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The Cost Effectiveness of Belimumab and Voclosporin for Patients with Lupus Nephritis in the United States

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Abstract

Background and objectives: Despite existing therapies, people with lupus nephritis progress to kidney failure and have reduced life expectancy. Belimumab and voclosporin are two new disease-modifying therapies recently approved for the treatment of lupus nephritis.

Design, setting, participants, and measurements: A *de novo* economic model was developed to estimate the cost-effectiveness of these therapies, including the following health states: "complete response", "partial response" and "active disease" defined by eGFR and proteinuria changes, kidney failure, and death. Short-term data and mean cohort characteristics were sourced from pivotal clinical trials of belimumab (BLISS-LN) and voclosporin (AURA-LV and AURORA). Risk of mortality and kidney failure were based on survival modelling using published Kaplan-Meier data. Each drug was compared to the standard of care as represented by the comparator arm in its respective pivotal trial(s), using US health care sector perspective, with a societal perspective also explored.

Results: In the healthcare perspective probabilistic analysis, the incremental cost-effectiveness ratio for belimumab compared to its control arm was estimated to be approximately $95,000 per quality-adjusted life year (QALY). The corresponding incremental ratio for voclosporin compared to its control arm was approximately $150,000/QALY. Compared to their respective standard care arms, the probability of belimumab and voclosporin being cost effective at a threshold of $150,000/QALY were 69% and 49%, respectively. Cost-effectiveness was dependent on assumptions made regarding survival in response states, costs and utilities in active disease, and the utilities in response states. In the analysis from a societal perspective, the incremental ratio for belimumab was estimated to be approximately $66,000/QALY and for voclosporin approximately $133,000/QALY.

Conclusions: Compared to their respective standard care arms, belimumab but not voclosporin met willingness to pay thresholds of $100,000 per QALY. Despite potential clinical superiority in the informing trials, there remains high uncertainty around the cost-effectiveness of voclosporin.

Introduction

Lupus nephritis, characterized by inflammation in the kidney, proteinuria, and progressive kidney damage, is caused by systemic lupus erythematosus (SLE).[1,2] Lupus nephritis is more common in women and in non-white populations,[3,4] with most patients diagnosed between age 20 to 40 years.[5,6] 10% to 30% of patients with lupus nephritis progress to kidney failure within 15 years of the diagnosis, requiring dialysis or kidney transplantation.[7-9] Lupus nephritis has a substantial socio-economic impact on the United States (US) population due to young age of patients at diagnosis and high impact of disease on patients' well-being.

Existing guidelines recommend treatments such as high dose corticosteroids combined with either mycophenolate mofetil or cyclophosphamide, [10,11], which have a relatively low response rate among lupus nephritis patients.[12] Recently the Food and Drug Administration (FDA) approved two drugs for lupus nephritis: belimumab, an intravenous (IV) B-lymphocyte inhibitor, and voclosporin, an oral calcineurin inhibitor.

In the Belimumab International Study in Lupus Nephritis (BLISS-LN) trial, belimumab increased the complete kidney response at two years compared with standard therapy alone, with benefits seen after the first year appearing stable at year two. In the AURORA trial, voclosporin also increased the complete and the partial kidney response at one year compared with standard therapy alone (table 1). While the preliminary clinical evidence supports the clinical benefits of both treatments [13 14], their cost-effectiveness has not been established.

Although cost-effectiveness models comparing alternative drug regimens for lupus nephritis have been developed for a range of healthcare settings over the last decade [15,16 17], there are no cost-effectiveness studies of belimumab or voclosporin in lupus nephritis. To assist decision/policymakers and payers in understand the cost-effectiveness and health gains associated with these therapies, this study aims to estimate the cost-effectiveness of these drugs in people with lupus nephritis from US health care sector and societal perspectives.

Materials and Methods

A *de novo* economic model was developed in Microsoft Excel to estimate the cost effectiveness of belimumab and voclosporin for a cohort of patients with lupus nephritis, with each drug compared to the standard of care as represented by the comparator arm in its own pivotal trial(s), from the US health care sector perspective. Costs, life years, and quality-adjusted life years (QALYs) were estimated using monthly time cycles and discounted at 3% per annum. This model was developed as part of the Institute for Clinical and Economic Review evaluation of belimumab and voclosporin for lupus nephritis, and input was sought from the manufacturers, patient groups, health economists, and clinical experts throughout the model development and analysis phase (supplementary materials).

Model overview

The model estimates the progression of lupus nephritis through the patients' lifetime based on response-to-treatment outcomes. It consists of two parts: (a) a short-term interpolation model concordant with data from the trials; and (b) a long-term (lifetime) model based on extrapolation using survival modeling.

The base case short-term model comprises three years for both belimumab and voclosporin. All patients start the short-term model in the active disease (AD) state and may transition to either CR, PR, kidney failure, or death (Figure 1). The proportions of patients in the different health states during the trial follow up are informed by key trials: Aurinia Urinary Protection Reduction Active – Lupus with Voclosporin (AURA-LV) and AURORA for voclosporin, and BLISS-LN for belimumab, with the longer-term transition to kidney failure and death from Two cohort studies.[9,18]

Key Assumptions

The key assumptions made during the modelling phase are described below, and a comprehensive list of assumptions and accompanying rationales is available in the supplementary materials. Both belimumab and voclosporin would be added on to standard therapy. Due to differences in the definitions in trials outcomes, [13,19] belimumab and voclosporin were not compared directly to each other but to their respective control arms.

Data from the trials and studies were used directly in the short-term model, and the response rates achieved at the end of clinical trial follow up (two years for belimumab and one year for voclosporin) were assumed to be sustained until the end of the three-year short-term model. The long-term model

was informed by estimates of long-term kidney failure-free survival conditional on whether the patients achieved response in the short-term model or not.

Treatment duration was assumed to be for three years, except for those discontinuing due to adverse events or lack of response, which was assumed to occur at 18 months.

Model inputs

Short-term model

Table 1 presents the proportions of patients reaching response, kidney failure, or death at the end of the follow-up in the published clinical trials. The data on the complete response for voclosporin was based on a random-effects meta-analysis of the AURA-LV and AURORA trials (each with one year follow-up) using the Mantel–Haenszel method, with the resulting risk ratio applied to the average control arm effect across the two trials (see supplementary material). As the clinical data are only reported at specific follow-up points, the proportions of patients in interim time cycles in the short-term model were estimated by applying linear interpolation to the efficacy data in Table 1.

Treatment duration

Based on expert clinical input, we assumed that belimumab and voclosporin will be used in patients in complete and partial response states for three years before discontinuation (except for those stopping treatment at 18 months due to adverse events based on the adverse event rates reported in their respective trials: 13% of patients taking belimumab and 11% taking voclosporin). For patients remaining in the active disease state, it is assumed that both drugs would be used for 18 months before treatment was discontinued due to non-response.

Long-term extrapolation

The long-term model used partitioned-survival modeling to estimate kidney failure-free survival for the different health states (active disease, partial and complete response) based on data from Davidson *et al.*,[18] with the proportion of kidney failure events and deaths estimated based on data from Chen et al.[9] The choice of sources in the long-term model was based on combined criteria of recent data, quality of reporting, and representativeness of the US lupus nephritis population. Davidson *et al*. included 53% Black patients[18] and reported similar kidney failure-free survival across the partial and complete response states. The base case model applied the same risk of kidney failure to partial and complete response states but different costs and utilities to patients while they were in these states. A scenario analysis was conducted using superior kidney failure free survival in complete

response state (hazard ratio 0.94) relative to partial response state based on differences in outcomes at 5 years using modified Aspreva Lupus Management Study criteria definitions from the same publication.

The survival curves used in the base-case analysis for long-term extrapolation are presented in Figure 2, with further detail provided in supplementary materials. The face validity of the survival curves was confirmed by clinical experts and the values obtained from them were as follows: in the complete and partial response health states, the mean kidney failure-free survival is 19.4 years, and the mean overall survival is 28.1 years, while in the active disease health state, the mean kidney failure-free survival is 13 years and the mean overall survival is 23.7 years.

Treatment, health state and non-medical costs

Costs and their sources are summarized in Table 2, and discussed in detail in the supplementary materials. The treatment costs for belimumab were estimated using the average sales price for IV (base-case) and subcutaneous preparations (scenario analysis) using the standard discount in the Federal Supply Schedule (6%). For IV belimumab, the mean dose was estimated using the dose of 10 mg per kilogram of body weight and the distribution of the body weights of the lupus nephritis population retrieved from the literature[14] and accounted for vial wastage and the induction dosing regimen. In the scenario analysis for subcutaneous belimumab, the regimen of one injection (200mg) per week was considered.

Voclosporin costs were assessed considering the average daily dose of 39.1 mg (mean dose weighted to the duration of patients in AURORA trial) and the price per "wallet" (containing 60 capsules of 7.9mg each) of $3,950 reported by the manufacturer. The mean discount of 22.5% was then applied to calculate the estimated net price for voclosporin [20].

The mean all-cause health care costs per lupus nephritis patient per year were reported as $45,469 in 2018 by Bartels-Peculis *et al. (*2020) based on data on 1,039 lupus nephritis patients (median age 47 years; 83% female)[21]. The costs for active disease, partial and complete response were then estimated using cost ratios between the different health states and proportions of populations in each state, estimated from published literature[22,23,21]. The costs in the kidney failure state were calculated as costs of people with lupus nephritis eligible for Medicare in 2016 based on kidney failure alone or in combination with disability.

In the modified societal perspective analysis, indirect costs were also considered, which included costs of unemployment, absenteeism (temporary productivity loss), and caregiving[24-26].

Quality of life

The health-related quality of life utility values for the health states were obtained from published literature, incorporating feedback from clinical experts and patients, as quality of life was not reported in the informing trials. The model assumed that utility values in the complete response state were equal to utility values of the population with SLE who have very low disease activity, based on data from a cohort of Swedish SLE patients.[27] We estimated the utility values for patients in the partial response, active disease, and kidney failure states by applying EQ-5D utility decrements compared to the complete response state based on a cost-utility analysis from Thailand.[16] In the model, all utilities were capped at the general population utility for that age group (see supplementary materials for details) to ensure they did not exceed the utilities of the general population.

For patients who have therapy with low-dose steroids (≤ 5mg/day) or no steroids (≤ 2.5 mg/day), we applied a positive increment in utilities and a reduction in costs compared to patients on high-dose steroids to the proportion of patients in active disease, complete and partial response states reported in corresponding steroid-use categories in the AURORA and BLISS-LN trials (see supplementary materials).

Base-case and Scenario Analyses

Base-case results were estimated from the probabilistic analysis, which was performed by jointly varying all model parameters, using 1,000 simulation runs. Due to the lack of data, the distributions used for costs and utilities in the probabilistic analysis were mean values ±10%. .

Deterministic one-way sensitivity analyses were performed using plausible ranges based on published data and expert opinion to identify the key drivers of model outcomes. For drug costs, 20% variability was applied. We conducted deterministic scenario analyses using alternative utility estimates, health state costs, survival estimates, treatment durations, and also from a societal perspective.

Results

Cost-effectiveness of belimumab

The base-case results for belimumab from the health care sector perspective are presented in Table 3. Belimumab treatment resulted in higher treatment costs and life years as well as higher QALYs gained, resulting in an incremental cost-effectiveness ratio (ICER) of approximately $95,000 per QALY and $113,000 per life year gained. Belimumab has 69% probability to be cost-effective at a willingness to pay threshold of $150,000 per QALY. This probability increased to 79% at a threshold of $200,000 per QALY and decreased to 52% at a threshold of $100,000 per QALY. The sensitivity of the ICER for belimumab to the variation in individual model costs and utility inputs is shown in figure 3A.

A number of scenario analyses were performed to identify the effect of alternative inputs and assumptions on the cost-effectiveness results (Table 3). The societal perspective (including the costs of unemployment, absenteeism, and caregiving costs) decreased the ICER for belimumab to around $66,000 per QALY gained. The results from the scenario analysis where the duration of the active disease state among those patients who eventually progressed to kidney failure was increased from 1.21 years in the base-case scenario to 3 and 5 years resulted in ICERs above the threshold of $100,000 per QALY but below the threshold of $150,000 per QALY. Worse kidney failure free survival in partial compared to complete response increased the ICER to $133,250 and the lower cost associated with the subcutaneous form of belimumab reduced the ICER to $70,077.

Cost-effectiveness of voclosporin

The base-case results for voclosporin, using the health care sector perspective, demonstrated that voclosporin treatment results in higher costs and higher QALY gained compared to the standard care, with an ICER of $150,000 per QALY gained and $172,000 per life year gained (Table 4). Voclosporin has 49% probability to be cost-effective at a willingness to pay threshold of $150,000 per QALY. This probability was 79% at a threshold of $200,000 per QALY and is 11% if the threshold is $100,000 per QALY. The sensitivity of the ICER for voclosporin to variation in individual model costs and utility inputs is shown in figure 3B.

A number of scenario analyses consider alternative modelling inputs and address uncertainty related to selected assumptions because of the limited and short-term data on voclosporin (Table 4). If a societal perspective is considered, voclosporin treatment may be considered cost-effective with the threshold of $150,000 per QALY but not with the lower threshold of $100,000 per QALY. A scenario analysis assuming a drop in kidney function in the long-term for patients on voclosporin (i.e., assuming

a 3-year reduction in overall survival and 5-year reduction in kidney failure-free survival in the complete and partial response states) increased the ICER for voclosporin treatment to $237,000 per QALY. If patients who remain in the active disease state discontinue the treatment after 12 months of the therapy, the ICER will decrease to $138,000 per QALY. Similarly, the ICER remains above the threshold of $100,000 per QALY if the mean discontinuation time for patients experiencing adverse events was set at 6 months (i.e., the mid-point in the AURORA trial). The scenario based on using the response rates from the AURORA trial (instead of the meta-analysis) and worse kidney failure free survival in partial respose compared to complete response did not change conclusions on cost-effectiveness for voclosporin treatment.

Discussion

With the demonstration of the clinical effectiveness of belimumab and voclosporin against standard of care (mycophenolate or cyclophosphamide) in their respective trials, this study evaluates the results from a cost-effectiveness model of belimumab and voclosporin for patients with lupus nephritis in the US setting. The incremental cost-effectiveness results were approximately $95,000 per QALY and $150,000 per QALY for belimumab and voclosporin respectively, each compared to the standard of care in their respective trials. Our analyses suggest that there is less uncertainty in the cost-effectiveness of belimumab, while the cost-effectiveness of voclosporin is uncertain.

Our work builds on existing cost-utility analyses performed in a range of settings comparing therapies currently considered standard of care and utilized in the control arms of the trials of the two treatments evaluated in this study. [16] [15,17] Common across these analyses are the disease states of active disease, partial and complete response, although other model structures which reflect GFR, proteinuria, and their ability to predict outcomes are possible. From a US perspective, the model by Nee *et al.* seems the most appropriate comparison, reporting the lifetime QALYs and costs for mycophenolate compared to azathioprine (inflated to 2019 values and without considering the reduction in mycophenolate cost) as 14.2-15.10 QALYs at a cost of $669,000-$677,000.[17] The predictions of the costs for standard care between our model and the Nee et al. model are comparable while the difference in QALYs can be explained by the different approach to utility measurement applied by Nee *et al*. [17].

Stakeholder engagement prioritized the disutility associated with steroid therapy, and the recognition that lupus nephritis differentially affects non-Caucasian racial groups in terms of incidence, outcomes, and access to therapies. It is likely that disease progression and treatment response will differ by ethnicity.[28,29] In addition to under-representation of these groups in the relevant trials, making conclusions for these specific groups unreliable, the use of lower health-related quality of life associated with these patient groups (which is partially explained by lower socioeconomic status) could reduce access to these therapies.[30]

Our study is fortunate to benefit from the wider initiative to conduct longer trials in lupus nephritis, incorporating clinical effectiveness data directly from the trials and aligning this with real-world data to inform life-time outcomes. Because data on the clinical effectiveness of the medications and disease progression by age, ethnicity, and other relevant factors were not available or uncertain, the cohort health economic model reports outcomes for an average lupus nephritis population similar to those in the informing clinical trials. Additional strengths include widespread stakeholder engagement through the model development process, which directed the study to additional information sources,

the use of contemporary data, and utility estimation techniques, which yield plausible values. Despite our efforts, these analyses have important limitations, which include lack of longer-term follow-up from the informing trials, broad health state definitions and assumed relationships between these and kidney failure-free and overall survival, and failure to capture any beneficial effects of these therapies on SLE beyond the kidney (e.g. fatigue, joint and skin involvement, cardiovascular disease, etc.). These uncertainties are reflected and explored in sensitivity and scenario analyses that evaluated different assumptions. Based on consultations with clinical experts, the model assumed continuation of treatments for up to three years, while the literature suggests standard care in stable patients should continue out to 5-6 years. The real-world use of these newer therapies is yet to be observed,[31] and more recent FDA labelling may result in patients discontinuing newer therapies because of the lack of clinical efficacy earlier than is currently considered in the model.

Further research in this area should include prospective data collection capturing longer-term outcomes, including the efficacy of the subcutaneous preparation of belimumab, rates of real-world use and discontinuation of these therapies, and methodological consensus on how the adverse effects of steroid therapy in chronic disease should be reflected in economic evaluations. Robust utility data were lacking for the lupus nephritis population in the US and may reveal greater value for these treatments than demonstrated in our analysis. Although these agents represent welcome additions to the therapeutic landscape for lupus nephritis, as the lupus community gains experience with these agents for this indication, additional data will be generated to inform more refined cost-effectiveness analyses. Meanwhile, given the uncertainty around its cost-effectiveness, decision-makers and commissioners should consider price negotiations for voclosporin before considering reimbursement schemes for this product.

Author Contributions

All authors conceptualized and designed the analysis, advised on methodology, drafted and re-reviewed the manuscript. Formal analysis was undertaken by OL, PT, and JF, SP and JT gave clinical input, MDS and RC gave economic input, SR gave statistical input, and SHS and FA conducted the meta-analysis.

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Disclosures

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Tables

Table 1. Trial characteristics, outcomes and associated assumptions for belimumab and voclosporin

	Belimumab		Voclosporin	
Informing studies	BLISS-LN		AURA-LV, AURORA	
Study Duration	104 weeks		52 weeks	
Inclusion/exclusion criteria	Patients 18+ with autoantibody-positive SLE that fulfills the 1982 ACR criteria, UPCR ≥ 1 and biopsy-proven LN of class II, IV, or V showing active lesions or active and chronic lesions in biopsy		SLE according to ACR criteria, kidney biopsy within 6 months of study entry confirming diagnosis of LN Class III, IV, or V (alone or in combination w/ class III or IV), proteinuria of ≥1.5mg/mg or ≥ 2 mg/mg for class V patients	
Standard Care Therapies	MMF/Corticosteroids or Cyclophosphamide/Corticosteroids		MMF/Corticosteroids	
Intervention Therapy	Above plus Belimumab 10 mg/kg every 2 weeks x 3 doses, then every 4 weeks		Above plus Voclosporin 23.7 mg twice daily	
Complete Response Endpoint Definition	Ratio of urinary protein to creatinine of <0.5, eGFR no worse than 10% below pre-flare value or ≥90 ml/min/1.73 m^2 with no use of rescue therapy		UCPR of ≤ 0.5 mg/mg, eGFR ≥ 60 mL/min/1.73 m^2, or no confirmed decrease from baseline in eGFR of > 20% with the presence of sustained, low-dose steroids and no administration of rescue medication.	
Partial Response Endpoint Definition	GFR >= 10% below baseline value or >60ml/min/1.73m^2 and >= 50% decrease in the ratio of urinary protein to creatinine with one of the following: ratio of urinary protein to creatinine <1.0 if baseline ratio ≤3.0, or ratio of urinary protein to creatinine of <3.0 if baseline ratio >3.0; no treatment failure; and not complete renal response.		≥50% decrease in UPCR from baseline with the presence of sustained, low dose steroids and no administration of rescue medication. *Proportions not in complete response presented	
Recruitment eGFR (mL/min/1.73m^2, mean (SD))	**Belimumab**	**Standard Care**	**Voclosporin**	**Standard Care**
	100.0 (37.7)	101.0 (42.7)	92.1 (30.6)	90.4 (92.0)
Recruitment PCR (mg/mg, mean(SD))	3.2 (2.7)	3.5 (3.6)	4.14 (2.71)	3.87 (2.36)
Complete Response rate	30.0	19.7	43.2	23.0
Partial Response rate	17.5	17.0	26.6*****	28.7
Intervention-Specific Model assumptions	Between years two and three in short term model patients remain in same response states		Between years one and three in short term model patients remain in same response states	

Table 2. Key Model Inputs

Parameter	Input	Source
Health-Related Quality of Life Utilities in model states		
Utility in complete response health state	0.80	Bexelius *et al.*[27]
Utility in partial response health state	0.71	Bexelius *et al.*, Mohara *et al.*[16,27]
Utility in active disease health state	0.62	
Utility in kidney failure health state	0.55	Bexelius *et al.*, Mohara *et al.*[16]
Steroid-related utility increase		
Increment in utilities for low-dose steroids	Utility value + 0.025	Cooper *et al.*[32]
Increment in utilities for treatments with no steroids	Utility value + 0.090	Cooper *et al.*[32]
Drug costs		
Belimumab cost in first month, IV form	$9,811*	ASP, WAC, FSS[33-35]
Monthly cost of belimumab (months 2-36), IV form	$3,560*	ASP, WAC, FSS[33-35]
Belimumab cost, subcutaneous forms	$3,246	ASP, WAC, FSS[33-35]
Monthly cost of voclosporin	$7,686	Data from Aurinia and assumed discount of 22.5%[20]
Health care costs by model states		
Annual cost in complete response health state	$7,871	Bartels-Peculis *et al.*,[21] Barber *et al.*,[36,37] Li *et al.*,[23] Medicare (data provided by the Lupus Research Alliance)
Annual cost in partial response health state	$8,185	
Annual cost in active disease health state	$42,510	
Annual cost in kidney failure health state	$120,920	
Steroid-related cost reduction compared to high-dose steroid use		
Annual cost reduction with low-dose steroids	$84.5	Redbook[33]
Annual cost reduction with no steroids	$126.8	Redbook[33]
Non-medical costs by health states		
Annual cost in complete response health state	$5,140	Cloutier *et al.*,[24] Garris *et al.*,[25] Bureau of Labor Statistics[26]
Annual cost in partial response health state	$5,140	
Annual cost in active disease health state	$14,777	
Annual cost in kidney failure health state	$24,157	

ASP: Average sales price, FSS: Federal Supply Schedule, WAC: wholesale acquisition cost

*Based on Federal Supply Schedule as of November 7, 2020

Table 3. Results for belimumab compared to standard care

Treatment	Total Cost	LYs	QALYs	ICER (costs per LY)	ICER (costs per QALY)
Base-case (probabilistic) analysis					
Belimumab	$934,663	17.92	11.70	$112,461	$95,269
Standard Care	$886,305	17.49	11.19		
Societal perspective					
Belimumab	$1,126,351	17.861	11.67	$83,933	$66,103
Standard Care	$1,094,193	17.478	11.18		
Increased duration of active disease prior to progressing to kidney failure in the long-term model					
3 years					
Belimumab	$935,194	17.861	11.35	$116,951	$108,245
Standard Care	$890,385	17.478	10.93		
5 years					
Belimumab	$941,026	17.861	10.99	$120,412	$138,501
Standard Care	$894,891	17.478	10.66		
Scenario analysis with pricing for the subcutaneuous drug form					
Belimumab	$920,434	17.861	11.67	$88,979	$70,077
Standard Care	$886,343	17.478	11.18		
Scenario analysis with lower kidney failure free survival in partial response state					
Belimumab	$1,068,154	16.76	10.16	$168,134	$133,250
Standard Care	$1,009,049	16.40	9.72		

Legend to Table 3: LY: life-years, QALY: quality-adjusted life year

Table 4. Results for voclosporin compared to standard care

Treatment	Total Cost	LY	QALYs	ICER (costs per LY)	ICER (costs per QALY)
Base-case analysis					
Voclosporin	$928,107	18.42	12.64	$171,927	$150,334
Standard Care	$783,688	17.58	11.68		
Scenario analyses					
Societal perspective					
Voclosporin	$1,095,833	18.408	12.640	$154,055	$131,962
Standard Care	$968,460	17.581	11.674		
Drop in kidney function within long-term timeframe					
Voclosporin	$1,004,382	17.466	11.649	$281,114	$237,389
Standard Care	$840,567	16.884	10.959		
Treatment discontinuation in non-response patients in 12 months					
Voclosporin	$917,523	18.42	12.64	$160,990	$137,903
Standard Care	$784,416	17.58	11.68		
Treatment discontinuation in patients with adverse events at midpoint in the AURORA trial (6 months)					
Voclosporin	$921,463	18.408	12.640	$165,755	$141,984
Standard Care	$784,416	17.581	11.674		
Scenario based on efficacy data from AURORA trial only					
Voclosporin	$928,684	18.408	12.607	$174,442	$152,899
Standard Care	$784,454	17.581	11.664		
Increased duration of active disease prior to progressing to kidney failure in the long-term model					
3 years					
Voclosporin	$936,174	18.408	12.171	$176,661	$173,127
Standard Care	$790,111	17.581	11.327		
5 years					
Voclosporin	$944,744	18.408	11.648	$179,349	$209,393
Standard Care	$796,459	17.581	10.940		
Scenario analysis with lower kidney failure free survival in partial response state					
Voclosporin	$1,162,891	16.73	10.36	$184,444	$154,934
Standard Care	$989,407	15.79	9.24		

Legend to Table 4: LY: life-years, QALY: quality-adjusted life year

Figure Legends

Figure 1. Short-Term Model Structure

Figure 2. Survival Curves Used in the Long-Term Extrapolation Model

Figure 2 legend: AD: active disease, , CR: complete response, PR: partial response

Figure 3. One-way sensitivity analysis for belimumab (3a) and voclosporin (3b)

Legend to Figure 3: CR: complete response, PR: partial response, AD: active disease, KF: Kidney Failure, QALY: quality-adjusted life year

*Lower input corresponds to higher incremental cost-effectiveness ratio and vice versa.