Cost-effectiveness of avacopan for ANCA-associated vasculitis in China

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Abstract

Objective

To evaluate the cost-effectiveness of avacopan plus immunosuppressants versus glucocorticoid (GC)-based regimens for adults with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in China, and to estimate the maximum avacopan unit price consistent with willingness-to-pay (WTP) thresholds.

Methods

A nine-state Markov model (active disease; three remission states; three relapse states; end-stage renal disease [ESRD]; death) was developed from the Chinese healthcare system perspective. Baseline characteristics were derived from the ADVOCATE trial. The intervention was avacopan plus cyclophosphamide (CYC) or rituximab (RTX) with reduced-dose GCs; the comparator was CYC/RTX plus standard GCs. Treatment shares followed trial allocation (35.2% CYC; 64.8% RTX). Outcomes included total costs, life-years (LYs), quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs), using a WTP threshold of one time China's 2024 GDP per capita per QALY. Uncertainty was assessed through one-way, probabilistic, and scenario analyses. Threshold price analyses back calculated the avacopan unit price at WTPs of one time, 1.2 times, and 1.5 times GDP per capita.

Results

Avacopan increased QALYs (5.81 vs. 5.26) and LYs (8.25 vs. 7.77) and increased total costs ($73,478 vs. $70,110), yielding an ICER of $6,146/QALY. At a WTP of $13,445/QALY, avacopan was cost-effective; results were robust in sensitivity and scenario analyses. The maximum cost-effective price was $11.12-$12.70 per 10 mg at WTPs of 1.0-1.5 times GDP per capita.

Conclusion

Avacopan-based regimens are cost-effective versus GC-based therapy for GPA/MPA in China and support value-based pricing of $11.12-$12.70 per 10 mg.

Key words

avacopan, cost effectiveness analysis, anti-neutrophil cytoplasmic antibody-associated vasculitis

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Introduction

Anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) is a rare, severe autoimmune small-vessel vasculitis included in China's second national rare disease catalogue (1, 2). AAV encompasses granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) (3). In China, the prevalence is 25 per 100,000 (4), with MPA accounting for about 80% of cases, GPA 15%, and EGPA 5% (5). The disease course is aggressive with frequent relapses; 80–90% of patients develop organ-threatening manifestations (6), most commonly renal involvement. Within five years, 15-38% of patients progress to end-stage renal disease (ESRD) (7). In China (8), mean annual costs were $15,100 for haemodialysis, $12,076 for peritoneal dialysis, and $15,767 for transplantation. Over eight years, cumulative costs reached $144,196, $122,398, and $122,511, respectively; this places a substantial burden on households and insurers. Roughly half experience relapse requiring prolonged immunosuppression (9). Mortality remains substantial: without treatment, 1- and 2-year mortality approach 82% and 90% (10), respectively; despite standard therapy, median 5-year mortality is around 25%, largely driven by severe infections, cardiovascular events, and dialysis-related complications (11).

Current treatment for GPA/MPA involves an induction phase followed by maintenance therapy. In China, glucocorticoids (GC) in combination with either cyclophosphamide (CYC) or rituximab (RTX) are used for induction. However, treatment is constrained by GC-related infectious, skeletal and metabolic toxicities, CYC-associated myelosuppression and malignancy risk, and infection risk from prolonged immunosuppression alongside suboptimal relapse control. Avacopan, an oral C5a receptor inhibitor, has demonstrated efficacy in reducing GC exposure while maintaining disease control, and is now recognised by international guidelines and recent systemic-vasculitis reviews as a key reduced-dose GC option in the contemporary management of AAV (12-15). With its recent approval in China, evaluating the economic value of avacopan in the local healthcare context is essential. However, a comprehensive evaluation of the cost-effectiveness of avacopan in China remains lacking.

This study aimed to evaluate the cost-effectiveness of avacopan in combination with immunosuppressants (CYC or RTX) and GCs compared with standard GC-based regimens in newly diagnosed or relapsing adult patients with GPA or MPA, from the perspective of the Chinese healthcare system.

Methods

Model structure

A Markov model with nine mutually exclusive health states was developed to simulate the progression of AAV and evaluate the cost-effectiveness of treatment strategies. The health states included: active disease, three remission states, three relapse states, ESRD, and death. ESRD was modelled as a distinct health state reflecting severe renal impairment, while death was treated as an absorbing state (13). The model structure is shown in Figure 1.

All patients were assumed to enter the model in the active disease state, representing either newly diagnosed or relapsing AAV requiring induction therapy. Patients who achieved remission transitioned to the maintenance phase. Relapse during maintenance prompted re-induction therapy, returning patients to remission once again. Thus, patients could cycle between remission and relapse until progression to ESRD or death. Refractory disease was defined as three relapse states; in this health state, patients were no longer eligible for further induction therapy and remained until progression to ESRD or death (13). At any cycle, patients could develop ESRD. Once in the ESRD health state, patients remained there until death, as recovery was not permitted, and no further induction or maintenance therapy was administered. Patients with ESRD were assumed to receive chronic renal replacement therapy until death or kidney transplantation.

The model used a cycle length of 4 weeks and applied half-cycle correction to improve accuracy. Given that

AAV requires lifelong management and may lead to long-term complications, a lifetime horizon was adopted to capture differences in costs and outcomes between treatment arms, as well as the long-term impact of the disease and its management on patient quality of life. Model outcomes included total costs, life years (LYs), quality-adjusted life years (QALYs), and incremental cost-effectiveness ratio (ICER). Costs incorporated drug acquisition, direct medical care, ESRD management, and adverse event (AE) treatment. Costs and health outcomes were discounted at 5% annually. The willingness-to-pay (WTP) threshold was set according to the 2024 per capita GDP in China ($13,445; €12,455/QALY) (16). This study adhered to the Consolidated Health Economic Evaluation Reporting Standards reporting guideline (17) (Supplementary Table S1).

Patient population

The target population consisted of adult patients (≥18 years) with newly diagnosed or relapsing GPA or MPA. Baseline characteristics were aligned with the phase 3 ADVOCATE trial, in which the mean patient age was 60 years and most participants presented with renal involvement (13) (Suppl. Table S2).

Treatment strategies

Treatment regimens were designed based on clinical protocols from the ADVOCATE trial, National Institute for Health and Care Excellence (NICE) technology appraisal guidance 825 (18), and Manuel's study (1).

Intervention

Induction phase. Patients received avacopan 30 mg orally twice daily, in combination with either RTX (375 mg/m2 intravenous infusion once weekly for 4 weeks) or CYC (15 mg/kg intravenous infusion on days 1, 15, 29, 49, 70, and 91), together with a reduced-dose GC taper. A weighted calculation was performed using the randomised controlled trial (RCT) treatment allocation proportions: 35.2% for CYC and 64.8% for RTX (13).

Maintenance phase. Avacopan was combined with azathioprine for 6 treatment cycles, followed by azathioprine monotherapy for 19 treatment cycles. From week 15, the azathioprine dose was titrated over 2 weeks to 2 mg/kg/day and maintained until week 52.

Refractory disease state. Based on NICE technology appraisal guidance 825 (18) and Manuel's study (1), patients not achieving remission after three induction courses entered a refractory disease state and received azathioprine at 2 mg/kg/day.

Comparator

Induction phase. CYC or RTX (administered at the same dosage as in the intervention regimen) in combination with a tapering course of GCs. A weighted calculation was performed using the RCT treatment allocation proportions: 35.2% for CYC and 64.8% for RTX (13).

Maintenance phase. Azathioprine monotherapy was administered at the same dose as in the intervention group.

Refractory disease state. Patients unresponsive after three induction courses entered a refractory disease state and received azathioprine, consistent with the comparator group.

Clinical efficacy

Clinical parameters were primarily derived from the ADVOCATE trial (13). Remission and relapse rates for the avacopan and GC groups were based on the proportions of patients in remission at weeks 26 and 52. For relapse between weeks 52 and 60, the intervention arm hazard ratio (HR) was estimated from the difference in remission rates at weeks 52 and 60 (8-week follow-up). This HR was applied to adjust the per-cycle relapse probability of the control arm, yielding relapse probabilities for the intervention arm. For the control arm, the relapse probability between weeks 52 and 60 was assumed to be the same as that between weeks 26 and 52, in line with NICE technology appraisal guidance 825 (18).

To account for the potential waning of avacopan efficacy after treatment cessation, a conservative approach informed by Manuel *et al*. was adopted. From week 60 onwards, efficacy was assumed to decline gradually at a constant rate over a 3-month period, based on the trend observed between weeks 26–52 and 52–60 (18). By the end of 2 years of maintenance therapy, relapse probabilities were assumed to be equivalent in both arms.

The probability of progression to ESRD varied by health state. For active disease (including relapse states), the risk of ESRD was estimated from data showing that the first 6 months after AAV onset carry a substantially higher ESRD risk compared with subsequent years. Cumulative 6-month ESRD incidence was extracted from long-term follow-up of six RCTs and converted into transition probabilities using an exponential distribution (19). For remission states, transition probabilities were derived from the cumulative ESRD incidence observed over 7.1 years in the same six RCTs, again using an exponential model (19).

For refractory disease, and consistent with NICE technology appraisal guidance 825, the risk of progression to ESRD was assumed to be 15 times higher than that of patients in remission (18). To reflect renal outcomes observed in ADVOCATE, the relative risk reduction in eGFR decline for avacopan versus control (HR=0.71) was applied to adjust annual transition probabilities to ESRD from both relapse and remission states, using cumulative ESRD incidence data from the six RCTs control arm as baseline (13, 19).

Background mortality was based on the Seventh National Population Census of China (20). As mortality rates for patients with AAV and ESRD are substantially higher than those of the general population, relative risks were applied to adjust general population mortality (21). Mortality was assumed to be equal across active disease, remission, and relapse states (22).

In addition, given the well-established association between glucocorticoid exposure and AEs, and the dose-dependent increase in toxicity, treatment-related grade ≥3 serious AEs with an incidence of at least 5% in either the avacopan or GC group of the ADVOCATE trial were incorporated into the model (13) (Table I).

Costs

The analysis considered direct medi-

cal costs, including drug acquisition, disease management, monitoring and follow-up, hospitalisation, ESRD management, and AE treatment. Costs of concomitant medications were obtained from the 2024 national median bid prices (23). Management and monitoring costs were derived from the median prices of medical service items across Chinese provinces. Hospitalisation and ESRD treatment costs were sourced from published literature, while AE management costs were estimated based on data from the Hospital Information System of the Third Affiliated Hospital of Sun Yat-sen University (24, 25) (Table I). All costs were initially collected in Chinese renminbi and then converted to US dollars using the average 2024 exchange rate ($1 = ¥7.12) (26). For key results, approximate values in euros were additionally reported using an exchange rate of €1 = $1.08 (26).

Utilities

Changes in health utility were primarily influenced by treatment regimen; within the same health state, between-group differences in utility were mainly attributable to reduced GC exposure and improvements in GC-related AEs in the avacopan group. Health utility values were sourced from NICE technology appraisal guidance 825 (18). To avoid double counting, the disutility associated with GC-related AEs was incorporated into health state utilities rather than modelled separately under treatment-related AEs. Therefore, only the disutility from treatment-related AEs unrelated to GC exposure was included in the AE component of the model (Table I).

Sensitivity analysis and scenario analysis

To evaluate the robustness of the model results, we conducted one-way, probabilistic, and scenario-based sensitivity analyses. In the one-way sensitivity analysis, model parameters were varied within predefined ranges, based on 95% confidence intervals when available or ±10% otherwise, to assess their impact on cost-effectiveness outcomes. Key parameters were identified and illustrated using tornado diagrams. In the probabilistic sensitivity analysis, we as-

Table I. Model input parameters.

Name	Mean	Low	Upper	Distribution	Source
Drug cost ($)					
Avacopan (10 mg)	9.41	7.53	11.29	Gamma	(31)
Rituximab (100 mg)	191.84	105.09	322.19	Gamma	(32)
Rituximab (500 mg)	673.01	538.41	1,104.58	Gamma	
Cyclophosphamide Injection (1000 mg)	22.47	17.97	26.96	Gamma	
Cyclophosphamide Injection (500 mg)	13.97	11.18	16.77	Gamma	
Cyclophosphamide Injection (200 mg)	3.37	3.19	3.39	Gamma	
Prednisone (5 mg)	0.26	0.21	0.31	Gamma	
Azathioprine (50 mg)	0.27	0.11	0.31	Gamma	
Monitoring and maintenance costs ($)					
Blood test per visit	2.81	2.25	4.91	Gamma	(18,23)
Liver function test per visit	11.23	9.83	13.34	Gamma	
Outpatient follow-up per visit	15.45	8.39	31.45	Gamma	
ESRD and mortality costs ($)					
Haemodialysis/year	13,306.20	10,644.96	15,967.44	Gamma	(33)
Peritoneal dialysis/year	11,340.60	9072.48	13,608.72	Gamma	
Kidney transplant surgery	20,365.25	18,328.73	22,401.78	Gamma	(34)
Post-transplant Treatment/year	13,792.88	11,034.30	16,551.45	Gamma	
Management costs ($)					
Intravenous infusion per visit	1.09	0.79	1.37	Gamma	(23)
Drug preparation	2.18	0.91	2.91	Gamma	
Infusion pump/hour	0.25	0.20	0.29	Gamma	
Hospitalisation costs ($)					
Annual hospitalisation	18,254.60	14,603.68	21,905.52	Gamma	(1)
Adverse event treatment costs ($)					
Infection (GC)	16,850.40	13,480.32	20,220.48	Gamma	(18,26)
Cardiovascular event (GC)	1,123.36	898.69	1,348.03	Gamma	
Ophthalmic disease (GC)	2,808.40	2,246.72	3,370.08	Gamma	
Orthopaedic disease (GC)	6,318.90	5,055.12	7,582.68	Gamma	
Endocrine and metabolic (GC)	1,404.20	1,123.36	1,685.04	Gamma	
Dermatological disease (GC)	47.31	37.85	56.77	Gamma	
Digestive system diseases (GC)	982.94	786.35	1,179.53	Gamma	
ANCA-associated Vasculitis adverse event management costs	1,151.13	920.91	1,381.36	Gamma	
Utility					
Active disease (Avacopan group)	0.78	0.74	0.82	Beta	(18)
Remission (Avacopan group)	0.85	0.83	0.87	Beta	
Relapse (Avacopan group)	0.81	0.71	0.91	Beta	
Active disease (GC group)	0.78	0.74	0.82	Beta	
Remission (GC group)	0.83	0.81	0.85	Beta	
Relapse (GC group)	0.74	0.62	0.86	Beta	
ESRD	0.44	0.40	0.49	Beta	(35)
Post-transplant	0.71	0.64	0.78	Beta	
AAV-related adverse event (disutility)	-0.05	-0.06	-0.04	Beta	(18)
Clinical parameters					
Remission rate at week 26 (Avacopan group)	0.72	0.65	0.80	Beta	(13)
Remission rate at week 52 (Avacopan group)	0.66	0.59	0.72	Beta	
Remission rate at week 26 (GC group)	0.70	0.63	0.77	Beta	
Remission rate at week 52 (GC Group)	0.55	0.49	0.60	Beta	
Incidence of ANCA-associated vasculitis (Avacopan group)	0.07	0.06	0.08	Beta	
Incidence of infection (Avacopan group)	0.04	0.03	0.05	Beta	
Incidence of cardiovascular event (Avacopan group)	0.43	0.39	0.48	Beta	
Incidence of ophthalmic disease (Avacopan group)	0.04	0.03	0.05	Beta	
Incidence of orthopaedic disease (Avacopan group)	0.11	0.10	0.13	Beta	
Incidence of endocrine and metabolic diseases (Avacopan group)	0.14	0.13	0.15	Beta	
Incidence of dermatological disease (Avacopan group)	0.08	0.07	0.09	Beta	
Incidence of psychological problems (Avacopan group)	0.16	0.15	0.18	Beta	

Name	Mean	Low	Upper	Distribution	Source
Incidence of gastrointestinal disease (Avacopan group)	0.02	0.01	0.03	Beta	
Incidence of ANCA-associated vasculitis (GC group)	0.12	0.11	0.13	Beta	
Incidence of infection (GC group)	0.07	0.06	0.08	Beta	
Incidence of cardiovascular event (GC group)	0.52	0.47	0.57	Beta	
Incidence of Ophthalmic disease (GC group)	0.07	0.06	0.08	Beta	
Incidence of orthopaedic disease (GC Group)	0.13	0.12	0.14	Beta	
Incidence of endocrine and metabolic diseases (GC group)	0.29	0.26	0.32	Beta	
Incidence of dermatological disease (GC group)	0.17	0.15	0.19	Beta	
Incidence of Psychological problems (GC Group)	0.24	0.21	0.26	Beta	
Incidence of gastrointestinal disease (GC group)	0.02	0.01	0.03	Beta	
Other					
6-month ESRD incidence in AAV patients	0.06	0.05	0.07	Beta	(36)
7.1-year ESRD Incidence in AAV patients	0.14	0.13	0.15	Beta	
Relative risk of ESRD in refractory patients	15.00	12.00	18.00	Gamma	(37)
Proportion choosing Haemodialysis for ESRD	0.82	0.66	0.99	Beta	(38)
Proportion choosing Peritoneal dialysis	0.11	0.09	0.13	Beta	
Proportion choosing Kidney transplant for ESRD	0.07	0.05	0.08	Beta	
Patient Body Surface Area (m^2)	1.60	1.28	1.92	Gamma	
Patient weight (kg)	60.00	48.00	72.00	Gamma	
Discount rate	0.05	0.00	0.08	Beta	

ESRD: end-stage renal disease; GC: glucocorticoids.

Table II. Results of base-case analysis.

	Avacopan group	GC group
Total costs ($)	**73,478.41**	**70,109.75**
Drug costs	22,104.21	6,070.52
Medical resource utilisation costs	4,984.99	7,738.26
ESRD costs	34,517.48	40,427.24
Treatment-related adverse event cost	341.81	337.20
GC-related adverse event treatment costs	11,529.92	15,536.54
Health outcomes		
LYs (years)	8.25	7.77
QALYs	5.81	5.26
ICER ($/QALY)	6,145.57	

CYC: cyclophosphamide; RTX: rituximab; ESRD: end-stage renal disease; GC: glucocorticoids; ICER: incremental cost-effectiveness ratio; LYs: life years; QALYs: quality-adjusted life years.

signed appropriate probability distributions to all model parameters and jointly propagated uncertainty via 10,000 second-order Monte Carlo simulations, from which cost-effectiveness acceptability curves were generated. In the scenario analysis, we evaluated alternative settings, including one or two courses of avacopan after relapse, drug wastage with RTX and CYC (wastage arising from mismatches between vial size and prescribed dose, with costs charged per full vial), and combinations with RTX only or CYC only.

Threshold price analysis

Given the absence of an official list price for avacopan in mainland China, we additionally conducted a WTP-based price threshold analysis to estimate the maximum unit price consistent with cost-effectiveness under alternative thresholds. All clinical effectiveness, utilities, non-drug medical costs, and discounting assumptions were fixed at base-case values; only the unit price of avacopan was varied.

For each WTP threshold (one time, 1.2 times, and 1.5 times China's 2024 per-capita GDP per QALY), we solved for the unit price P* such that the ICER equals the threshold:

$ICER(P^*) = \Delta Cost(P^*) / \Delta QALY = WTP$.

Results

Base case

In the base case, the avacopan strategy generated more QALYs (5.81 *vs*. 5.26) and life-years (8.25 *vs*. 7.77) than the GC strategy. Total costs were $73,478 (€67,741) in the avacopan group and $70,110 (€ 64,642) in the GC group, corresponding to an ICER of $6,146/QALY (€ 5,666/QALY). At a WTP threshold of one time China's 2024 GDP per capita ($13,445; €12,455 per QALY), avacopan was cost-effective.

Compared with the GC group, total costs were higher in the avacopan group by $3,368 (driven by higher drug acquisition costs: $22,104 *vs*. $6,071), partly offset by lower medical resource utilisation costs ($4,985 *vs*. $7,738). ESRD-related costs were lower with avacopan ($34,517 *vs*. $40,427), and costs for GC-related AEs were also lower ($11,530 *vs*. $15,537). Costs for managing treatment-related AEs were similar between groups ($342 *vs*. $337). Detailed results are reported in Table II.

Sensitivity analyses

Sensitivity analyses supported the robustness of the base-case results. In the one-way sensitivity analysis, the unit price of avacopan was the most influential driver of the ICER. For avacopan group versus GC group, the ICER ranged from $329/QALY to $11,962/QALY. None of these variations changed the conclusion that avacopan remained cost-effective at a WTP threshold of one time per-capita GDP. The sensitivity analysis results are shown in Figure 2.

Results of the probabilistic sensitivity analysis are presented in Figure 3. In the avacopan group *versus* the GC group, the probability of cost-effective-

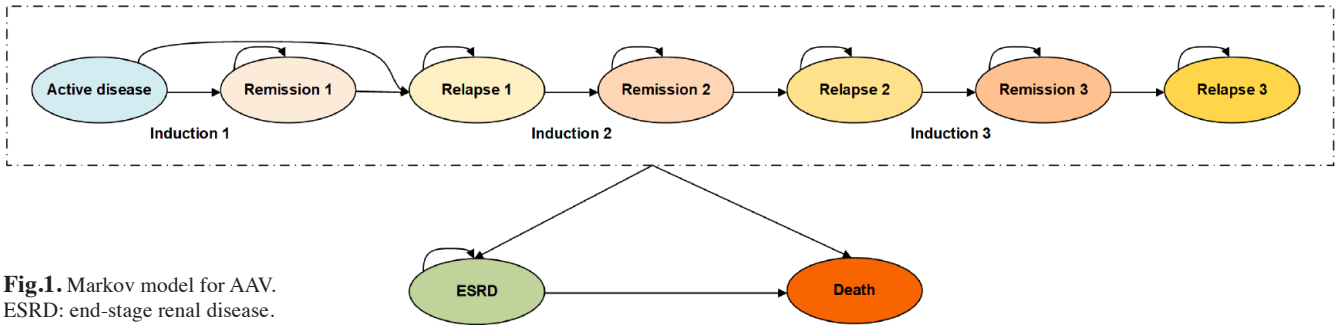

Fig.1. Markov model for AAV.
ESRD: end-stage renal disease.

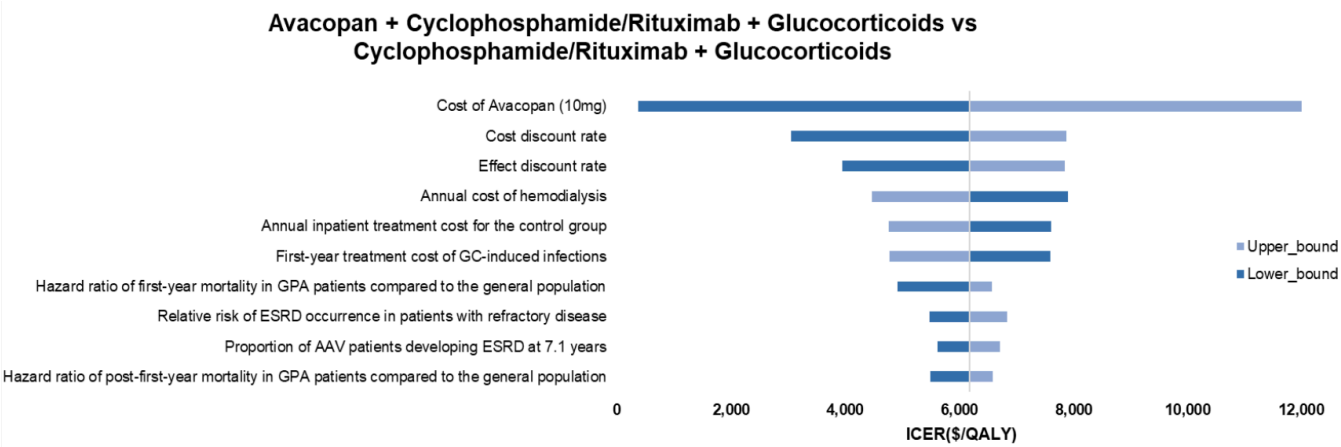

Fig. 2. Tornado diagram of one-way sensitivity analysis: avacopan group *vs*. GC group.
Each bar shows the change in the ICER when the corresponding parameter is varied from its lower to upper bound, with longer bars indicating greater influence on the cost-effectiveness results.
AAV: ANCA-associated vasculitis; ESRD: end-stage renal disease; GPA: granulomatosis with polyangiitis; GC: glucocorticoids.

ness was 94.44% at a WTP threshold of one time per-capita GDP and 99.47% at 1.5 times per-capita GDP.

Scenario analyses yielded consistent findings. When avacopan was administered once after relapse, the ICER for avacopan group *versus* GC group was $10,611/QALY; when administered twice after relapse, the corresponding ICER was $11,562/QALY. In scenarios with drug wastage for RTX and CYC, the ICER for the avacopan group versus the GC group was $6,150/QALY. When combined only with RTX, the ICER was $6,227/QALY; when combined only with CYC, the corresponding ICER was $6,101/QALY (Supplementary Table S3). In all cases, avacopan was considered cost-effective at a WTP threshold of one time per-capita GDP.

Threshold price back-calculation

The results of the threshold price back-calculation are shown in Figure 4. At a WTP threshold of one time per-capita GDP, the upper-bound unit price for avacopan was $11.12 (€10.25) per 10 mg. At 1.2 times per-capita GDP, the corresponding upper-bound unit price was $11.75 (€10.83) per 10 mg, and at 1.5 times per-capita GDP it was $12.70 (€11.71) per 10 mg.

Discussion

This study evaluated the cost-effectiveness of avacopan combined with immunosuppressants and GCs for treating adults with newly diagnosed or relapsing GPA/MPA in China. From the Chinese healthcare system perspective, avacopan-based regimens were cost-effective compared with standard GC-based regimens at a WTP threshold of one time the per-capita GDP. These findings were robust across base-case, deterministic, probabilistic, and scenario analyses. The clinical advantages of avacopan observed in the ADVOCATE trial (13) were key drivers of cost-effectiveness. Avacopan improved sustained remission rates and reduced relapse risk compared with conventional GC regimens, thereby delaying progression to ESRD, a major contributor to long-term costs and morbidity in AAV. In our model, the avacopan arm was associated with lower ESRD-related costs and reduced GC-related AEs, which partially offset its higher drug acquisition cost.

Renal outcomes play a central role in the economic burden of AAV. Approximately 81% of patients in the ADVOCATE trial had kidney involvement (13). Progression to ESRD significantly increases healthcare expenditures due to dialysis and transplantation. A study using Shanghai insurance data estimated cumulative 8-year costs of $22,165-144,633 for renal replacement therapy (8). Avacopan's renal benefits, including improved eGFR and delayed ESRD onset, suggest clinical and economic advantages, particularly in patients with advanced renal impairment (13). The management of relapsing disease also substantially affects both patient outcomes and cost. Scenario analyses demonstrated that re-treatment with avacopan after relapse-either once or twice-remained cost-effective at a WTP

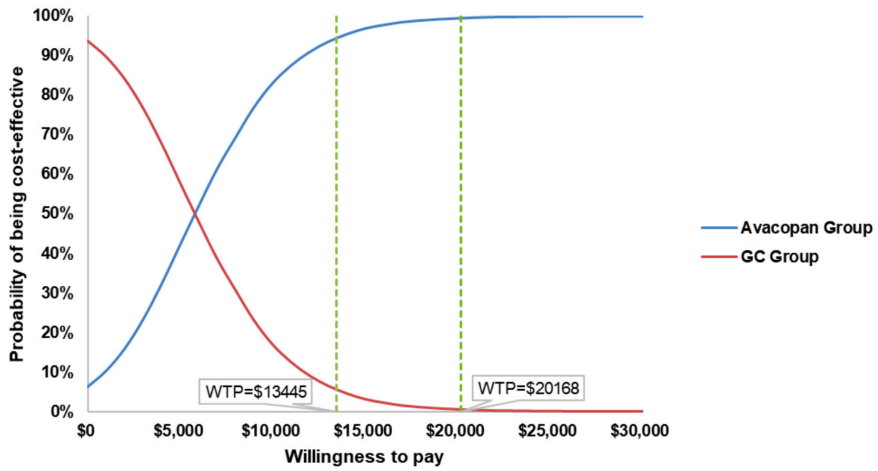

Fig. 3. Cost-effectiveness acceptability curve of probabilistic sensitivity analysis: avacopan group *vs.* GC group.
The cost-effectiveness acceptability curves show the probability that the avacopan group (blue) and the GC group (red) are cost-effective over a range of willingness-to-pay thresholds. As the WTP threshold increases, the probability that the avacopan group is cost-effective rises and exceeds that of the GC group beyond the intersection point. The two vertical green lines indicate WTP thresholds at one time and 1.5 times of China's 2024 per-capita GDP.
AVA: avacopan; CYC: cyclophosphamide; RTX: rituximab; GC: glucocorticoids.

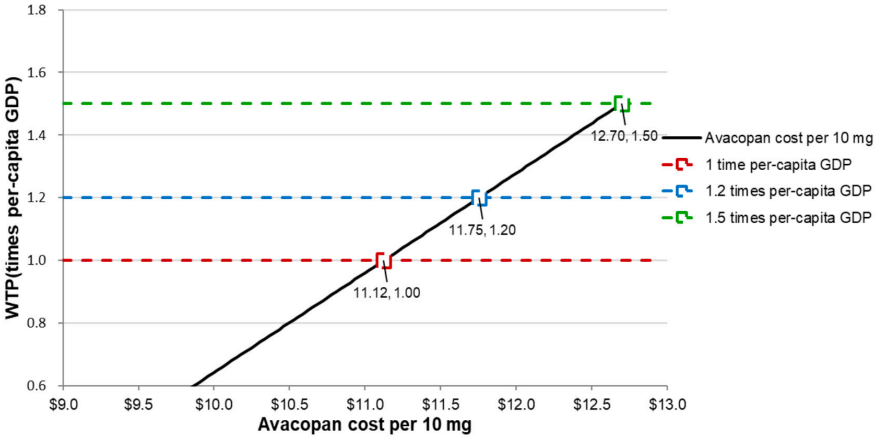

Fig. 4. Drug prices under different willingness-to-pay thresholds.
The curve depicts the threshold unit prices of avacopan (per 10 mg) corresponding to different WTP thresholds, expressed as multiples of China's 2024 per-capita GDP. For each WTP level, the point on the curve indicates the avacopan price at which the avacopan group remains cost-effective compared with the GC group.

threshold of one time per-capita GDP. These findings are aligned with recent guideline updates and narrative reviews, which support avacopan as a GC-sparing option, particularly in relapsed or refractory cases (12, 14, 15, 27).

Using WTP as a negotiation anchor offers a transparent basis for value-based pricing. If one times WTP is adopted, the unit price should not exceed $11.12 per 10 mg; under a rare-disease context with 1.5 times WTP, the cap could be relaxed to $12.70 per 10 mg (and $11.75 per 10 mg at 1.2 times WTP).

Importantly, conventional cost-effectiveness thresholds may underestimate the value of rare disease therapies. In this study, we adopted a WTP threshold of one time per-capita GDP. Xu *et al*. (28) estimated a WTP threshold of 2.06 times per-capita GDP for rare diseases in China, exceeding the base-case threshold used in this study. Internationally, agencies such as NICE (29) apply higher thresholds for ultra-rare conditions, and Australia's Life Saving Drugs Program (30) provides reimbursement beyond standard thresholds. These perspectives support adopting flexible or tiered thresholds in rare disease evaluations like AAV. In addition, cross-country differences in healthcare prices and WTP thresholds mean that direct comparison of ICERs across settings may be misleading. Future work should consider purchasing power parity-adjusted analyses to enable more meaningful global comparisons.

To our knowledge, this is the first cost-effectiveness analysis of avacopan in the Chinese healthcare context. Our findings are consistent with international evaluations. A Spanish study (1) reported an ICER of €45,638/QALY, and a UK analysis (18) showed an ICER of £18,537/QALY from the NHS perspective. These results suggest the global value of avacopan in AAV management. However, this study has several limitations. First, clinical efficacy inputs were derived from the ADVOCATE trial (13), which had a 52-week follow-up. Long-term effectiveness beyond treatment discontinuation was extrapolated based on conservative assumptions. Second, due to limited local data, some transition probabilities and utility values were obtained from international sources. These assumptions may introduce parameter uncertainty, although sensitivity analyses confirmed the robustness of the findings. Third, all unit prices, medical costs, and WTP thresholds in this study reflect the Chinese healthcare system and benefit package; these inputs may differ from those in European or North American settings, which could limit the external generalisability of our cost-effectiveness results.

In summary, avacopan offers clinical and economic benefits for patients with GPA/MPA in China by improving disease control, reducing relapse, and delaying ESRD. Its use may alleviate the long-term burden on patients and the healthcare system and may inform reimbursement deliberations and future updates to clinical practice guidelines in China.

Conclusion

This study evaluated the cost-effectiveness of avacopan in combination with immunosuppressants and gluco-

corticoids compared with immunosuppressants plus glucocorticoids for the treatment of newly diagnosed or relapsing adult patients with GPA/MPA in China. From the perspective of the Chinese healthcare system, avacopan was cost-effective at a WTP threshold of one time per-capita GDP in 2024 ($13,445; €12,455/QALY). Although avacopan was associated with higher drug acquisition costs, it delayed progression to ESRD, reduced glucocorticoid exposure, and achieved better disease control by increasing sustained remission and lowering relapse risk. These benefits translated into substantially lower costs for healthcare resource utilisation, ESRD management, and GC-related AEs, while improving patient outcomes and quality of life.

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