Efficacy of Sonrotoclax Versus Pirtobrutinib in Post–Bruton Tyrosine Kinase Inhibitor Relapsed/Refractory Mantle Cell Lymphoma: An Indirect Comparison

Authors: Toby A. Eyre,[1] Swetha Challagulla,[2] Kaijun Wang,[2] Leyla Mohseninejad,[3] Piotr Wojciechowski,[4] Natalia Kut,[4] Priscille Bourquelot,[2] Keri Yang,[2] Alvaro Alencar[5]

Affiliations: [1]Oxford Cancer and Haematology Centre, Churchill Hospital, Headington, Oxford, UK; [2]BeOne Medicines, Ltd, San Carlos, CA, USA; [3]BeOne Medicines, Ltd, Schiphol, The Netherlands; [4]Clever-Access, Kraków, Poland; [5]University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA

Background: Sonrotoclax (BGB-11417-201) and pirtobrutinib (BRUIN MCL trial; NCT03740529) have demonstrated efficacy in separate single-arm post-Bruton tyrosine kinase inhibitor (BTKi) relapsed/refractory (R/R) mantle cell lymphoma (MCL) studies, but there are currently no head-to-head randomized trials that compare both therapies.

Aims: To compare the efficacy of sonrotoclax versus pirtobrutinib in a post-BTKi R/R MCL setting in an unanchored matching-adjusted indirect comparison (MAIC).

Methods: An unanchored MAIC compared individual patient-level data from the sonrotoclax trial (n=103 [efficacy set]; median overall survival (OS) follow-up, 15.2 months) with aggregate data from the pirtobrutinib trial (n=120 [US Food and Drug Administration efficacy cohort]; median OS follow-up, 9.3 months). Matching covariates were selected based on literature review and clinical expert input. The base-case model maximized covariate adjustment while maintaining an effective sample size (ESS) >50. Sensitivity analyses with adequate sample size (ESS >50) and alternative covariates were conducted to validate the base-case model results. Outcomes included overall response rate (ORR), duration of response (DOR), progression-free survival (PFS), and OS. Weighted Cox proportional hazards and logistic regression models were used for time-to-event and binary endpoints, respectively. Hazard ratios (HR) and odds ratios (OR) with 95% confidence intervals (95% CI) were reported.

Results: In the base-case analysis, sonrotoclax showed a nonsignificant, numerically higher ORR (OR, 1.54; 95% CI, 0.80-2.97), as well as a numerically longer DOR (HR, 0.75; 95% CI, 0.37-1.54), versus pirtobrutinib. Consistent numerical improvements in the sonrotoclax cohort were observed for PFS (HR, 0.73; 95% CI, 0.48-1.11) and OS (HR, 0.66; 95% CI, 0.37-1.15). Sensitivity analyses using alternative covariate sets generated broadly consistent results (Table).

Summary/Conclusion: Based on the data currently available, the MAIC findings suggest a nonsignificant trend of potential difference in efficacy outcomes between sonrotoclax and pirtobrutinib. Future studies with longer follow-up are warranted.

MAIC Results Comparing Efficacy Outcomes With Sonrotoclax Versus Pirtobrutinib in Post-BTKi R/R MCL

Model	ESS n (%)	ORR-IRC OR (95% CI) *P* value	DOR-IRC HR (95% CI) *P* value	PFS-IRC HR (95% CI) *P* value	OS HR (95% CI) *P* value
Base case[a-c]	55 (53)	1.54 (0.80-2.97) .20	0.75 (0.37-1.54) .43	0.73 (0.48-1.11) .14	0.66 (0.37-1.15) .14
Sensitivity analysis 1[a,b]	97 (94)	1.15 (0.67-1.97) .62	0.77 (0.44-1.36) .37	0.90 (0.64-1.25) .52	0.92 (0.59-1.44) .71
Sensitivity analysis 2[a]	102 (99)	1.14 (0.67-1.94) .64	0.76 (0.43-1.32) .32	0.89 (0.64-1.23) .48	0.92 (0.59-1.43) .70

Covariates include: [a]sMIPI, no. of prior therapy lines; [b]PD to last BTKi ; and [c]blastoid MCL.
BTKi, Bruton tyrosine kinase inhibitor; IRC, independent review committee; PD, progressive disease; sMIPI, simplified Mantle Cell Lymphoma International Prognostic Index.