A COST-UTILITY ANALYSIS OF SPARSENTAN FOR THE TREATMENT OF IMMUNOGLOBULIN A NEPHROPATHY IN THE UK

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INTRODUCTION

- Immunoglobulin A nephropathy (IgAN) is a rare disorder associated with reduced kidney function and increased risk of end-stage renal disease (ESRD) that imposes a significant burden on both patients and payers.
- IgAN is the most common cause of chronic kidney disease (CKD) in patients <40 years of age; a chronic condition characterised by declining kidney function which can ultimately lead to the requirement for renal replacement therapy (RRT). Furthermore, IgAN can result in faster disease progression than other causes of CKD.
- RRT has a significant impact on patient health-related quality-of-life (HRQOL), potentially requiring frequent visits to receive in-centre haemodialysis. Similarly, kidney transplant recipients require lifelong immunosuppression, and may also need subsequent re-transplant as the disease progresses.
- IgAN itself has no cure, with the goal of treatment being to slow down its rapid advancement. Standard of care (SOC) includes renin angiotensin-angiotensin system inhibitors (RAASi). Patients with persistent proteinuria may also receive immunosuppressants. SGLT2 inhibitors are also becoming an increasingly common option for patients who have already optimised other treatments.
- Sparsentan is a non-immunosuppressive, single molecule dual endothelin angiotensin receptor antagonist. PROTECT (NCT03762850) was a phase 3 randomised controlled trial that demonstrated that treatment with sparsentan resulted in statistically significant reductions in proteinuria and delays in kidney decline versus irbesartan (a frequently used RAASi therapy).

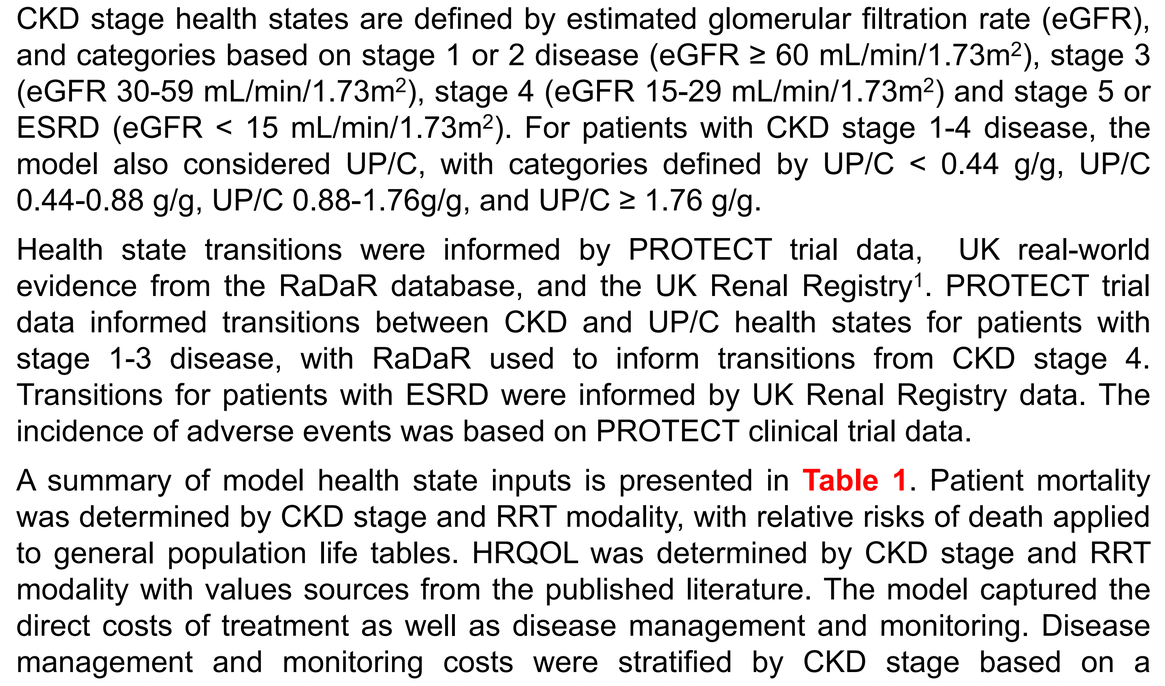
OBJECTIVE

- This study evaluated the cost-effectiveness of sparsentan compared with maximally tolerated dose of irbesartan for the treatment of adults with IgAN from a UK NHS perspective.

METHODS

- A lifetime Markov state-transition model was developed to simulate disease progression in patients treated with sparsentan compared with SOC, informed by the irbesartan arm of PROTECT.
- The modelled patient population was aligned with the indication for sparsentan (proteinuria ≥1.0 g/day or UP/C 0.75 g/g, despite maximal supportive care), with patient baseline characteristics informed by the PROTECT trial.
- The model includes 16 health states, with 12 defined by CKD stage and urine protein to creatine ratio (UP/C), 3 describing ESRD (pre-renal-replacement therapy, dialysis, and transplant), and death (**Figure 1**).
- CKD stage health states are defined by estimated glomerular filtration rate (eGFR), and categories based on stage 1 or 2 disease (eGFR ≥ 60 mL/min/1.73m^2), stage 3 (eGFR 30-59 mL/min/1.73m^2), stage 4 (eGFR 15-29 mL/min/1.73m^2) and stage 5 or ESRD (eGFR < 15 mL/min/1.73m^2). For patients with CKD stage 1-4 disease, the model also considered UP/C, with categories defined by UP/C < 0.44 g/g, UP/C 0.44-0.88 g/g, UP/C 0.88-1.76g/g, and UP/C ≥ 1.76 g/g.
- Health state transitions were informed by PROTECT trial data, UK real-world evidence from the RaDaR database, and the UK Renal Registry[1]. PROTECT trial data informed transitions between CKD and UP/C health states for patients with stage 1-3 disease, with RaDaR used to inform transitions from CKD stage 4. Transitions for patients with ESRD were informed by UK Renal Registry data. The incidence of adverse events was based on PROTECT clinical trial data.
- A summary of model health state inputs is presented in **Table 1**. Patient mortality was determined by CKD stage and RRT modality, with relative risks of death applied to general population life tables. HRQOL was determined by CKD stage and RRT modality with values sources from the published literature. The model captured the direct costs of treatment as well as disease management and monitoring. Disease management and monitoring costs were stratified by CKD stage based on a microcosting approach reported in the published literature combined with unit costs reported by the Personal Social Services Research Unit (PSSRU).
- Direct costs and benefits were discounted at a rate of 3.5% per annum, consistent with NICE guidance.

Figure 1. **Markov state-transition model structure**



CKD, chronic kidney disease; ESRD, end-stage renal disease; RRT, renal replacement therapy; Transpl, transplant; UP/C, urine protein creatinine ratio.

Table 1. **Summary of model inputs**

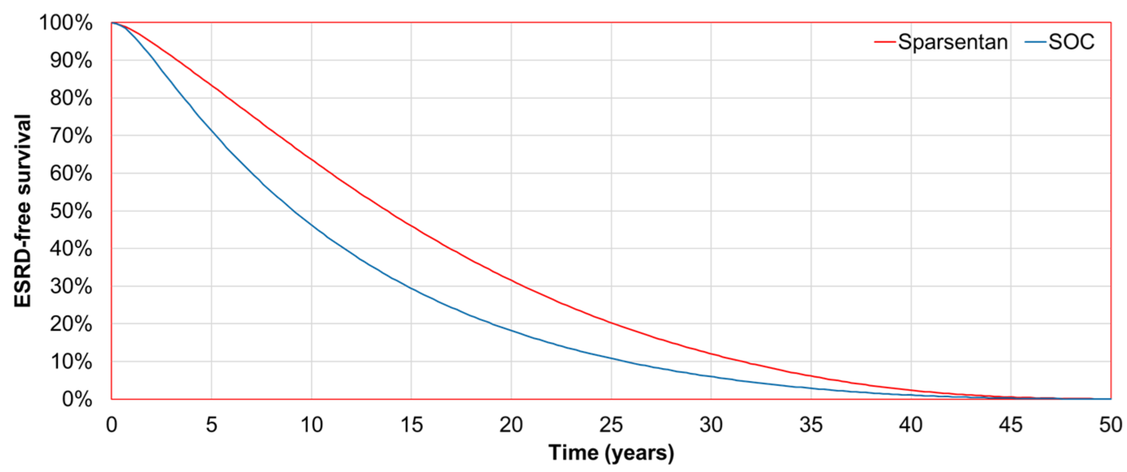
	Utility[2,3]	Annual costs[4,5]	Mortality relative risk[6]
CKD stage 1/2	0.850	£1,440	1.00
CKD stage 3	0.800	£1,440	1.55
CKD stage 4	0.740	£4,888	2.80
CKD stage 5 (pre-RRT)	0.730	£16,619	4.60
Dialysis	0.451*	£34,499	6.96
Transplant	0.710	£8,573	1.40

* Calculated as a weighted average of utility values for peritoneal and haemodialysis based on UK Renal Registry data.
RRT, renal replacement therapy.

RESULTS

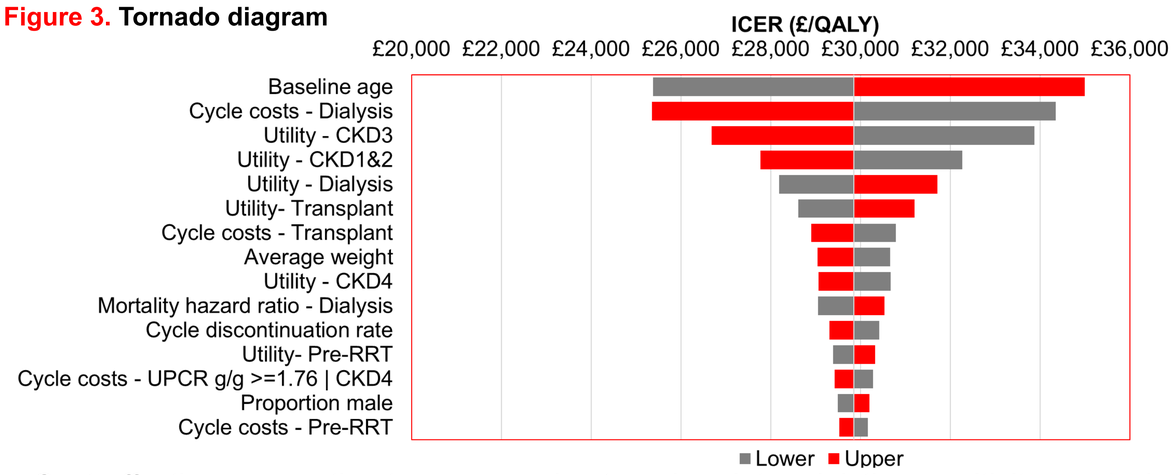
- Treatment with sparsentan was estimated to delay progression to ESRD in patients with IgAN in comparison with SOC. (**Figure 2**). Patients treated with sparsentan spent a total of 15.6 years prior to ESRD, in comparison with 11.6 for patients treated with SOC, an increase of 4.0 years. Furthermore, patients treated with sparsentan spent 2.9 years less time with ESRD in comparison with those treated with SOC This translated to improved life expectancy and patient HRQOL, resulting in a total life year gain of 1.15 years, and 0.88 additional discounted quality-adjusted life years (QALYs).
- In addition to improved patient health outcomes, reduced rates of disease progression and time spent with ESRD resulted in significant cost-offsets. Reduced requirements for RRT provision reduced total per-patient costs by £49,629 for patients treated sparsentan in comparison with SOC.

Figure 2. **ESRD-free survival**



- The estimated incremental cost-effectiveness ratio (ICER) of sparsentan in comparison with SOC was £29,845/QALY, which would be considered cost-effective at willingness-to-pay thresholds typically used in the UK.

Figure 3. **Tornado diagram**



- Cost-effectiveness estimates were robust under deterministic sensitivity analysis (DSA), with the all scenarios resulting in ICERs under £35,000/QALY (**Figure 3**). The model was most sensitive to patient age as a result of mortality risk, followed by costs associated with dialysis provision, and health state utilities.
- Probabilistic sensitivity analysis (PSA) was consistent with the results of the deterministic base case analysis, with a probabilistic ICER of £32,132/QALY, and a 38.9% probability of being cost-effective at a willingness-to-pay threshold of £30,000/QALY.

CONCLUSION

Sparsentan may ameliorate the substantial burden imposed by IgAN on patients, with significant offsets to treatment cost that could positively impact service provision in the NHS. Sparsentan represents a cost-effective treatment option for IgAN patients in the NHS at conventional willingness-to-pay thresholds, offering improved patient outcomes by delaying CKD progression and consequently initiation of renal-replacement therapy.

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