ISPOR Europe 2024, 17th-20th November 2024, Barcelona, Spain

EE400

Cost-effectiveness of avacopan for the treatment of granulomatosis with polyangiitis or microscopic polyangiitis in adult patients in Austria

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Objectives

The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) are a group of rare diseases, comprising granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Diagnosis of AAV is often delayed due to the non-specific disease course. The disease can be rapidly progressive and can result in organ damage and death.

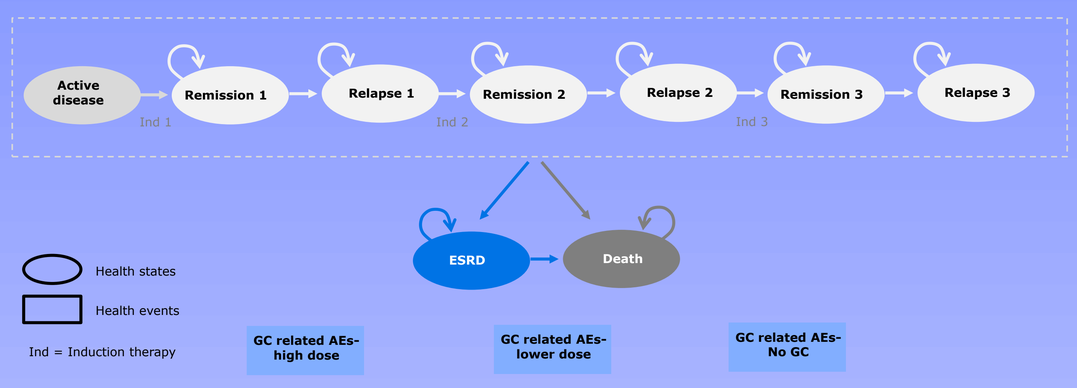
It is estimated that between 617 and 1,257 people have been diagnosed with AAV in Austria. Of these, about 441 to 828 cases are attributable to GPA, about 83 to 233 to MPA and 53 to 196 to EGPA.

This analysis aims to evaluate the cost-effectiveness of avacopan (AVA) in combination with either a rituximab (RTX) or cyclophosphamide (CYC) dosing regimen, compared to prednisolone plus RTX or CYC in adult patients with severe active GPA or MPA.

Methods

A multistate Markov-cohort-model was developed to simulate costs, life-years (LYs) and quality-adjusted life-years (QALYs) with a lifetime horizon. The model comprises 9 health states: an active disease state, three remission and three relapse states, end-stage renal disease (ESRD) and death, with a cycle length of 4 weeks. Clinical data from the phase 3 clinical trial ADVOCATE were used. Direct costs (year 2024) were derived from published sources. All drug costs, including avacopan, are based on the reimbursement list-price. A univariate deterministic sensitivity analysis and probabilistic sensitivity analysis (PSA) were performed. QALYs, LYs and costs were discounted.

Figure 1: Model design



Transition probabilities for the population included were used to model the following (Figure 1):

- Newly diagnosed patients with recurrence enter model in "active disease" state and get first induction therapy with AVA+RTX/CYC or GC+RTX/CYC
- Patients stay in "remission 1" or experience a recurrence and switch to "relapse 1" where they get second induction.
- The model considers two re-induction phases with RTX or CYC.
- Max. duration induction phase is 6 months.
- Once the induction phase is completed and patients are in remission, maintenance therapy for 24 months is recommended (Hellmich et al. 2023).
- In accordance with the ADVOCATE study protocol, patients in remission will receive azathioprine for 26 cycles.
- Patients get azathioprine until they switch to ESRD state or death (absorbing state)
- Max. duration maintenance phase is 24 months.
- Patients can enter the ESRD state or death at anytime during the model period.
- Cost and QALYs in alive-states are calculated for each alternative and each patient during each cycle.

Table 1: Overview of methods applied

Methods	
Type of study	Cost-effectiveness analysis (CEA) and cost-utility analysis (CUA)
Type of the model	A Markov-cohort-state-transition model using 9 health states
Perspective	Austrian healthcare payer perspective
Time horizon	Lifetime (40 years)
Cycle length	4 weeks
Discount rate	5% per annum for costs & 3% per annum for outcomes
Population	Patients with newly diagnosed or recurrent GPA or MPA, a mean age of 60, a mean body weight of 77 kilograms, a mean body surface area of 1.92 square meters, AVA arm: 64.8% used AVA+RTX, 35.2% used AVA+CYC
Intervention	AVA+RTX/CYC (30 milligram [mg] AVA twice daily per oral [one capsule = 10mg AVA])
Comparator	GC+RTX/CYC
Outcomes	LYs saved; QALYs saved; total cost; Incremental cost-utility ratio (ICUR) & incremental cost-effectiveness ratio (ICER)
Utilities	Health state-dependent utilities are based on Dutch EQ-5D-3L value set from Versteegh et al. (2016) Age-dependent utilities are based on Ara & Brazier (2011) Only "Serious Adverse Events" (SAEs) with an incidence of > 2% in one of the two treatment arms of the ADVOCATE study were used to calculate the disutilities.
Timing	2024

Clinical Data

- The patient groups modelled (intention-to-treat population) corresponds to patients included in the ADVOCATE trial (Jayne et al. 2021).
- This study is a global, multicenter, randomized, double-blind, pivotal-Double-Dummy phase 3 clinical trial to investigate the efficacy and safety of avacopan as combination therapy for the treatment of GPA or MPA over 52 weeks. The primary endpoint was remission in week 26 (intervention arm versus comparator arm: 72.3% versus 70.1%) and sustained remission in week 52 (intervention arm versus comparator arm: 65.7% versus 54.9%) (Jayne et al. 2021).
- Distribution of ESRD treatments was used to inform the model ESRD health-state: peritoneal dialysis (~9.3%), hemodialysis (~87.6%), and renal transplant (~3.1%)
- Safety data were taken directly from ADVOCATE (Jayne et al. 2021).
- A relative risk to die is applied to the life table of the Austrian general population to account for the increased mortality rate in the AAV patient population and in patients with ESRD compared to the Austrian general population.

Resource Use and Costs

- Direct costs: drug acquisition costs, drug administration costs, monitoring costs, ESRD costs, hospitalization costs, and adverse event (AE) costs
- All direct cost components are based on values for 2024.
- All drug costs (incl. avacopan) are based on reimbursement list prices.
- Vial sharing was used for all intravenously applicated drugs.
- Drug administration costs are applied for all intravenously applicated drugs.

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Funding: This study was sponsored by CSL Vifor Flughofstrasse 61, 8152 Glattbrugg, Switzerland

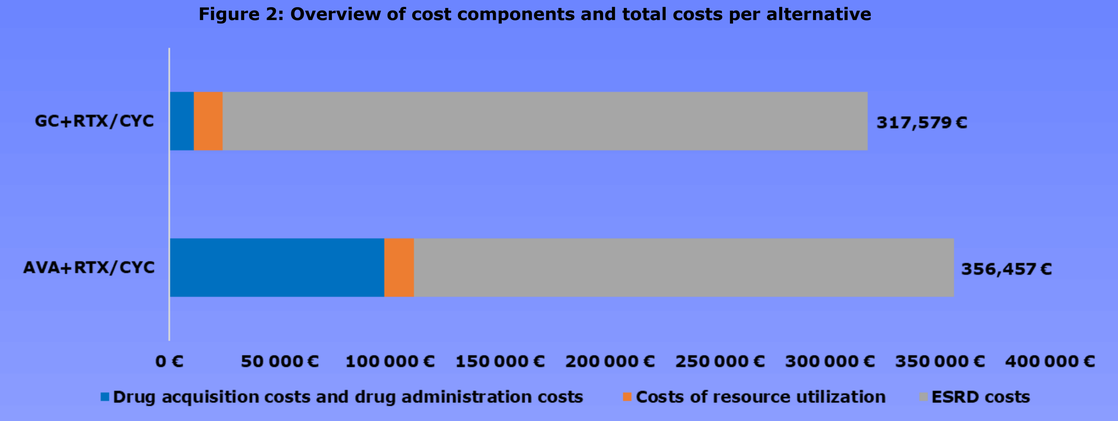
Results

Total costs and cost components

Over a lifetime horizon, AVA+RTX/CYC leads to total cost of 356,457 € and GC+RTX/CYC results in total cost of 317,579 €. This causes incremental cost of 38,878 € for AVA+RTX/CYC versus GC+RTX/CYC regarding adult patients with this rare and severe active conditions (Figure 2; Table 2).

ESRD costs is the most considerable cost component in both treatment arms. A comparison of these two alternatives reveals significantly higher ESRD related costs of +48,385.62 € in the GC+RTX/CYC treatment arm. This saving leads to a cost compensation of 55.9% for drug acquisition and administration costs (Figure 2; Table 2).

Figure 2: Overview of cost components and total costs per alternative



Source: own calculations

Cost-effectiveness results

AVA+RTX/CYC is associated with a QALY benefit of 0.67 QALYs compared to GC+RTX/CYC. In addition, the intervention leads to a survival benefit of 0.47 LYs. Incremental cost of 38,878 € and incremental QALYs of 0.67 result in an ICUR of 57,684 €/QALY regarding AVA+RTX/CYC versus GC+RTX/CYC (Table 2).

Table 2: Cost-effectiveness results

Cost components	AVA + RTX/CYC	GC + RTX/CYC	Difference
Drug acquisiton and administration costs	97,811.07 €	11,195.51 €	86,615.56 €
Other health care costs*	13,604.03 €	12,956.13 €	647.90 €
ESRD costs	245,041.76 €	293,427.38 €	-48,385.62 €
Total costs	**356,456.86 €**	**317,579.03 €**	**38,877.84 €**
Total QALYs	6.34	5.67	0.67
ICUR per QALY gained		**57,683.90 €**	
Total LYs	10.04	9.57	0.47
ICER per LY gained		**82,589.77 €**	

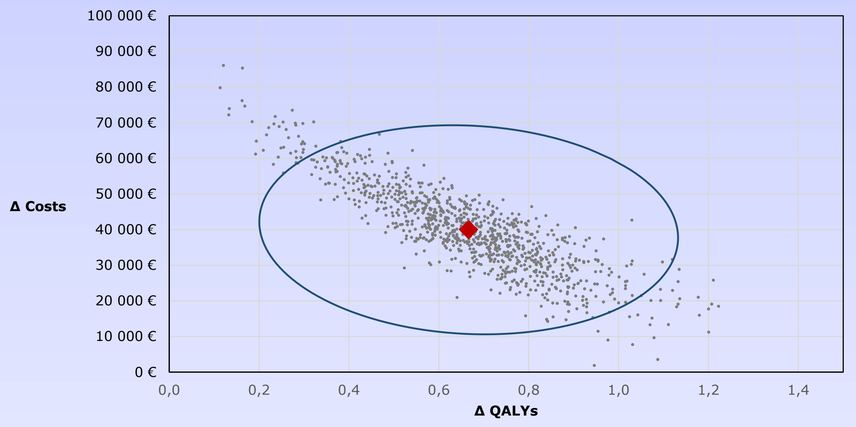
*Costs of resource utilization comprise monitoring costs, hospitalization costs, and AE costs.

Source: own calculations

Sensitivity Analysis

A one-way sensitivity-analysis (OWSA) and a probabilistic sensitivity-analysis (PSA) were performed to examine the robustness of the model.

Figure 3: Scatterplot, AVA+RTX/CYC versus GC+RTX/CYC



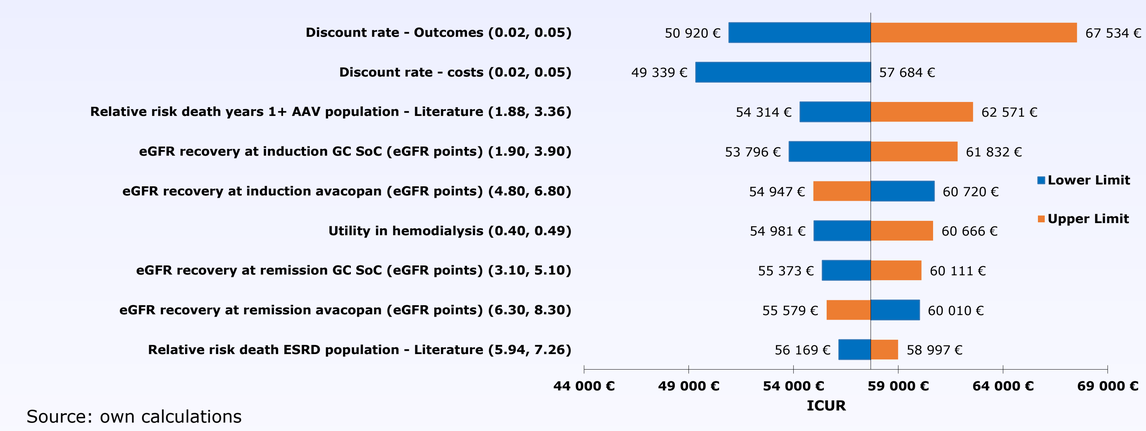
- The Monte-Carlo PSA results of 1,000 second-order simulations plotting incremental cost versus incremental effects (Figure 3).
- The acceptability-curve revealed that in case of a WTP for an ultra orphan diseases of £300.000 [~ 346.364 €; maximum threshold for highly specialized treatments] AVA+RTX/CYC was a highly cost-effective strategy in 100.0% of the simulations.

Source: own calculations

The OWSA uses a tornado diagram to depict the effect of variations on base case results.

- The highest impact was identified for "discount rate-outcomes" (50,920 €; 67,534 €)
- and the lowest impact for "relative risk of death in the ESRD population" (56,169 €; 58,997 €) (Figure 4).

Figure 4: OWSA tornado diagram, AVA+RTX/CYC versus GC+RTX/CYC



Source: own calculations

Conclusion

In adult patients with this rare and severe active condition (AAV), avacopan shows a good and affordable cost-effectiveness relationship from the Austrian payer perspective.

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