Background

Study Rationale

To determine the safety and maximum tolerated dose (MTD) of umbralisib (U), a selective inhibitor of phosphatidylinositol 3-kinase delta (PI3Kδ) in patients with relapsed/refractory follicular lymphoma (FL) and B cell chronic lymphocytic leukemia (B-CLL) with target engagement.

Study Objectives

Primary Objectives

- To determine the Safety and Maximum Tolerated Dose (MTD) of U2 + Bendamustine Secondary Objectives

- To evaluate efficacy (overall response rate, time to response, duration of response, progression-free survival) Key Eligibility Criteria

- Confirmed diagnosis of Diffuse Large B-Cell Lymphoma (DLBCL) or Follicular Lymphoma (FL)
- Relapsed after radiotherapy at least prior to 36 months
- Expression of CD20, CD27 and/or FRα

Results

Demographics

Efficacy

Best Overall Response Rate

Phase 2a BUNY-NHL Study

- 77 y/o Male with 3 prior lines: R-Benda (refractory), R-idelbela (refractory), and an investigational EZH2 inhibitor (refractory)
- Attained a PR (72% reduction) at first assessment, CR by Week 44, now ongoing for >29 months
- 58 y/o Male with 3 prior lines of therapy: CHOP, R-IKE, and ASCT
- Attained a PR (86% response) at first assessment, and PET-NC by Week 32, ongoing for >19 months
- 48 y/o Male with 3 prior lines of therapy: R-Benda, R-CHOP, and R-CHOP
- Attained a PR (86% reduction) within 6 months, and PET-NC by Week 32, ongoing for >19 months

Conclusions

- The non-commercial doublet of umbralisib + ublituximab is a safe and efficacious backbone regimen on to build novel multi-d rag combinations.
- The combination of umbralisib + ublituximab + bendamustine is well tolerated and highly active in patients with advanced NHL, even in heavily pretreated, indolent and aggressive NHL, including those not eligible for HD/CT or ASCT 12 chemotherapy.
- An 80% CR with 54% CR rate in relapsed or refractory FL, including a 75% ORR in refractory FL.
- The activity demonstrated with the triple combination of umbralisib + ublituximab + bendamustine is being explored further in registration directed studies (UNITY-NHL).