THE COST SAVINGS POTENTIAL ASSOCIATED WITH THE USE OF NEFECON FOR ADULTS WITH PRIMARY IGA NEPHROPATHY IN THE UNITED STATES

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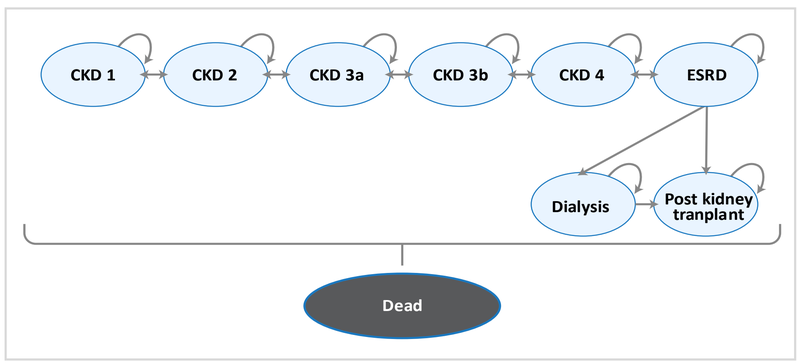
BACKGROUND

- Immunoglobulin A Nephropathy (IgAN) is a rare, chronic autoimmune disease that often leads to end stage renal disease (ESRD).[1]
- The goal of treatment is to slow disease progression so that patients are less likely to develop kidney failure in their lifetime.[1]
- The Phase 3 NefIgArd clinical trial provides confirmatory results that 9 months of treatment with Nefecon slows kidney function decline in patients with primary IgAN at high risk of progression.[2]
- This model assesses the cost-effectiveness of Nefecon in conjunction with best supportive care (BSC), relative to BSC alone, for US adult primary IgAN patients based on the full data set from the Phase 3 NefIgArd clinical trial.

METHODS

- A semi-Markov model structure was used to compare health outcomes and associated costs of Nefecon plus BSC versus BSC alone for the treatment of patients with primary IgAN.
- The model consisted of nine health states: CKD stage 1, CKD stage 2, CKD stage 3a, CKD stage 3b, CKD stage 4, ESRD with or without dialysis, post-kidney transplant, and death (***Figure 1***).

Figure 1: Semi-Markov model structure



- Patient distribution across the different health states at the start of the model was based on the distribution of the NefIgArd trial participants at baseline.[3]
- Transition probabilities (TP) between CKD states were calculated using regression analysis of individual patient-level data (IPD) from NefIgArd trial. Alternate transition probabilities were calculated using robust regression.[3]
- In the base case analysis, transition probabilities were assumed to be continuously maintained over the model time horizon with 1 round of treatment with Nefecon.
- Main model features are presented in ***Table 1.***

Table 1: Key features of the cost-effectiveness analysis model

Time horizon	Lifetime
Treatment cycle length	30.44 days [(3)]
Comparators	Nefecon + BSC vs BSC alone
Starting age	43.49 years [(3)]
Discount rate	3% per year; 0.25% per cycle [(4)]
Inflation	4.90% [(5)]
Perspective	U.S payer perspective

Cost Inputs

- Best Supportive Care (BSC) costs included prescription costs, outpatient costs, emergency department costs, and inpatient costs associated with Chronic Kidney Disease and were obtained from Golestaneh 2017.[6]
- Cost for one round of treatment with Nefecon was calculated using the 2023 monthly WAC and a treatment duration of 9.5 months (16 mg/day for 9 months followed by 8 mg/day for 2 weeks; this was numerically considered as 16 mg/day for 9.25 months in the model) as per the NefIgArd trial.[3,7]
- AE costs were calculated based on unit costs and proportion of patients treated as outpatient and inpatient. The proportion treated as inpatient was assumed to be equal to the proportion of TEAE that were categorized as severe in the NefIgArd trial.[3]
- Commercial and Medicare costs for dialysis were obtained from various sources. Of note, given the average baseline age of 43, the cost of dialysis was classified as Commercial for the first 33 months after which Medicare becomes responsible. After age 65, the cost of dialysis was always classified as Medicare[8,9]
- Costs for transplantation were obtained from 2020 Milliman Research Report.[10]
- Mortality costs for the last three months of life were calculated using data from Kerr 2017.[11]
- Indirect productivity costs were excluded in the base case analysis and only evaluated for the societal perspective (sensitivity analysis).
- Key clinical, HRQoL and cost inputs are presented in ***Table 2.***

Table 2: Key Clinical, HRQoL and Cost Parameters

Key Clinical Parameters	Key HRQoL Parameters
CKD stage at diagnosis of IgAN [(3)] CKD 1: 2% CKD 2: 38% CKD 3a: 37% CKD 3b: 22% CKD 4: 0%	**Health-state utility values** [(12)] CKD 1: 0.76 (0.75 for BSC alone) CKD 2: 0.76 (0.75 for BSC alone) CKD 3: 0.63 CKD 4: 0.51 ESRD without dialysis: 0.38 ESRD with Dialysis: 0.42 Post transplant: 0.71

Key Cost Parameters	
Nefecon 16 mg – 2023 Monthly WAC [(7)] Cost per treatment cycle: $15,123	**Dialysis: Commercial, inflated USD** [(8)] Hemodialysis (90%): $333,114 Peritoneal dialysis (10%): $281,462
AE costs outpatient, inflated USD [(13)] $74.87	**Dialysis: Medicare, inflated USD** [(9)] Hemodialysis (90%): $130,257 Peritoneal dialysis (10%): $110,060
AE costs inpatient, inflated USD [(14)] Hypertension:$34,849 WBC count increase: $57,549 Edema peripheral :$32,195 Dyspepsia: $51,888 Neutrophil count increase: $20,990 Face edema: $41,668 Cushingoid: $101,356	**Kidney transplant, inflated USD** [(10)] $510,787 **Mortality Cost** [(11)] $20,565

RESULTS

- Overall, the base case results of the cost-effectiveness analyses show that adding Nefecon to BSC in the treatment of patients with IgAN results in clinical benefits while reducing overall net costs from the payer perspective in the US. (***Tables 3 & 4***)

Table 3: Cost-effectiveness model results, base case analyses

	Nefecon + BSC	BSC alone	Difference
Costs	$1,292,318	$1,613,482	$ -321,164
LYs	15.549	14.913	0.635
evLYs	9.592	8.478	1.114
QALYs	9.437	8.478	0.959

Table 4: Incremental Cost-effectiveness ratios (ICER)

	ICER Value	ICER Interpretation
Cost per LY gained	-505,575	Nefecon Dominant
Cost per evLY gained	-288,184	Nefecon Dominant
Cost per QALY gained	-334,750	Nefecon Dominant

- The model estimated that fewer patients would reach ESRD within ten years with Nefecon plus BSC versus BSC alone, respectively (23.27% vs 55.70%) (***Figure 2***).
- Patients treated with Nefecon plus BSC had a median delay of 13.42 years in reaching ESRD compared with BSC alone (***Table 5***).

Figure 2: Estimated ESRD cumulative incidence within 10 years

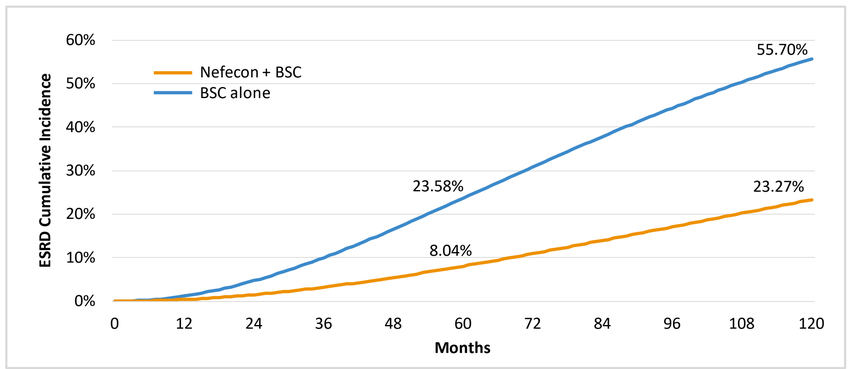


Table 5: Median Delay in Time to ESRD

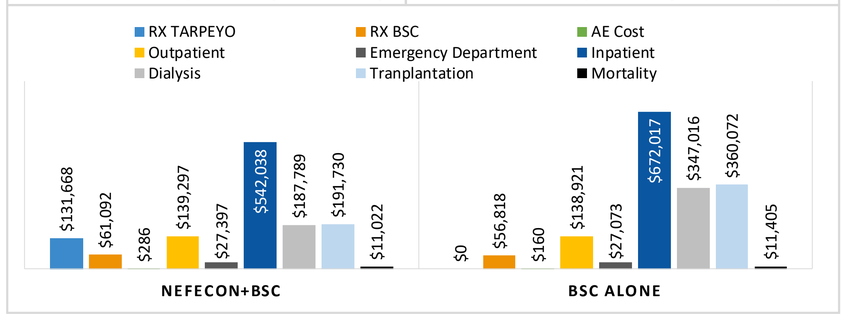
	Time to 50% reaching ESRD	Median Delay from Nefecon
Nefecon + BSC	22.42 years	13.42 years
BSC alone	9.0 years	

- The cost effectiveness of Nefecon in the model is likely explained by the proportionally greater amount of time spent in earlier health states versus later health states (i.e., CKD 4, ESRD, and post kidney transplant).
- In ***Figure 3, when comparing*** the Nefecon plus BSC scenario against the BSC alone scenario, there is an increase in prescription costs as expected; however, there is a large reduction in medical costs which are typically associated with late-stage disease (inpatient, dialysis and transplantation costs).

Figure 3: Summary of Discounted Costs (1 round of treatment)

Nefecon plus BSC Scenario:
Total Costs: $1,292,318
Prescription Costs: $192,760
Medical Costs and mortality: $1,099,558 [ESRD= $379,518]

BSC alone scenario:
Total Costs: $1,613,482
Prescription Costs: $56,818
Medical Costs and mortality: $1,556,664 [ESRD= $707,088]



Sensitivity Analysis

- The base case model assumed that the transition probabilities between health states were continuously maintained over the model horizon after 1 round of treatment. It is not known whether the kidney function benefit observed during the clinical trial (and hence the transition probabilities generated from them for this model) will extend indefinitely over the patient's lifetime.
- To address this limitation in the model, we considered two approaches. First, the transition probability assumption was adjusted. Second, additional rounds of treatment were considered to maintain the transition probability over the model horizon. Both approaches resulted in Nefecon remaining dominant. (***Table 6***)

Table 6: Sensitivity analyses
(Assumes 1 round of Nefecon treatment unless noted)

Scenario	Description	δ costs	δ QALYs	ICERs ($/QALY)
Transition Probability Assumption	Maintained for 3 years	-9,050	0.25	-36,351
	Maintained for 5 years	-79,681	0.38	-211,628
	Maintained for 10 years	-194,995	0.62	-315,521
	Continuously Maintained	-321,164	0.96	-334,750
Rounds of Treatment	4 rounds of treatment	-55,805	0.96	-58,173
	3 rounds of treatment	-124,759	0.96	-130,048
	2 rounds of treatment	-212,336	0.96	-221,329
	1 round of treatment	-321,164	0.96	-334,750
Model Perspective	Societal Perspective*	-326,797	0.96	-340,622
	Payer Perspective**	-321,164	0.96	-334,750
TP Calculation Method^	Robust Regression Method	-480,355	1.12	-428,319
	Regression Analysis of IPD	-321,164	0.96	-334,750

*Societal Perspective Includes: Nefecon Drug Costs, AE related costs for Nefecon & BSC, BSC Drug Costs, Outpatient Costs, Emergency Department Costs, Inpatient Costs, Dialysis Costs, Transplant Costs, Mortality Costs and Productivity Costs.
**Payer Perspective Includes: Nefecon Drug Costs, AE related costs for Nefecon & BSC, BSC Drug Costs, Outpatient Costs, Emergency Department Costs, Inpatient Costs, Dialysis Costs, Transplant Costs, Mortality Costs.
^In the logistic regression approach, eGFR values were assigned to CKD states at baseline and after 24 months of treatment. The independent variable in this case was the arithmetic mean change in eGFR value. Transition probabilities were then derived from the results of the logistic regression applied to individual patient data. In the robust regression method, we adapted the logistic regression model to calculate transition probabilities. This means that we utilized the predicted eGFR values from the robust regression method, which were based on the geometric least squares (LS) mean change in eGFR from baseline to 24 months. These values were then mapped to CKD stages to estimate transition probabilities.

Probabilistic Analysis

Results of probabilistic sensitivity analyses (PSA) using 5000 iterations demonstrated that Nefecon remains dominant when considering a continuously maintained treatment effect assuming up to 4 rounds of treatment with Nefecon. (***Figures 4 & 5 and Table 7***).

Figure 4: Cost-effectiveness plane of probabilistic cost per QALY ICERs (1 round of treatment)

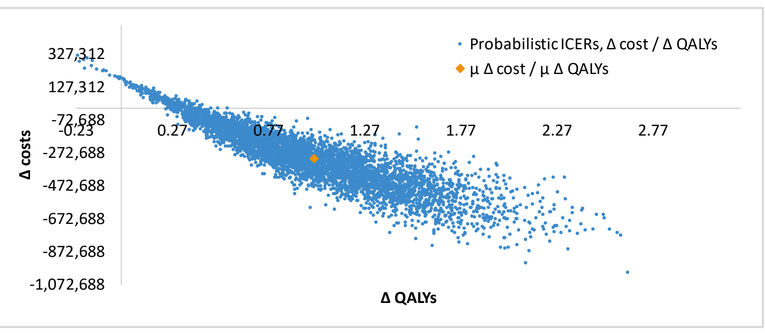


Figure 5: Cost-effectiveness plane of probabilistic cost per QALY ICERs (4 rounds of treatment)

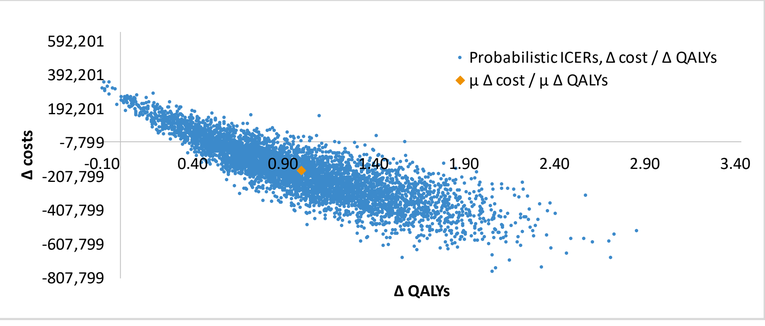


Table 7: Summary of Probabilistic Sensitivity Analyses (PSA)

	1 round of treatment	4 rounds of treatment
Average lifetime cost reduction	$ 299,059	$170,413
Average lifetime QALYs gained	0.989	0.999
% of Iterations Below WTP < $0 (i.e., Cost Saving)	95%	85%
% of Iterations Below WTP < $150K	97%	92%

CONCLUSION

- Model results suggest that adding Nefecon to BSC can help preserve kidney function by slowing eGFR loss in patients with IgAN while reducing overall net costs from the payer and societal perspective in the US.
- The projected long-term benefit for Nefecon in this model correlates closely with other modelling projections.[15]

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