy; those who additionally had HF (41.9%) were modelled through New York Heart Association classes.
- MACE, hospitalisation and mortality events, stratified by disease status, were informed by published event rates[7-9], with potassium levels and RAASi use impacting their incidence through the application of relevant hazard ratios (HRs) and odds ratios (ORs)[10-13].

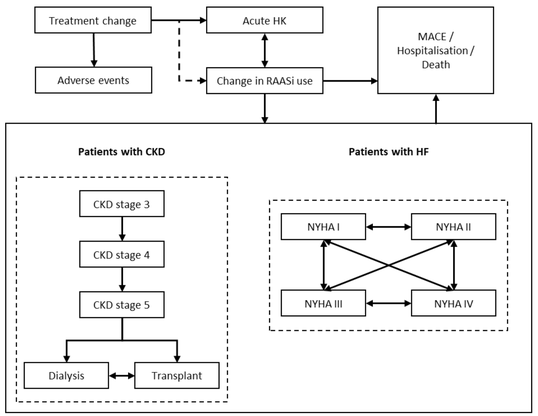

Figure 1: Flow diagram summarising the Patiromer model health states and events

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

- Mortality risk was estimated from disease status, comorbidity and RAASi use.[14] Potassium levels influence RAASi discontinuation and down-titration. Initially, RAASi use was modelled based on the observed trial data.[15] From month 4 onwards published RAASi discontinuation rates, stratified by potassium level were used.[16] Input values are presented in **Table 1** and **Table 2**. Patients could return to optimal RAASi use independent of their potassium 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+)			
	$K^+ \leq 5$	$K^+ > 5$ to ≤ 5.5	$K^+ > 5.5$ to ≤ 6	$K^+ > 6$
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%

RAASi: Renin-angiotensin-aldosterone system inhibitors; [a] Assumed to be the same as optimal RAASi discontinuation

- 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 potassium levels of K+ >5 to ≤5.5 and K+ > 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 RRT[15]; patients could repeat treatment if their potassium levels reached a user-defined value prior to renal replacement therapy (RRT).
- Healthcare costs (2019-2020 GBP) were sourced from NHS Reference Costs 2020, Personal Social Services Unit (PSSRU) 2020, Public Health Scotland, NICE Clinical guidelines for CKD and other published literature and inflated to 2019/20 values were relevant[17-33]; utility values (EQ-5D), stratified by disease status, were sourced from published literature[34-38]; costs and benefits were discounted at an annual rate of 3.5%.

Results

- With patiromer treatment, discounted life years and quality adjusted life years (QALY) were predicted to increase from 6.88 to 6.94 (+0.06) and 5.13 to 5.19 (+0.06), respectively.
- Incremental discounted costs were predicted at £970.60 per patient (**Figure 2**)**,** with an incremental cost-effectiveness ratio of £16,667 per QALY gained.
- Probabilistic analysis is presented in **Figure 3.** At willingness-to-pay thresholds of £30,000 and £50,000 per QALY, treatment with patiromer was estimated to have an 80% and 89% chance of cost-effectiveness, respectively.
- Probabilistic and one-way sensitivity analyses (**Figure 4)** 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.

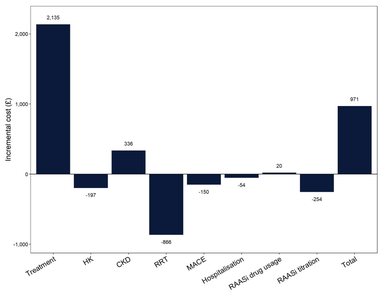

Figure 2: Incremental cost breakdown

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

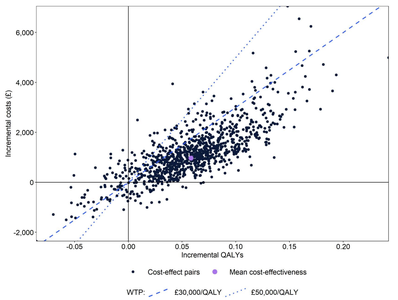

Figure 3: ICER scatterplot

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

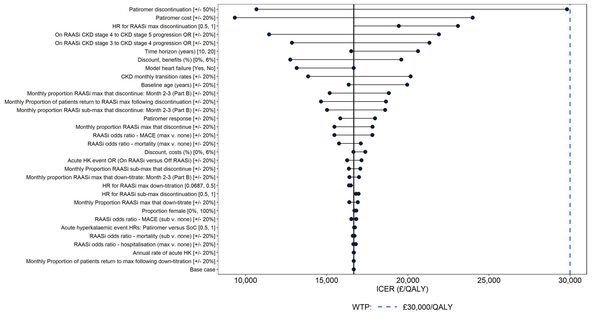

Figure 4: Impact of one-way sensitivity analyses on cost-effectiveness outcomes

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 the standard of care in the UK.
- The result is predominantly attributed to the ability of patiromer to enable the continuation of RAASi use, and was relatively stable across sensitivity analyses.

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