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Efficacy of sonrotoclax vs pirtobrutinib in post–Bruton tyrosine kinase inhibitor (BTKi) relapsed/refractory (R/R) mantle cell lymphoma (MCL): an indirect comparison

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Background: Sonrotoclax (BGB-11417-201) and pirtobrutinib (BRUIN MCL trial; NCT03740529) have demonstrated efficacy in separate single-arm post-BTKi R/R MCL studies. In the absence of head-to-head randomized trials, a matching-adjusted indirect comparison (MAIC) was conducted to compare the efficacy of both therapies in a post-BTKi R/R MCL setting.

Methods: An unanchored MAIC compared individual patient-level data from the sonrotoclax trial (n=103 [efficacy set]; median 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 overall survival (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**).

Conclusions: 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.

Table. MAIC Results Comparing Efficacy Outcomes With Sonrotoclax vs 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.

IRC, independent review committee; PD, progressive disease; sMIPI, simplified Mantle Cell Lymphoma International Prognostic Index.