Duvelisib (DUV) is a first-in-class oral dual phosphoinositide 3-kinase (PI3K)-δ/γ 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 systemic therapies.1

Dose interruption (DI) or reduction (DR) to 15, 10, or 5 mg BID was permitted per appropriate intervention via dose modifications, routine medical care, and prophylactic measures.7,8

Here, we report results from retrospective analyses conducted to examine dose-modification patterns and their impact on response to DUV in the DUO trial (NCT02304542)14-16; an open-label, 2-arm, randomized, phase 3, superiority trial designed to evaluate the safety and efficacy of DUV compared with OPA in patients who were diagnosed with R/R CLL/SLL.1

Figure 1. Duvelisib Significantly Improved PFS vs OPA in Patients With R/R CLL/SLL

DESCRIPTION

In the phase 3 DUO trial, DUV monotherapy 25 mg twice daily (BID) significantly improved overall response rate (ORR) vs OPA 40 mg BID (25 mg for patients >65 years old) (Figure 1). The median duration of R/R CLL/SLL was consistent with previous reports and manageable with appropriate intervention via dose modifications, routine medical care, and prophylactic measures.7,8

Figure 2. DUO Trial Design

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RESULTS

Among 158 R/R treated patients, the median duration of DUV exposure was 11.8 months (range, 0.2 to 36.8 months).

The median overall DUV dose intensity (total dose taken/total expected dose [25 mg BID] × 100) was 97.2% (range, 34.7 to 100%)

- Median dose intensity was highest during the first 3 months, then decreased slightly among patients with ≥3 prior lines of therapy (0.2 to 36.8 months).

- Median time to onset of AEs was 2.0 to 4.3 months (Figure 3A).

- Proportion of patients experiencing AEs was stable or decreased over time after 3 to 6 months (Table 1).

Figure 3. Onset and Duration of AEs

- Median duration of AEs was 7.8 months (range, 22 days to 9 months).

- Among responders (n = 118), median time to first response on DUV was 1.3 months (range, 0.6 to 3 months).

- PFS was similar between patients with ≥1 DI and those without DI for ≥3 months of therapy (Figure 5).

- PFS was similar between patients with ≥1 DR and those without DR within the first 3 and 6 months of therapy (Figure 6).

- Baseline characteristics of patients with DI or DR are described in Table 2.

- Response to DUV was maintained in patients after a DR (≥ 30 days, 53%; ≥ 60 days, 47%).

- Efficacy and Dose Modification

- Among responders (n ≥ 1), median time to first response on DUV was 1.3 months, and estimated median duration of response was 11.1 months.

- Response to DUV was improved or maintained in most evaluable responders for whom response had ≥ 1 DR for 21 days (94%) or ≥ 2 weeks (82%) followed by 3 to 6 months on DUV (Table 4).

- Response to DUV was maintained in patients after a DR (> 30 days, 53%; ≥ 90 days, 45%, 120 days, 44%).

- Among 23 patients who had a DR after a complete response (CR) or partial response (PR), the median time to DUV was 5.6 months (range, 1 to 21.3 months), and the median duration at reduced dose was 3.4 months.

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Table 1. Rates of AEs Over Time

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