Cost-utility Analysis of Avacopan for the Treatment of ANCA-Associated Vasculitis (AAV) Patients in the UK

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Objectives

- The objective of this study was to evaluate the cost-utility of avacopan compared to glucocorticoids in combination with cyclophosphamide or rituximab for patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) in the UK National Health Service (NHS).

Background

- AAV is an autoimmune condition characterised by inflammation and destruction of small and medium blood vessels. It is a group of rare, serious, and often life-threatening diseases, including microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) (1,2).
- Guidelines for the treatment of AAV recommend treatment with cyclophosphamide (CYC) or rituximab (RTX), plus glucocorticoids (GCs) for patients with organ- or life-threatening disease (3,4).
- Avacopan is an orally administered C5a receptor inhibitor which is recommended for the treatment of severe active GPA or MPA in combination with CYC or RTX in adults in the UK (5) and has been shown to be effective in sustaining remission in GPA and MPA compared to standard of care (SoC) treatment with GCs (6).

Methods

- A state-transition Markov model was designed to reflect clinical practice for induction of remission in patients with AAV, with up to three induction courses.
- The model comprises 9 health states to represent active disease, up to three remission and relapse states, end-stage renal disease (ESRD) and death (Figure 1).
- The clinical efficacy for avacopan was based on the ADVOCATE trial (6), and included disease remission at 26, 52, and 60 weeks, change in estimated glomerular filtration rate (eGFR) and health-related quality of life measured using EQ-5D. Transition probabilities to ESRD were sourced from literature. Cost data were obtained from published literature, including adverse events (AEs), and clinical management of AAV, and were reported in 2021 British pounds (£).
- The results of the analysis were presented in terms of incremental cost-effectiveness ratio (ICER). Uncertainty was characterised using one-way sensitivity analyses and a probabilistic sensitivity analysis (PSA).

***Figure 1**. Structure of the Markov model*

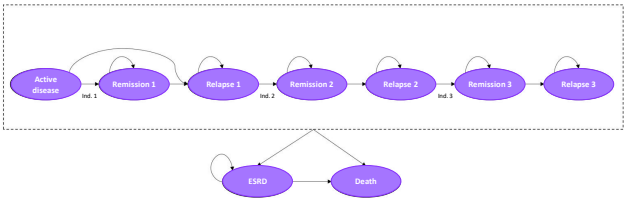

***Table 1.** Summary cost-effectiveness analysis results*

Endpoint	Avacopan + CYC/RTX	CYC+RTX + GCs	Difference
Total cost	£156,549	£151,451	£5,097
Drug costs	£27,281	£11,563	£15,718
AAV management including AEs	£29,956	£31,846	-£1,891
ESRD	£99,312	£108,043	-£8,730
Total QALYs	6.79	6.52	0.26
Total life-years	10.40	10.17	0.23
ICER per QALY			£19,441
Probability of cost-effectiveness (£20k/QALY threshold)			47.3%
Probability of cost-effectiveness (£30k/QALY)			68.5%

Results

- The incremental cost and QALYs of a regimen including avacopan compared to GC, both as an add on to CYC (35%) or RTX (65%), are reported in Table 1. The base case ICER was £19,441 per QALY, which is considered to be cost-effective below the willingness-to-pay threshold of £20,000 per QALY in the UK.
- The univariate sensitivity analysis demonstrated that eGFR recovery at induction from the ADVOCATE trial, discount rates applied to costs and outcomes, and the cost of maintenance dialysis were the main drivers of uncertainty (Figure 2).
- A probabilistic analysis with 5,000 runs demonstrated substantial parametric uncertainty in the model, with a probability of cost-effectiveness of 49% and 70% at willingness to pay (WTP) per QALY of £20k and £30k per QALY, respectively (Figures 3 and 4).
- The model results were sensitive to assumptions for impact of relapse on renal function (measured using estimated glomerular filtration rate, eGFR) and the impact of eGFR on the probability of ESRD. Other assumptions related to the choice of treatments and data sources had an impact on the ICER, although the ICER remained below the NICE £30k/QALY threshold with more conservative assumptions (Table 2).

***Figure 2.** Tornado diagram representing the top 10 parameters which contributed to model uncertainty*

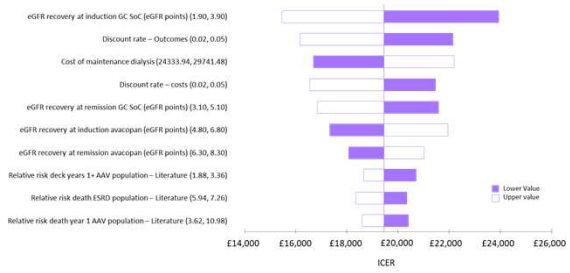

***Figure 3.** Scatter diagram for the PSA*

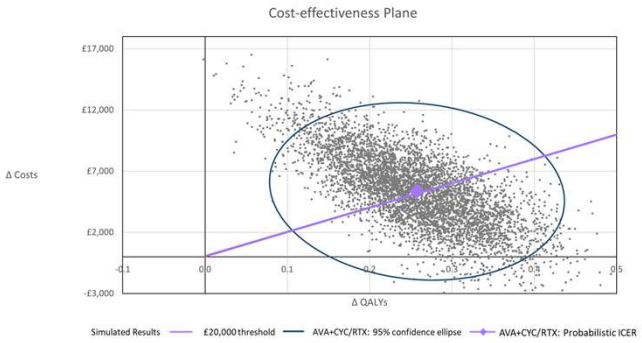

***Figure 4.** CEAC for the PSA*

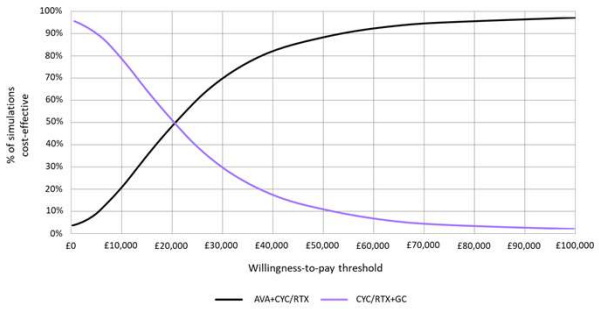

***Table 2.** Scenario analysis results*

Scenario	Δ Cost	Δ QALYs	ICER per QALY
Base case	£5,097	0.26	£19,441
Re-induction with avacopan	£11,578	0.52	£22,454
RTX maintenance for eligible patients	£5,911	0.25	£23,704
AE source from CPRD (RWE dataset in UK)	£5,097	0.20	£26,203
HR for ESRD per unit eGFR: 0.947 (Literature pooled estimate)	£6,823	0.22	£30,888
eGFR decrease with each relapse: 15ml/min	£3,884	0.29	£13,391
Treatment-specific utility values from ADVOCATE trial	£5,097	0.28	£18,261

Conclusions

- Avacopan in combination with cyclophosphamide and rituximab is cost-effective compared to current SoC in the UK. Avacopan was superior compared to GC-based SoC in terms of sustained remission, which resulted in improved QALYs and reduced cost of treating relapse and ESRD over a lifetime horizon.
- The model was informed by phase III trial data restricted to 52 weeks, and the long-term cost-effectiveness of avacopan is uncertain, particularly in terms of renal function and probability of ESRD. Studies using real-world registry data could inform long-term outcomes and reduce uncertainty.

References

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Disclosure statement

This study was funded by CSL Vifor. Vladislav Berdunov (presenting author) has no further conflicts of interest to declare.

Footer: AE = adverse event; ANCA = anti-neutrophil cytoplasmic antibody; AVA = avacopan; CEAC = cost-effectiveness acceptability curve; CYC = cyclophosphamide; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; GC = glucocorticoid; GPA = granulomatosis with polyangiitis; HR = hazard ratio; ICER = incremental cost-effectiveness ratio; MPA = microscopic polyangiitis; NICE = National Institute of Health and Care Excellence; PSA = probabilistic sensitivity analysis; QALY = quality-adjusted life-year; RTX = rituximab; SoC = standard of care; WTP = willingness to pay.

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