Comparative Efficacy of Zanubrutinib versus Rituximab in Relapsed Marginal Zone Lymphoma (MZL): Matching-Adjusted Indirect Comparison (MAIC)

Abstract P1113

Catherine Thieblemont,[1] Kaijun Wang,[2] Sam Keeping,[3] Ina Zhang,[3] Keri Yang,[2] Boxiong Tang,[2] Leyla Mohseninejad[2]

[1]Hôpital Saint-Louis, Paris, France; [2]BeiGene USA, Inc., San Mateo, CA, USA, and BeiGene Switzerland GmbH, Basel, Switzerland; [3]PRECISIONheor, Vancouver, BC, Canada

INTRODUCTION

- Although standard chemoimmunotherapy incorporating anti-CD20 monoclonal antibodies can be used for relapsed MZL, alternative treatment options for patients are limited
- Zanubrutinib, a second-generation Bruton tyrosine kinase inhibitor, has shown deep and durable responses in non-Hodgkin lymphoma subtypes, including Waldenstrom macroglobulinemia, chronic lymphocytic leukemia, and mantle cell lymphoma
- Rituximab is also used to treat patients with relapsed MZL; therefore, estimates of the efficacy of zanubrutinib compared with rituximab are of interest
- In the absence of head-to-head randomized controlled trials, comparative estimates must come from unanchored between-trial comparisons of reported treatment effects

OBJECTIVE

- To assess the comparative efficacy of zanubrutinib vs rituximab for the treatment of relapsed MZL

METHODS

Data Sources

- Zanubrutinib has been evaluated in 2 single-arm trials in relapsed or refractory MZL (phase 2 MAGNOLIA trial [NCT03846427]; phase 1/2 BGB-3111-AU-003 trial [NCT02343120])[1,2]
- Rituximab has been evaluated in a phase 3 randomized controlled trial in relapsed MZL (CHRONOS-3 [NCT02367040])[3]

Statistical Analysis

- Propensity score models were used to match the baseline characteristics in the MAGNOLIA and BGB-3111-AU-003 trials to those observed in the rituximab arm of CHRONOS-3
- Prognostic factors were ranked by clinical experts (presented in order of importance in **Table 1**)
- In the base-case model, variables that were balanced included prior lines of therapy, MZL subtype, relapse after prior therapy, and age
- Sensitivity analyses incorporating additional characteristics were not possible due to a lack of reporting of additional factors from CHRONOS-3; however, the impact of each covariate in the base model was explored via a leave-one-out analysis
- Logistic regression models for binary outcomes (objective response rate [ORR]) and Cox proportional hazards models for time-to-event outcomes (overall survival [OS], progression-free survival [PFS]) were used to estimate relative treatment effects of zanubrutinib and rituximab

RESULTS

Patient Demographics and Disease Characteristics

- MAIC convergence was achieved using the full set of base-case covariates, and baseline characteristics were balanced between the 2 treatment groups after matching (**Table 1**)

Table 1. Baseline Characteristics in Zanubrutinib Treatment Group Before and After Matching to Rituximab Treatment Group

Covariate	Zanubrutinib		Rituximab (N=29)
	Observed (N=86)	Weighted base-case model (ESS=39)	
2 prior treatment lines, %	30.2	20.7	20.7
≥3 prior treatment lines, %	25.6	13.8	13.8
MZL subtype: nodal, %	36.6	41.4	41.4
MZL subtype: splenic, %	22.0	20.7	20.7
Relapse to last therapy, %	69.9	100	100
Age, median, years	68	63	63

Matching-Adjusted Indirect Comparison Results

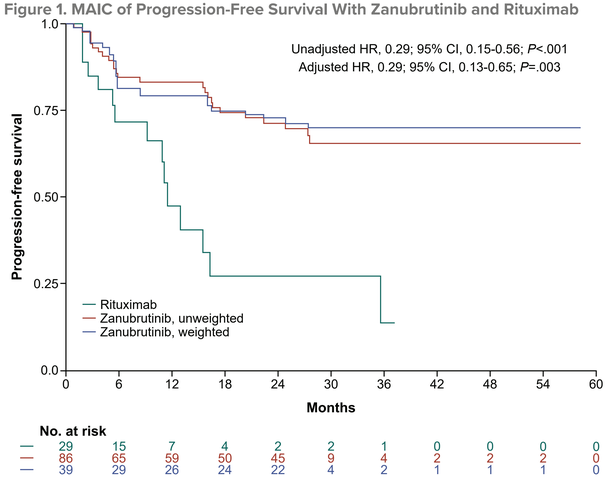
- Results from the MAIC are reported in **Table 2**, with unadjusted comparisons presented for informative purposes only
- Zanubrutinib significantly reduced the risk of progression (**Figure 1**) and had a significantly higher probability of response compared with rituximab
- OS was comparable for zanubrutinib and rituximab, which is consistent with survival expectancy for indolent lymphomas, although point estimates were in favor of zanubrutinib (**Figure 2**)
- The leave-one-out analysis showed that removing any of the characteristics from the propensity score model yielded comparable results

Table 2. Relative Treatment Effect Estimates of Zanubrutinib vs Rituximab

Model	Zanubrutinib ESS	ORR OR (95% CI)	PFS HR (95% CI)	OS HR (95% CI)
Unadjusted	86	**3.51 (1.46-8.44)** ***P*<.01**	**0.29 (0.15-0.56)** ***P*<.01**	0.79 (0.28-2.20) *P*=.65
Base-case (all covariates)	39	**5.09 (1.84-14.08)** ***P*<.01**	**0.29 (0.13-0.65)** ***P*<.01**	0.73 (0.26-2.01) *P*=.54
Base-case (excluding age)	52	**4.96 (1.88-13.11)** ***P*<.01**	**0.25 (0.12-0.53)** ***P*<.01**	0.77 (0.29-2.08) *P*=.61
Base-case (excluding relapse to last therapy)	54	**4.13 (1.61-10.59)** ***P*<.01**	**0.26 (0.12-0.56)** ***P*<.01**	0.58 (0.22-1.58) *P*=.29
Base-case (excluding MZL subtype)	39	**5.10 (1.86-14.00)** ***P*<.01**	**0.28 (0.13-0.63)** ***P*<.01**	0.71 (0.26-1.97) *P*=.51
Base-case (excluding number of prior lines)	41	**4.54 (1.66-12.44)** ***P*<.01**	**0.31 (0.14-0.69)** ***P*<.01**	0.79 (0.29-2.14) *P*=.64

All **bolded** values are statistically significant at the 0.05 significance level.

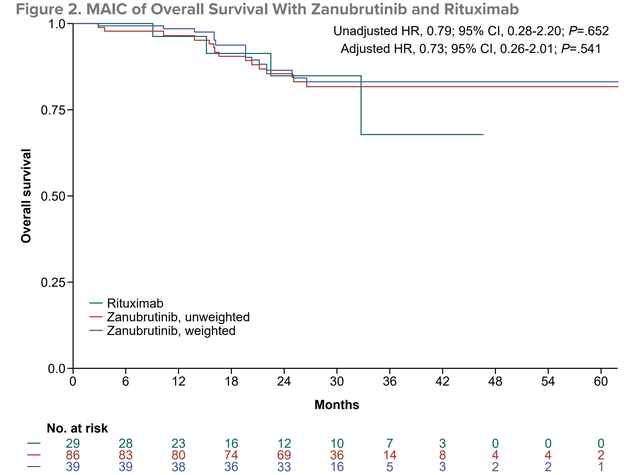
Figure 1. MAIC of Progression-Free Survival With Zanubrutinib and Rituximab



CONCLUSIONS

- MAIC results suggest that zanubrutinib is associated with improved PFS and ORR compared with rituximab in relapsed MZL

Figure 2. MAIC of Overall Survival With Zanubrutinib and Rituximab



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DISCLOSURES

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CORRESPONDENCE

Leyla Mohseninejad
leyla.mohseninejad@beigene.com

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