**Effect of Dose Modifications on Response to Duvelisib in Patients With Relapsed/Refractory CLL/SLL in the DUO Trial**

**Pablo Ghia, Ian W. Flinn, Nicole Lamanna, Marco Montillo, Árpád Illés, Gabriel Etienne, Julio Delgado, Bryone J. Kuss, Constantine S. Tam, Fritz Offner, Francesc Bosch, Matthew S. Davids, Ulrich Jünger, Florence Cymbalista, David T. Weaver, Stephanie Lustgarten, Hagop Yossoufian, Stephan Stilgenbauer**

**University of Texas Southwestern Medical Center and KDTC, Radiation Oncology, Dallas, TX.**

**Background**
- Duvelisib (DUO) is a first-in-class dual phosphoinositide 3-kinase (PI3K) inhibitor approved by the US Food and Drug Administration for the treatment of patients with relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after ≥ 2 prior therapies or R/R follicular lymphoma after ≥ 2 prior systemic therapies.
- In a phase 3 DUO trial, DUO monotherapy 25 mg twice daily (BID) significantly improved efficacy vs obinutuzumab (OBA) in patients with R/R CLL/SLL:
  - Median progression-free survival (mPFS) 11.3 vs 9.9 months (HR, 0.52; P = 0.001) (Figure 1).
- In a randomized controlled trial comparing DUO at 25 mg twice daily for 28-day treatment cycles until progressive disease or unacceptable toxicity vs placebo (Figure 2), Grade ≥ 3 adverse events (AEs) of any severity were more frequent with DUO (45.5% vs 34.1%; P = 0.014) (Table 2).  
- The most common treatment-emergent adverse events (TEAEs) of any severity were diarrhea (42.5% vs 34.1%; P = 0.014), neutropenia (16.9% vs 10.5%; P = 0.042), and infections (13.9% vs 7.9%; P = 0.042) (Figure 3).

**Methods**

- **DUO-IH: 150-07; NCT03066232** is an open-label, 2-arm, randomized, phase 3, superiority trial designed to evaluate the efficacy and safety of DUO compared with OBA in patients with R/R CLL/SLL (Figure 4).
- **DUO-IH: 150-08; NCT03066233** is an open-label, 2-arm, randomized, phase 3, superiority trial designed to evaluate the efficacy and safety of DUO compared with OBA in patients with R/R SLL (Figure 4).
- **DUO-IH: 150-09; NCT03066234** is an open-label, 2-arm, randomized, phase 3, superiority trial designed to evaluate the efficacy and safety of DUO compared with OBA in patients with R/R SLL (Figure 4).

- **DUO-IH: 150-10; NCT03066235** is an open-label, 2-arm, randomized, phase 3, superiority trial designed to evaluate the efficacy and safety of DUO compared with OBA in patients with R/R SLL (Figure 4).

**Results**

- Among 319 DUO-treated patients, the median duration of DUO exposure was 11.6 months (range, 0.2 to 36.8 months) (Figure 1).
- Median time to onset of AESI after 28 days was 20 days (range, 1 day to 36 weeks) (Figure 2).
- **Grade ≥ 3 TeAEs:**
  - Diarrhea: 31% vs 22% (P = 0.042) (Table 3).
  - Neutropenia: 17% vs 12% (P = 0.042) (Table 3).
  - Infections: 13% vs 7% (P = 0.042) (Table 3).
- **Grade ≥ 3 TeAEs of any duration:**
  - Diarrhea: 7% vs 3% (P = 0.042) (Table 3).
  - Neutropenia: 5% vs 2% (P = 0.042) (Table 3).
  - Infections: 5% vs 3% (P = 0.042) (Table 3).
- **Rate of Grade ≥ 3 TeAEs of any duration:**
  - Diarrhea: 7% vs 3% (P = 0.042) (Table 3).
  - Neutropenia: 5% vs 2% (P = 0.042) (Table 3).
  - Infections: 5% vs 3% (P = 0.042) (Table 3).

**Conclusion**

- **DI and DR did not negatively impact efficacy outcomes with DUO:**
  - Among responders (n = 118), median time to first response on DUO was 1.9 months, and estimated median duration of response was 11.1 months (Table 4).
  - Response to DUO was improved in most patients evaluated for response who had ≥ 1 DI for 1 week (HR, 0.79; 95% CI, 0.6-1.0; P = 0.03) (Table 5).

- **PFM was similar between patients with ≥ 1 DI and those without DI for ≥ 1 week or ≥ 2 weeks:**
  - Among 25 patients who had a DI after a complete response (CR) or partial response (PR), the median time to DI was 5.6 months (range, 1 to 23 months) (Figure 6).

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**References**