Number Needed to Treat Analyses of Zanubrutinib vs Acalabrutinib in Relapsed/Refractory Chronic Lymphocytic Leukemia

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CONCLUSIONS

- The number needed to treat (NNT) model analysis demonstrates that using zanubrutinib compared to acalabrutinib, to treat patients with relapsed/refractory chronic lymphocytic leukemia (R/R CLL) is associated with more favorable clinical and economic outcomes in the US
- Notably, treating **10** patients with zanubrutinib instead of acalabrutinib could prevent one additional disease progression or death, along with an estimated cost saving of **$7,335 per patient** in the US
- Applying these results to a hypothetical clinical practice of 100 patients suggests 10 patients would avoid progression or death within 24 months, and the practice would save $733,500 by treating patients with zanubrutinib instead of acalabrutinib

INTRODUCTION

- Bruton tyrosine kinase inhibitors (BTKis), including zanubrutinib and acalabrutinib, have become a standard of care in CLL. However, there is a lack of head-to-head comparative trial data of these treatments
- In the phase 3 ALPINE study (NCT03734016), zanubrutinib showed favorable progression-free survival (PFS) compared to ibrutinib in the treatment of R/R CLL[1]
- In the ASCEND study (NCT02970318), acalabrutinib showed improved PFS vs rituximab-idelalisib/bendamustine in R/R CLL[2]
- A previously published matching-adjusted indirect comparison (MAIC) reported significantly improved PFS and complete response rates for zanubrutinib compared to acalabrutinib in R/R CLL[3]

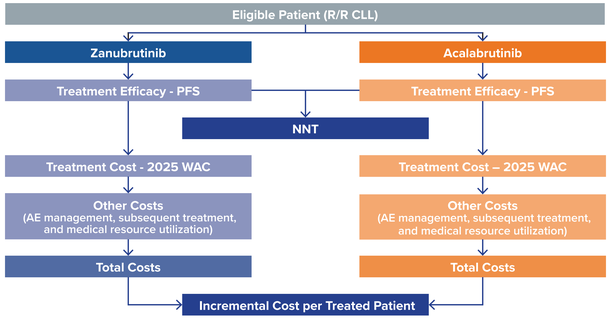
OBJECTIVES

- This study aimed to compare zanubrutinib versus acalabrutinib in R/R CLL by calculating the NNT to avoid one progression or death and associated incremental costs

METHODS

- A health-economic model (**Figure 1**) was developed to estimate the number of patients with R/R CLL needed to be treated to avoid one progression or death from the US payer perspective

Figure 1. Structure of NNT Health Economic Model Comparing Zanubrutinib to Acalabrutinib in Patient with R/R CLL



AE; adverse event; CLL, chronic lymphocytic leukemia; NNT, number needed to treat; PFS, progression-free survival; R/R, relapsed/refractory; WAC, wholesale acquisition cost.

- Clinical efficacy data from a MAIC of ALPINE and ASCEND trials were extracted for key model inputs of PFS values (**Table 1**). Final analysis results of 24-month PFS were used for the base-case analysis in the model[3]
- Costs associate with direct treatment (2025 wholesale acquisition costs), adverse event (AE) management, healthcare resource utilization, and subsequent treatment were considered in the model (**Table 2**)[4-11]
- The model accounted for the impact of all Grade 3+ AEs related to BTKi treatment
- Subsequent costs were calculated based on the treatment and additional healthcare resource utilization during the progression stage
- The NNT, incremental cost per treated patient, and incremental cost per additional patient with progression or death were estimated
- Deterministic sensitivity analyses were conducted to assess parameter uncertainties and explore key model drivers. Scenario analyses was conducted to test the impact of alternative PFS rates from the unadjusted population of the MAIC (**Table 1**)

Table 1. PFS Value Inputs

	Zanubrutinib		Acalabrutinib	
PFS Source	**12 months**	**24 months**	**12 months**	**24 months**
PFS – MAIC adjusted	93.2%	85.5%	88.1%	75.1%
PFS – ITT unadjusted	91.9%	82.0%	88.1%	75.1%

ITT, intent-to-treat; MAIC, matching-adjusted indirect comparison; PFS, progression-free survival.

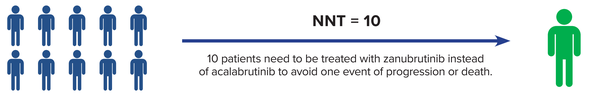
Table 2. Key Model Inputs

Key Inputs	**Zanubrutinib**	**Acalabrutinib**	
Treatment Cost ($2025)[4]	$15,744.00	$15,829.15	
Adverse Events (Grade 3+)	**Zanubrutinib Rate[1]**	**Acalabrutinib Rate[2]**	**Costs[5-9]**
Anemia	2.2%	11.7%	$432
Atrial fibrillation/flutter	1.9%	1.3%	$16,524
Hemorrhage (major bleeding)	3.4%	1.9%	$21,314
Hypertension	14.8%	1.9%	$2,938
Infection (pneumonia)	5.9%	5.2%	$13,863
Neutropenia	16.0%	15.6%	$1,508
Second primary malignancy	6.8%	0.6%	$15,484
Thrombocytopenia	2.8%	3.9%	$1,327
Healthcare Resource Utilization (per treated member per month)	**Progression-Free[10]**	**Progression[10,11]**	
Hospitalization	$237.25	$2,771.13	
Emergency department visit	$16.28	$16.28	
Office visit	$140.72	$140.72	
Other services	$1,249.06	$1,249.06	

RESULTS

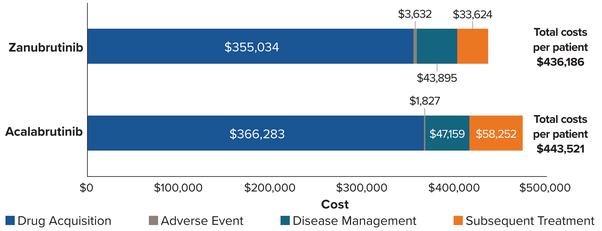
Base Case Results

- The base case results from the NNT model showed that **10** patients need to be treated with zanubrutinib instead of acalabrutinib to avoid one event of progression or death



- The total costs per patient treated with zanubrutinib and acalabrutinib are $436,186 and $443,521, respectively, with an estimated cost savings of $7,335 per patient treated with zanubrutinib in a 24-month timeframe (**Figure 2**)
- Applying the base case model result to a hypothetical scenario of a clinical practice of 100 patients treated with zanubrutinib versus acalabrutinib suggests that approximately 10 patients will avoid disease progression events or death in 24 months, and the practice would realize savings of $733,500

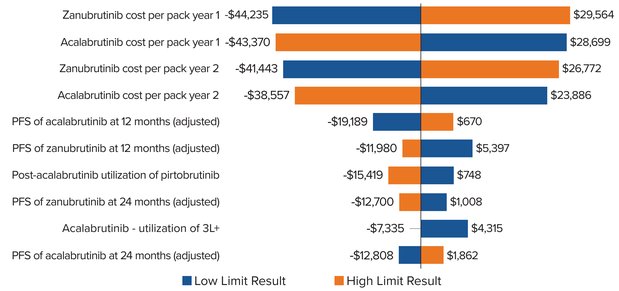
Figure 2. Base Case Disaggregated Costs for Zanubrutinib to Acalabrutinib



Sensitivity Analyses

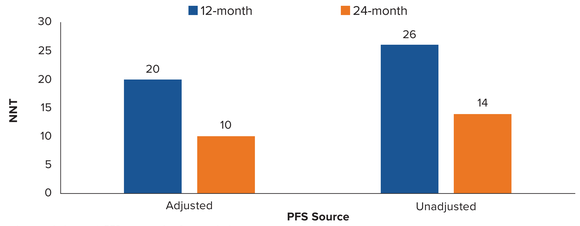
- A deterministic sensitivity analysis (DSA) was conducted by setting the model input parameter values (one at a time) to the upper and lower bound of their reported uncertainty (95% confidence interval or published ranges); results are displayed in **Figure 3**
- The DSA indicates that the model estimates are most sensitive to changes in the drug acquisition costs, and the PFS rates for acalabrutinib vs zanubrutinib at 12 months
- Subsequent treatment utilization and costs among those patients who progressed to the next line of therapy after zanubrutinib or acalabrutinib also impact the incremental cost per treated patient between the two treatments

Figure 3. Deterministic Sensitivity Analysis on Incremental Cost Per Treated Patient



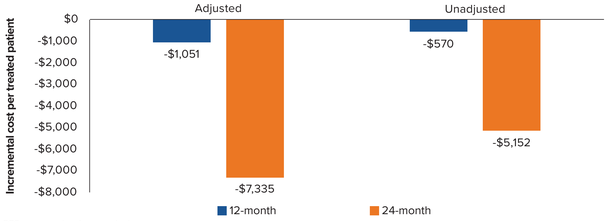
- Scenario analysis was conducted using PFS from an unadjusted population from the MAIC analysis. The NNT result changed from 10 to 14, and is associated with cost savings of $5,152 per zanubrutinib-treated patient in a 24-month time frame (**Figure 4** and **Figure 5**)
- Across the scenario analysis of alternative PFS inputs, zanubrutinib remains cost-saving

Figure 4. Scenario Analysis: NNT Results Per PFS Scenarios and Duration



NNT, number needed to treat; PFS, progression-free survival.

Figure 5. Scenario Analysis: Cost Per Treated Patient Per PFS Scenario and Duration



PFS, progression-free survival.

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DISCLOSURES

MS: Employment with Bristol Myers Squibb; consulting or advising roles for AbbVie, Genentech, AstraZeneca, Pharmacyclics, BeOne, Bristol Myers Squibb/ Celgene, MorphoSys, Kite (a Gilead company), Fate Therapeutics, Lilly, Genmab, Merck, Nurix, and ADC Therapeutics; research funding from Pharmacyclics, Acerta Pharma, Merck, TG Therapeutics, BeOne, Celgene, Genentech, MustangBio, AbbVie, Sunesis Pharmaceuticals, Bristol Myers Squibb/ Celgene, Genmab, and Vincerx Pharma; and stock options in Koi Biotherapeutics. **DC**: Employment with Curta. Curta received funding for the study. **MX**: Employment and equity holder in BeOne. **MM**: Employment and equity holder in BeOne. **KY**: Employment and equity holder in BeOne. **RW**: Employment and equity holder in BeOne. **ACK**: Employment with Mayo Clinic; consulting fees and honoraria from BeOne; current equity and stock holdings in Ascentage, Cellectar, Starton, and Alpha2; patents and royalties from Alpha2; and membership on the Board of Directors or advisory committees for Ascentage, Cellectar, Starton, and Alpha2.

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