PCN122

Cost-effectiveness of a 24-month fixed duration of venetoclax in combination with rituximab in relapsed or refractory chronic lymphocytic leukemia in the United States

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INTRODUCTION

- The randomized, open-label, Phase III MURANO study (NCT02005471) evaluated the efficacy of a fixed duration of the oral, selective, potent BCL-2 inhibitor venetoclax[1] in combination with rituximab (VenR) versus bendamustine in combination with rituximab (BR) in patients with relapsed or refractory (R/R) chronic lymphocytic leukemia (CLL).[2,3]
- After a median 23.8 months' follow-up, investigator-assessed progression-free survival (PFS) was significantly higher with VenR than BR; 2-year PFS 84.9% versus 36.3%, respectively (hazard ratio [HR], 0.17 [95% confidence interval (CI): 0.11, 0.25]; p<0.001), with benefit maintained across clinical and biologic subgroups, including patients with del(17p).[2] PFS benefit continued after all patients had completed treatment.[3]
- The economic value of fixed-duration VenR versus BR and oral treat-to-progression agents, such as ibrutinib and idelalisib, has not been formally evaluated in patients with CLL.
- The current analysis aimed to estimate the cost-effectiveness of VenR in the treatment of R/R CLL from a US-payer perspective.

METHODS

- A three-state (PFS, disease progression [PD], and death) partitioned-survival model **(Figure 1)** was used to extrapolate PFS and overall survival (OS) over a lifetime horizon.
- The second MURANO data cut-off (May 2018)[3] estimates of investigator-assessed PFS and OS were used to model long-term survival **(Figure 2)**.
- Cost-effectiveness of VenR was compared with BR using MURANO data. VenR was also compared with ibrutinib (IBR), IBR + BR, and idelalisib + rituximab (IR); relative efficacy of VenR versus the other agents was estimated using matched-adjusted indirect comparisons.[4,5] HRs for VenR PFS and OS versus the comparators were: BR, 0.19 (95% CI: 0.14, 0.27) and 0.51 (95% CI: 0.30, 0.86), respectively; IBR, 0.80 (95% CI: 0.53, 1.20) and 0.45 (95% CI: 0.25, 0.80), respectively; IBR + BR, 1.19 (95% CI: 0.68, 2.10) and 0.59 (95% CI: 0.22, 1.57), respectively; and IR, 0.17 (95% CI: 0.09, 0.34) and 0.19 (95% CI: 0.07, 0.53), respectively.[4,5]
- Health state utilities, and adverse event (AE) probabilities and disutilities were derived from the literature.[2,6–12]
- Drug costs for CLL treatment were based on the dosing regimen from the drug prescribing information and average wholesale acquisition costs in 2018.[13] Frequency of routine monitoring,[14] used to derive the cost of routine care,[5] and cost of end-of-life care[15] were based on published data. PD treatment costs were estimated from data for the second-line treatment of CLL. Model parameters are displayed in **Table 1**.
- Sensitivity analyses (including a one-way deterministic sensitivity analysis of key model parameters, probabilistic sensitivity analysis, and scenario analyses) were conducted to assess uncertainty in the results.

Figure 1. Model.

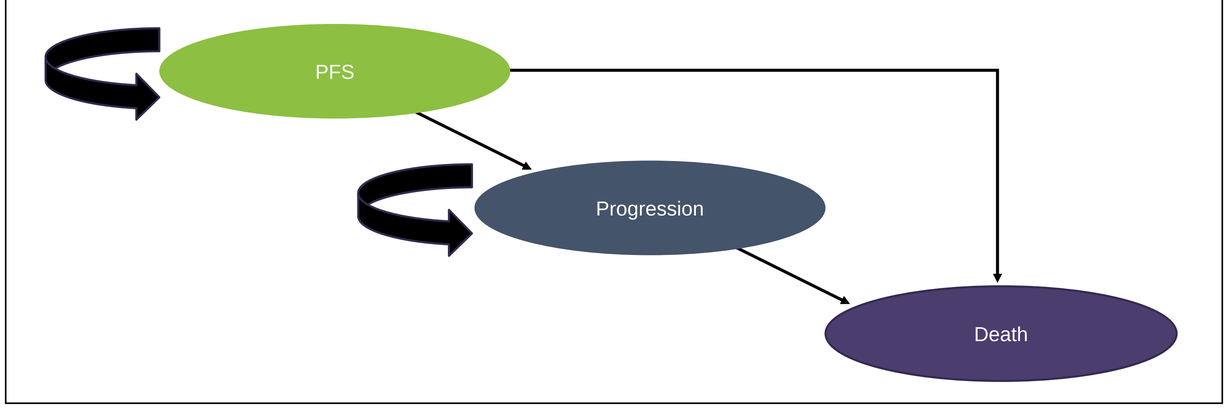
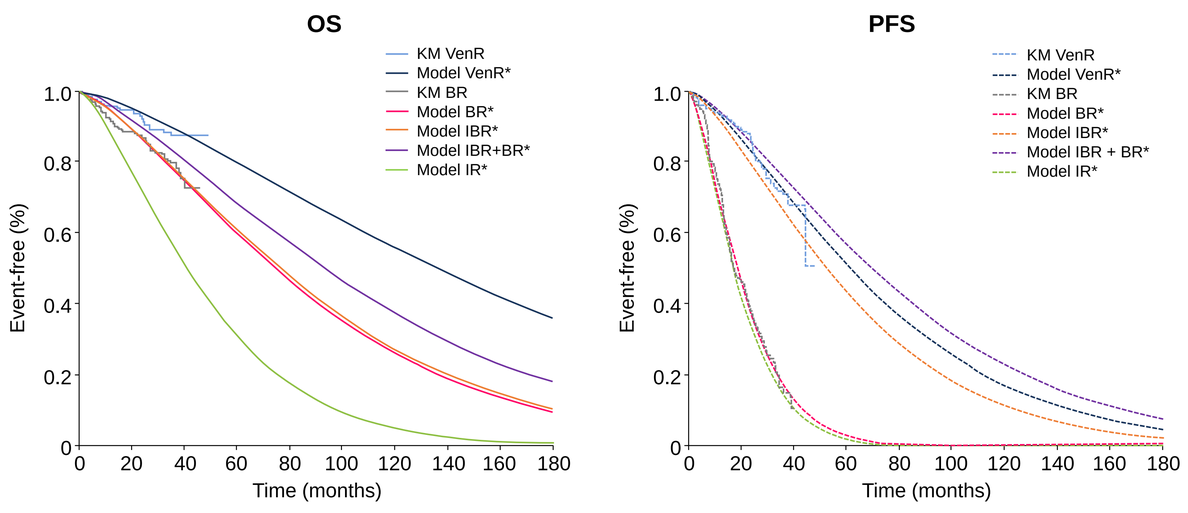


Figure 2. Modeled survival curves.



*Model OS and PFS fit using Weibull distribution. KM, Kaplan–Meier

Table 1. Model parameters.

GENERAL SETTINGS	Value
Time horizon	30 years
Discount rate: costs	3.0%
Discount rate: efficacy	3.0%
Starting age	64.18 years
PFS MODELING	**Value**
Distribution used	Weibull
Treatment effect assumption	Maintained over time
OS MODELING	**Value**
Distribution used	Weibull
Treatment effect assumption	Maintained over time
UTILITIES[8,12]	**Value**
PFS – VenR	0.75
PFS – BR	0.75
PFS – IBR	0.75
PFS – IBR + BR	0.75
PFS – IR	0.75
PD	0.60
END OF LIFE COSTS[15]	**Value**
$ most likely (upper–lower)	38,879 (31,103–46,654)
ROUTINE MONITORING COSTS[5,14]	**Value, $**
TLS monitoring	8916.00
Pneumonitis monitoring	300.80
Liver function test	42.20
Office/outpatient visit	51.13
Blood tests	80.00

DRUG COSTS[13]	Pack size	Cost, $
Venetoclax	120 × 100mg pills	11,150.54
Rituximab	10mg/mL (10mL)	903.38
Bendamustine	25mg/mL (4mL)	2425.30
Ibrutinib	90 × 140mg pills	12,179.90
Idelalisib	60 × 150mg pills	10,216.53
AE PROBABILITIES[2,6–8]	**Value, % (VenR/BR/IBR/IBR + BR/IR)**	
IRRs	1.6/5.3/–/0/0	
Neutropenia	57.7/38.8/16.6/53.7/33.6	
Thrombocytopenia	6.2/10.1/5.5/15.0/10.0	
Pneumonia	6.2/8.0/6.6/0/7.3	
Anemia	10.8/13.8/4.6/3.5/5.5	
ADVERSE EVENT DISUTILITIES[9,10]	**Value**	
IRRs	0.200	
Neutropenia	0.163	
Thrombocytopenia	0.108	
Pneumonia	0.195	
Anemia	0.090	
ADVERSE EVENT COSTS[11]	**Value, $**	
IRRs	5011	
Neutropenia	6193	
Thrombocytopenia	14,458	
Pneumonia	8206	
Anemia	10,189	
PD COSTS	**Value, $ (VenR/BR/IBR/IBR + BR/IR)**	
PD treatment (per cycle)	437/540/1255/1318/1269	

IRR, infusion-related reaction; TLS, tumor lysis syndrome

RESULTS

- VenR increased quality-adjusted life years (QALYs) compared with BR, IBR, IBR + BR, and IR **(Table 2)**, with incremental benefits for VenR of 2.83 versus BR, 2.31 versus IBR, 1.43 versus IBR + BR, and 4.43 versus IR.
- Oral treat-to-progression agents incurred higher incremental costs compared with fixed-duration venetoclax; $406,818 for IBR, $705,318 for IBR + BR, and $17,065 for IR. Compared with these treatments, VenR was more efficacious and had lower total costs.
- VenR was more costly than BR (incremental cost: $175,591), resulting in an incremental cost-effectiveness ratio (ICER) of approximately $62,000 per QALY gained.
- A one-way deterministic sensitivity analysis showed that the VenR versus BR ICER was mainly sensitive to utilities in PFS in both arms (driven by differences between arms as utilities varied independently), and discounting rates for costs and effects. The OS HR (treatment effect in the model) was the parameter with greatest influence on the model outcomes **(Figure 3)**.
- A probabilistic sensitivity analysis **(Figure 4)** showed that VenR is the most cost-effective treatment at a willingness to pay above $65,000/QALY. At a willingness-to-pay rate of $150,000/QALY, the probability of VenR being cost effective was 88%.

Table 2. Model results.

						Difference			
OUTCOME	**VenR**	**BR**	**IBR**	**IBR + BR**	**IR**	**VenR vs BR**	**VenR vs IBR**	**VenR vs IBR + BR**	**VenR vs IR**
Mean total cost, $	486,606	311,015	893,424	1,191,924	503,671	175,591	-406,818	-705,318	-17,065
Cost of PFS, $	317,294	109,797	705,756	1,014,649	289,905	207,497	-388,462	-697,355	27,389
Cost of PD, $	116,226	137,154	123,913	116,430	143,560	-20,928	-7687	-205	-27,334
End of life cost, $	53,086	64,065	63,755	60,846	70,206	-10,979	-10,668	-7759	-17,120
Mean QALYs gained	6.931	4.101	4.620	5.498	2.501	2.829	2.311	1.432	4.430
Mean life years gained	10.228	6.412	6.541	7.689	3.768	3.816	3.688	2.539	6.460
Treatment duration, mo	22.2	5.3	62.0	82.6	20.2				
Cost per QALY gained, $						**62,063**	**Dominant**	**Dominant**	**Dominant**
Cost per life year gained, $						**46,016**	**Dominant**	**Dominant**	**Dominant**

Figure 3. One-way deterministic sensitivity analysis.

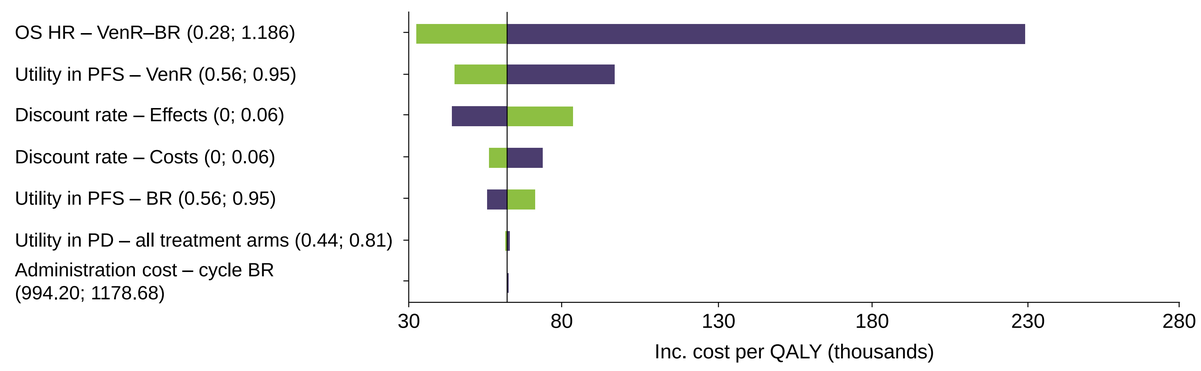
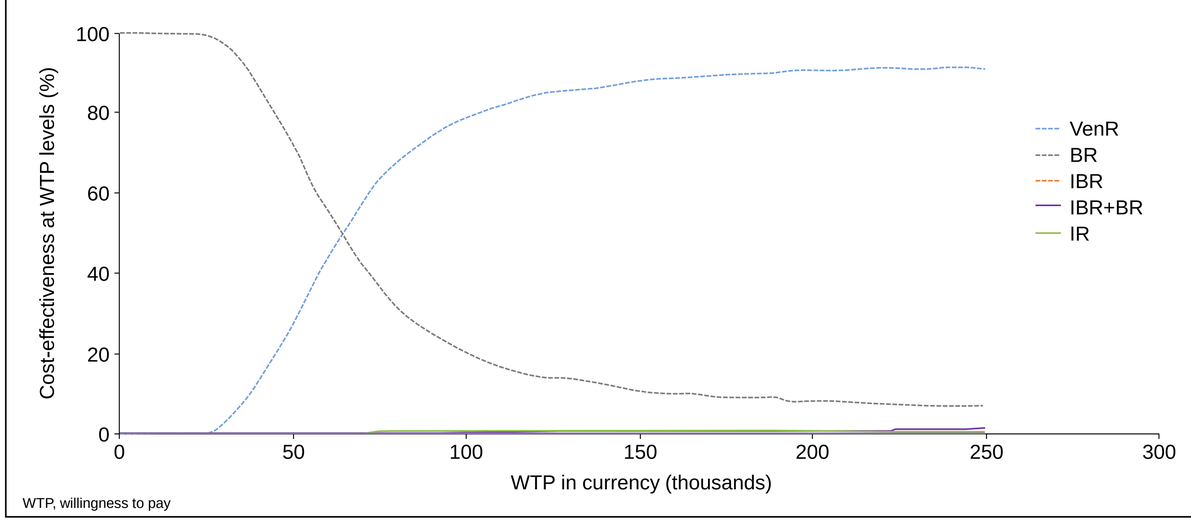


Figure 4. Probabilistic sensitivity analysis.



WTP, willingness to pay

CONCLUSIONS

- Our analysis suggests that treatment with VenR is cost effective compared with BR in patients with R/R CLL, within accepted US cost-effectiveness thresholds.
- The findings also demonstrated that 24-month fixed-duration treatment with VenR is more efficacious and cost saving compared with the treat-to-progression oral agents IBR, IBR + BR, and IR.
- Taken together, our analysis suggests that VenR is a cost-effective treatment for patients with R/R CLL, and should be considered as a standard treatment option in this setting.

Acknowledgments and disclosures

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References

1. Souers AJ, et al. Nat Med 2013;19:202–8; 2. Seymour JF, et al. N Engl J Med 2018;378:1107–20; 3. Kater AP, et al. J Clin Oncol 2019;37:269–77; 4. Mato A, et al. Poster presented at EHA 2018 [Abstract PF358]; 5. AbbVie. Data on file: H18.DoF.019; 6. Chanan-Khan A, et al. Lancet Oncol 2016;17:200–11; 7. Byrd JC, et al. N Engl J Med 2014;371:213–23; 8. Furman RR, et al. N Engl J Med 2014;370:997–1007; 9. Beusterien KM, et al. Health Qual Life Outcomes 2010;8:50; 10. Tolley K, et al. Eur J Health Econ 2013;14:749–59; 11. Monberg MJ, et al. Value in Health 2014;17:A79; 12. Dretzke J, et al. Health Technol Assess 2010;14(suppl 2):19–26; 13. Truven Health Analytics. Red Book (Accessed March 2018); 14. Chen Q, et al. J Clin Oncol 2017;35:166–74; 15. Lafeuille MH, et al. Leuk Lymphoma 2012;53:1146–54.