A cost-utility analysis of avacopan for the treatment of antineutrophil cytoplasmic antibody-associated vasculitis, a rare disease, in Spain

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INTRODUCTION AND OBJECTIVE

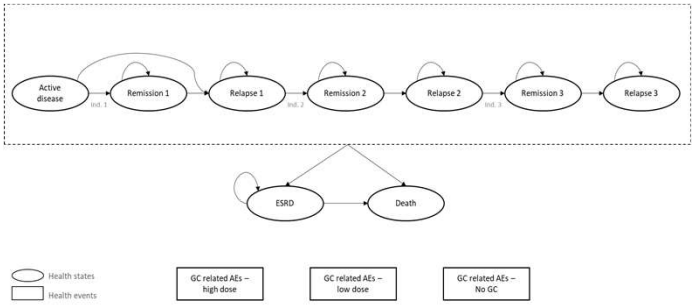
- Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) is a rare, heterogeneous, life or organ-threatening, autoimmune condition affecting small and medium blood vessels, including microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA)[1,2].
- In Spain, the prevalence of GPA and MPA is estimated to be 15.8 and 23.8 cases per million inhabitants, respectively[3], and the incidence varies between 2.1-2.9 and 3.4-7.9 new cases per million habitants, respectively[3,4].
- Avacopan is an orally administered small molecule that is a highly selective inhibitor of the complement C5a receptor 1 (C5aR1). Avacopan, in combination with a rituximab (RTX) or cyclophosphamide (CYC) regimen, is indicated for the treatment of adult patients with severe, active GPA or MPA[5].
- **This study aimed to evaluate the cost-utility of avacopan in combination with RTX or CYC compared with glucocorticoids (GC) and RTX or CYC for the treatment of severe, active AAV from the Spanish National Health System perspective.**

METHODS

Model Structure

- A 9-state Markov model was developed to reflect clinical practice for achieving and sustaining remission in patients with AAV over a lifetime horizon, comprising an active disease state where patients start, three remission and three relapse states, end-stage renal disease (ESRD) and death. Additionally, patients can experience GC-related adverse events (AEs) depending on the GC dosage (high, low or no GC)(FIGURE 1).

Figure 1. Markov Model Structure



Note: The cycle duration is 4 weeks.
AE: Adverse event; ESRD: End stage renal disease; GC: Glucocorticoids.

Inputs & assumptions

- Demographic characteristics were obtained from the phase 3 ADVOCATE trial[6] and validated by a panel of Spanish clinical experts. A cohort of patients with a baseline mean age of 61 years and a male proportion of 59% were considered[6].
- Transition probabilities from the active disease/relapse state to remission and remission to relapse were determined from the proportion of patients in remission at 26 and 52 weeks in ADVOCATE trial[6].
- The probability of progression from active disease/relapse state to ESRD and remission to ESRD was sourced from literature and adjusted with the change in estimated glomerular filtration rate observed in the ADVOCATE trial[6], but this resulted in a high variability in the progression to ESRD. In the base case, the risk of ESRD reported by Robson et al. (2015)[7] was assumed. Additionally, different scenario analyses based on data from Spanish studies[8-10] were performed (TABLE 1).

Table 1. Cumulative incidence of progression to ESRD

References	Follow-up (years)	Cumulative incidence
Robson et al., 2015[7]	**0.5**	**6.4%**
	7.1	**13.9%**
Solans-Laqué et al., 2017[8]	6.8	16.8%*
Villacorta et al., 2020[9]	3.4	32.7%
Marco et al., 2018[10]	3.6	35.1%

ESRD: End-stage renal disease; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis.
*Considering GPA/MPA patients requiring dialysis.
Note: For the base case, different probabilities from active disease/relapse and remission state to ESRD were applied, according to the data at 6 months and 7.1 years, respectively.

- Mortality data included the increased mortality rate in AAV and ESRD patients, compared to the general population. This was done by applying a relative risk obtained from the literature[11] to the Spanish life tables[12].
- Costs (€, 2022) were sourced from national databases, including drug acquisition, management of AAV (hospitalisations, monitoring and maintenance), ESRD and AEs[13-18].
  - The cost of ESRD was derived by including the cost of the different treatment options: peritoneal dialysis (€32,432), hemodialysis (€51,792), and renal transplant (first year: €49,318; subsequent years: €6,777)[17,18]; and the corresponding distribution of use: peritoneal dialysis (5.4%), hemodialysis (43.8%) and renal transplant (50.8%)[18].

METHODS

- Health outcomes were expressed as quality-adjusted life years (QALYs) and life years gained (LYG). QALYs were determined by multiplying the duration of time spent in each health state by the associated health-related quality of life weight (i.e., utility). The utilities for each health state (active disease, remission, and relapse) were obtained from the EQ-5D-5L questionnaire used in the ADVOCATE trial[5], and the utility decrements for adverse events were included separately and obtained from the literature[16,19,20] (TABLE 2).
- An annual discount rate of 3% was applied to costs and health outcomes[21,22].

Table 2. Utilities used for each health state and AE

Parameter	Utility values	
Health state	**Avacopan**	**GC**
Active disease[6]	0.708	0.697
Remission[6]	0.790	0.766
Relapse[6]	0.738	0.678
ESRD[6]	0.453	0.453
AE	**Acute**	**Follow-up period**
Infections	-0.100	NA
CV disease[19]	-0.049	-0.049
Renal disease[19]	-0.053	-0.053
Bone disease[16]	0.000	0.000
Ocular disease[20]	-0.050	NA

Note: Utility values for infections are assumed.
AE: Adverse event; CV: Cardiovascular; ESRD: End-stage renal disease; GC: Glucocorticoids; NA: Not applicable.

RESULTS

Base case

- Considering an average annual progression to ESRD of 2.0%, a regimen including avacopan compared to GC, as an add on to CYC (35%) or RTX (65%)[5], respectively, was more effective (6.63 vs. 6.32 QALYs), and resulted in an incremental cost of €8,918.
- The drug acquisition cost represented 19% of all costs in avacopan arm and 7% in GC arm.
- Avacopan compared to GC yielded an incremental cost-utility ratio (ICUR) under a threshold of €30,000 per additional QALY gained (TABLE 3).

Table 3. Base case analysis

	Avacopan+ RTX/CYC	GC+ RTX/CYC	Incremental
Costs			
Total costs	**€ 159,867**	**€ 150,949**	**€ 8,918**
Drug acquisition	€ 30,676	€ 10,689	€ 19,987
Management of AAV	€ 21,435	€ 22,439	-€ 1,004
ESRD management	€ 107,756	€ 117,821	-€ 10,065
Effectiveness			
QALY	6.63	6.32	**0.31**
LYG	9.75	9.42	**0.33**
Results			
ICUR		**€ 29,020/QALY**	
ICER		**€ 27,259/LYG**	

CYC: Cyclophosphamide; ESRD: End stage renal disease; GC: Glucocorticoids; ICER: Incremental cost-effectiveness ratio; ICUR: Incremental cost-utility ratio; LYG: life year gained; QALY: quality-adjusted life year; RTX: Rituximab.

Scenario analyses

- The ICER increased according to the probabilities of progression to ESRD.
- In the different scenarios, avacopan compared to GC, was more effective (5.77-6.58 vs 5.59-6.37 QALYs), and resulted in an incremental cost (€13,667-14,191), yielding a ICUR under a threshold of €100,000 per additional QALY gained (TABLE 4).
- Drug costs accounted for 15%-19% of total costs in avacopan arm, and 5%-7% in GC arm.

Table 4. Scenario analyses

	Solans-Laqué et al., 2017	Villacorta et al., 2020	Marco et al., 2018
Δ Costs	€ 14,418	€ 14,160	€ 14,191
Δ LY	0.19	0.18	0.18
Δ QALYs	0.20	0.18	0.18
ICUR	**€ 73,920**	**€ 77,447**	**€ 78,142**

ICUR: Incremental cost-utility ratio; LY: life year; QALY: quality-adjusted life year

CONCLUSIONS

- **Avacopan is a new cost-effective option for AAV patients in Spain since it reduces relapse rates, the risk of progression to ESRD and GC-related infections and complications, considering a threshold for orphan drugs of €30,000-100,000/QALY gained[23].**
- **This model facilitates the approach to economic evaluation of orphan drugs where the evidence is scarce.**

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