A phase II multicenter study of abexinostat, an oral histone deacetylase inhibitor, in patients with relapsed/refractory follicular lymphoma.

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Background: Epigenetic alterations are major drivers of Follicular lymphoma (FL). Histone deacetylase (HDAC) inhibitors have potential to counteract the loss of histone acetylation that results from *CREBBP* or *EP300* mutations. Abexinostat (Abx) is a novel potent oral pan-HDAC inhibitor with a pharmacokinetic profile that allows maintenance of sufficient drug concentrations for anti-tumor activity with twice daily (BID) dosing. Abx was shown to be well-tolerated with significant response in pts with relapsed/refractory (R/R) FL. **Methods:** This phase II study evaluated Abx 80 mg administered orally BID 4 hours apart in a "one week on, one week off" schedule (days 1 to 7 & 15 to 21 of a 28-day cycle) in pts with R/R FL (grade 1-3a). Key inclusion criteria included age ≥18 years, ≥ 2 prior treatment regimens, ECOG of 0-2, and measurable disease per Lugano 2014 criteria. Pts undergo efficacy assessment by enhanced CT/MRI every 8 weeks for the first 24 weeks, and every 12 weeks thereafter, and PET-CT at weeks 12 and 24 and to confirm a complete response (CR), in accordance with the Lugano 2014 criteria. Bone marrow (BM) evaluation was mandated in pts with baseline BM involvement who achieved radiographic CR. The primary endpoint is independent review committee (IRC)-assessed overall response rate (ORR). Secondary endpoints include duration of response (DoR), progression-free survival (PFS), overall survival (OS), and safety. **Results:** At the data cut-off date of December 15, 2023, data were available for 90 pts. Median age was 55.0 (range 27-79), 57.8% of pts were male, and 22.2% had ≥ 3 FLIPI-2. Pts had a median of 3 prior lines of therapy (range 2-9), and 24.4% were refractory to the last prior regimen, 27.8% of pts had been treated with PI3K inhibitors before. With a median follow-up of 20.8 months, of 82 pts evaluable for efficacy, the IRC-assessed ORR was 67.1% (95% CI: 55.8%-77.1%), including 12.2% CR. The ORR for pts with > 3 lines of prior therapy was 69.0% (95% CI: 49.2%-84.7%). The median PFS and median DoR was 13.77 (95% CI: 9.69-not evaluable [NE]) months and 13.96 (95% CI: 8.34-NE) months, respectively. Median OS was not reached, and the 42-month OS rate was 74.3% (95% CI: 58.1%-85.0%). Of 90 pts evaluable for safety, the most common (≥ 40%) treatment-emergent adverse events (TEAEs) were thrombocytopenia (85.6%), neutropenia (58.9%), leukopenia (52.2%), nausea (50.0%), anemia (48.9%) and diarrhea (46.7%); ≥grade 3 TEAEs (≥ 5%) included thrombocytopenia (37.8%), neutropenia (23.3%), leukopenia (7.8%), and lymphopenia (5.6%). TEAEs led to dose reductions and discontinuations in 28.9% and 3.3% of all pts, respectively. **Conclusions:** Abx was well tolerated at dose of 80 mg BID as monotherapy, and demonstrated a significant response in pts with heavily pretreated R/R FL. Clinical trial information: NCT03934567. Research Sponsor: None.