Number Needed to Treat Analyses of Zanubrutinib in Relapsed/Refractory Chronic Lymphocytic Leukaemia

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Introduction: Chronic lymphocytic leukaemia (CLL) is the most common leukaemia type. In 2020, there were an estimated 207,463 people living with CLL, with an annual incidence of approximately 4.9 per 100,000 in the United States (US). Zanubrutinib is a Bruton tyrosine kinase inhibitor that is FDA-approved and an NCCN preferred and recommended treatment of CLL. In the phase 3 ALPINE trial (NCT03734016), zanubrutinib elicited a significantly higher overall response rate and significantly longer progression-free survival (PFS) than ibrutinib. This study aimed to compare zanubrutinib versus ibrutinib in Relapsed/Refractory (R/R) CLL by calculating the number needed to treat (NNT) to avoid one progression or death and associated incremental costs.

Methods: A health-economic model was developed to evaluate the number of R/R CLL patients needed to be treated to avoid a progression or death from the US payer perspective. Payer blend was assumed with 40% Commercial and 60% Medicare payer mix. Clinical efficacy data were extracted from the ALPINE trial. Final analysis result of 24-month PFS (79.5% for zanubrutinib and 67.3% for ibrutinib) was used for the base-case analysis in the model. Treatment, adverse event management, other medical resource use, and subsequent treatment costs were considered in the model. The NNT, incremental cost per treated patient, and incremental cost per additional patient with progression or death were captured. Deterministic sensitivity analyses were conducted to assess parameter uncertainties and explore key model drivers. Scenario analyses were conducted to test the impact of different PFS estimates.

Results: The base-case results from the NNT model showed that for every 8 patients treated with zanubrutinib, 1 event of progression or death would be avoided compared to using ibrutinib. The total costs per patient treated with zanubrutinib and ibrutinib are $370,558 and $430,150, respectively, with a cost savings of $59,593 associated with using zanubrutinib (Table). Drug costs and PFS have the greatest impact on the incremental cost per patient. Varying the PFS scenarios, including adjustment with drug interruption, COVID death, or treatment discontinuation, change the NNT from 8 to 12, and are associated with cost savings of $58,179 to $67,153 per zanubrutinib-treated patient in a 24-month time frame. Applying the model result to a hypothetical scenario of a clinical practice of 100 patients treated with zanubrutinib versus ibrutinib suggest that approximately 13 patients will avoid disease progression events or death.

Conclusions: The NNT model suggests that using zanubrutinib to treat R/R CLL patients, compared to ibrutinib, will result in more favorable clinical and economic outcomes in the US.

Table. Number Needed to Treat to Avoid One Progression or Death and Cost Difference in a 24-Months Time Horizon (Base-case results)

	24-Month PFS	Total Cost per Treated Patient
zanubrutinib	79.5%	$370,558
ibrutinib	67.3%	$430,150
Results	**Number Needed to Treat with zanubrutinib**	**Cost Savings with zanubrutinib**
	8 patients	$59,593