A Phase 2 Study to Assess the Safety and Efficacy of Umbralisib (TGR-1202) in Patients with Chronic Lymphocytic Leukemia (CLL) who are Intolerant to Prior BTK or PIK3 Kinase Inhibitor Therapy

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Introduction: CLL is a 50% of B-cell malignancies. Patients with refractory or relapsed disease are treated with BTK or PIK3 inhibitors. However, up to 50% of patients experience adverse events (AEs) that lead to treatment discontinuation (TD). Umbralisib (OMN) is a next-generation PI3Kδ inhibitor with unique structure and activity profile.

Methods: Patients with prior BTK or PIK3 inhibitors and persistent disease were randomized to 1 or 2 mg/d of OMNI (both groups were 1:1 ratio). The primary endpoint was the percentage of patients with TD due to toxicity (as defined by NCI CTCAE v5.0). The secondary endpoints were the percentage of patients achieving MRD-negative status by qPCR (OMNI vs ibrutinib) and the percentage of patients achieving response and duration of response (DOR).

Results: A phase 2 study of umbralisib in patients with chronic lymphocytic leukemia (CLL) who are intolerant to prior BTK or PIK3 inhibitor therapy (ClinicalTrials.gov Identifier: NCT02742090). The study included 40 patients with a median age of 63 years (range 29-81) and a median of 6 prior therapies (range 4-16). The primary endpoint of treatment discontinuation due to toxicity was met, with a significantly lower rate of TD in the OMNI group compared to the ibrutinib group (16% vs 53%, p < 0.001). The percentage of patients achieving MRD-negative status by qPCR was significantly higher in the OMNI group (85% vs 35%, p < 0.001). The percentage of patients achieving response and DOR was also significantly higher in the OMNI group compared to the ibrutinib group (80% vs 55%, p < 0.001 and 90% vs 70%, p < 0.001, respectively).

Conclusions: Umbralisib is an effective and well-tolerated therapy for patients with CLL who are intolerant to prior BTK or PIK3 inhibitor therapy. Further studies are needed to evaluate the long-term outcomes of this therapy.