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439 | SAFETY AND EFFICACY OF ACALABRUTINIB, BENDAMUSTINE, AND RITUXIMAB IN PATIENTS WITH TREATMENT-NAIVE OR RELAPSED/REFRACTORY MANTLE CELL LYMPHOMA: PHASE IB TRIAL

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Background: Acalabrutinib (A) is a next-generation Bruton tyrosine kinase inhibitor approved for relapsed/refractory (R/R) mantle cell lymphoma (MCL). Bendamustine (B) + rituximab (R) is used for treatment-naive (TN) and R/R MCL. We present updated ABR safety and efficacy data in patients (pts) with TN or R/R MCL.

Methods: Eligible adults received ABR (phase 1b; NCT02717624) as follows: ABR for 6 28-d cycles, maintenance A+R for up to 2 y (TN cohort responders), then oral A continuously until progressive disease (PD) or treatment discontinuation due to toxicity (both cohorts). Primary endpoint was safety. Secondary endpoints were overall response rate (ORR), progression-free survival (PFS), and duration of response (DOR), all per Lugano.

Results: Overall, 38 pts were enrolled (TN, $n = 18$; R/R, $n = 20$) with median age 66 y (range 47–86). Baseline characteristics were (TN and R/R cohorts, respectively): stage IV disease, 88.9% and 95.0%; high-risk simplified MIPI score, 11.1% and 15.0%; bulky disease >5 cm, 16.7% and 30.0% or ≥10 cm, 5.6% and 10.0%; blastoid morphology, 5.6% and 15.0%. R/R pts had a median of 2 prior lines of therapy. At data cutoff (6/15/22), 6 (33.3%) TN pts and 4 (20.0%) R/R pts were receiving A monotherapy (Table). Most common any-grade AEs were nausea ($n = 14$, 77.8%; TN) and neutropenia ($n = 11$, 55.0%; R/R). Grade 3–4 AEs occurred in 13 (72.2%) TN pts and 17 (85.0%) R/R pts, most commonly neutropenia ($n = 7$, 38.9% [TN]; $n = 10$, 50.0% [R/R]). Serious AEs occurred in 11 (61.1%) TN pts and 13 (65.0%) R/R pts. There were no reports of ventricular tachyarrhythmia. Grade 3 atrial fibrillation occurred in 1 pt outside the safety reporting period and was unrelated to study treatment. Grade ≥3 major hemorrhage was reported in 2 (11.1%) TN pts and 3 (15.0%) R/R pts. Grade ≥3 hypertension was reported in 3 (16.7%) TN pts and 2 (10.0%) R/R pts. Five TN pts died (AE: pneumonitis, $n = 1$; unknown, $n = 4$) and 6 R/R pts died (AE: COVID and cerebrospinal meningitis, $n = 2$; PD, $n = 2$; unknown, $n = 2$). ORR was 94.4% ($n = 17$) in the TN cohort and 85.0% ($n = 17$) in the R/R cohort, with CR rates of 77.8% ($n = 14$) and 70.0% ($n = 14$), respectively. Median DOR was not estimable (NE) in the TN cohort and 43.5 mo in the R/R cohort. Median PFS and overall survival were NE in the TN cohort (median follow-up 47.6 mo) and 28.6 mo and NE, respectively, in the R/R cohort (median follow-up 20.4 mo).

Conclusions: Triple-combination ABR was tolerable and effective in pts with TN or R/R MCL.

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Table. Disposition

Patients, n (%)	TN (n=18)	R/R (n=20)	Total (N=38)
Time on study, median (min–max), mo	47.6 (0.6–72.4)	20.4 (1.2–64.2)	26.4 (0.6–72.4)
Completed 6 cycles of BR	15 (83.3)	10 (50.0)	25 (65.8)
Completed 6 cycles of ABR	14 (77.8)	10 (50.0)	24 (63.2)
Receiving A at end of study	6 (33.3)	4 (20.0)	10 (26.3)
Discontinued A	12 (66.7)	16 (80.0)	28 (73.7)
AE	6 (33.3)	9 (45.0)	15 (39.5)
Disease progression	2 (11.1)	5 (25.0)	7 (18.4)
Withdrawal by PI	2 (11.1)	1 (5.0)	3 (7.9)
Other	2 (11.1)	1 (5.0)	3 (7.9)

M. Wang

Consultant or advisory role: AbbVie, Acerta Pharma, ADC Therapeutics America, Amphista Therapeutics Limited, AstraZeneca, Be Biopharma, BeiGene, BioInvent, Deciphera, DTRM Biopharma (Cayman) Limited, Genentech, InnoCare, Janssen, Kite Pharma, Leukemia & Lymphoma Society, Lilly, Merck, Miltenyi Biomedicine, Milken Institute, Oncternal, Parexel, Pepromene Bio, Pharmacyclics, VelosBio

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440 | PHASE 1/2 STUDY OF ZILOVERTAMAB AND IBRUTINIB IN MANTLE CELL LYMPHOMA (MCL), CHRONIC LYMPHOCYTIC LEUKEMIA (CLL), OR MARGINAL ZONE LYMPHOMA (MZL)

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Background: Zilovertamab (Zilo) is a humanized monoclonal antibody that inhibits the tumor promoting activity of the cancer stem cell receptor, ROR1, which is highly expressed in many hematologic malignancies but not on normal adult tissues.

Methods: Patients (Pts) with relapsed or refractory (RR) MCL or MZL or treatment-naïve (TN) or RR CLL were enrolled. Part 1 (Dose Escalation in CLL & MCL) evaluated multiple doses up to Zilo 600 mg IV q4wks + Ibr 420 mg (CLL) or 560 mg (MCL) daily which was selected for Part 2 (Dose Expansion in CLL, MCL & MZL) and Part 3 (CLL only; pts randomized 2:1 to Zilo+Ibr vs. Ibr alone).

Results: To date, 33 MCL, 62 CLL & 4 MZL (99) pts were treated in Parts 1, 2 & 3. In Parts 1&2, 28 RR MCL and 34 CLL (12 TN and 22 RR) on zilo+ibr were efficacy evaluable (MZL not yet evaluable). In Part 3, 23 CLL pts on Zilo+Ibr (16) or Ibr (7) were evaluable. Safety & efficacy results were as of 11 October 2022.