Patterns of Duvelisib-Induced Lymphocytosis in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Including Those With High-Risk Factors Treated in the DUO Trial

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**Abstract**

A phase III trial of duvelisib (DUV), a first-in-class dual PI3K-δ/PI3K-γ inhibitor, in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) was conducted. Lymphocytosis is a proven adverse event (AE) of PI3K inhibitors, and the incidence and impact of lymphocytosis on patient outcomes were assessed.

**Methods**

Study Design: Duo Trial

- **DUV 450-500 mg twice daily (BID) vs. placebo (PBO) in 28-day treatment cycles until progressive disease or unacceptable toxicity.**

**Assessment of Lymphocytosis**

- **Absolute lymphocyte count (ALC) measured by local laboratories for determination of peak ALC and median reduction from baseline (BL) and median time to first and second ALC peak**.
- **Lymphocytosis was defined as an ALC of ≥ 30 × 10^9/L and ≥ 150 × 10^9/L increases of ALC at BL**.
- **Lymphocytosis follow-up visit was defined as ≥ 10% increase or ≥ 15 × 10^9/L increase in ALC at ALC peak**.
- **Lymphocytosis follow-up visit was defined as the time of onset of peak lymphocytosis in relation to resolution of lymphocytosis or last ALC value, whichever occurred first**.

**Assessment of Response**

- **Response summary and duration (CR/PR) determined at the best response of complete response (CR) or partial response (PR) at the end of frontline therapy or progression.**
- **Duration of response was calculated from the date of CR/PR to the date of loss of response (progression)**.

**In Vivo Assessment of PI3K-δ or PI3K-γ Inhibition of CLL in a Patient-Derived Xenograft Mouse Model**

- **A phase III trial of DUV vs. placebo (PBO) in 28-day treatment cycles until progressive disease or unacceptable toxicity**.

**Lymphocytosis and Resolution**

- **Lymphocytosis and resolution were assessed on Cycle 1, day 8 and Cycle 3, day 1 (first nodal assessment)**.

**Figure 4. Mean Changes From BL in ALC and Lymph Node SP02 Time Over Duo**

**Figure 5. Median Changes From Baseline ALC and LMR**

**Table 1. DUO Baseline Characteristics**

**Table 2. Summary of Lymphocytosis in Patients With R/R CL/LGG**

**Table 3. Median Change From Baseline ALC and LMR**

**Table 4. Lymphocytosis in High-Risk Patients With R/R CL/LGG Receiving Duo**

**CONCLUSIONS**

- **DUV monotherapy induced rapid lymphocytosis that occurred within 1 week in the majority of patients**.
- **The median time to onset of lymphocytosis was the same regardless of response to DUV**.
- **The median time to onset of lymphocytosis was the same regardless of response to DUV**.
- **The incidence of prolonged lymphocytosis and hyperleukocytosis was low among patients**.

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