Characterization of Duvelisib in Patients With Refractory Marginal Zone Lymphoma: Data From the Phase 2 DYNAMO Trial

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BACKGROUND
Duvelisib (DUV) is a first-in-class, oral dual inhibitor of phosphoinositide 3-kinase (PI3K)-δ and PI3K-γ approved in the United States for the treatment of relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma after ≥ 2 prior therapies and for follicular lymphoma after ≥ 2 prior systemic therapies.1

• DUV targets key signaling pathways that promote the growth and survival of hematologic malignancies2–4 (Figure 1) – In preclinical studies, dual PI3K-δ inhibition with duvelisib was more effective at inhibiting B cells and modifying cells in the tumor microenvironment in vivo than PI3K-δ inhibition alone.5

• DUV offers a novel therapeutic approach for patients with marginal zone lymphoma (MZL), for which few effective treatment options exist.6

RESULTS
• DUV was well tolerated overall with ≥ 1 adverse event in all 18 patients and most AEs were mild to moderate in nature (grade ≤ 2).7

• All patients experienced ≥ 1 adverse event (AE) – Most AEs were mild to moderate in nature (grade ≤ 2) – Neutropenia and diarrhea were among the most common grade ≥ 3 AEs, occurring in 28% and 17% of patients, respectively

• Treatment-emergent AEs (Table 5) resulted in 33% of patients discontinuing treatment – Causes of discontinuation: diarrhea (4 patients), pneumonitis (2 patients), pneumocytomegaly (2 patients), and asepsis (2 patients).

CONCLUSIONS
• DUV demonstrated clinical meaningful antitumor activity in patients with high-risk MZL, double-refractory to previous anticancer therapy – 67% of patients were refractory to ≥ 2 prior regimens

• The ORR with DUV was 39% (95% CI, 17.3%-64.3%), with 35% achieving partial response (PR) and 4% achieving complete response (CR) (Table 4)

• The median time to response with DUV was 3.7 months (range, 1.8-6.4 months) (Table 3) – Of the 3 in PR at discontinuation, follow-up imaging was not available for 1 patient, but the other 2 had sustained responses of > 1 year as of the most recent imaging after treatment discontinuation

Table 2. Prior Regimens and Degree of Refractory Disease

Table 3. Exposure to Selected Anticancer Therapies

Table 4. DCR and ORR in Patients With MZL

Table 5. Treatment-Emergent Adverse Events in ≥ 20% of Patients

REFERENCES


3Wang S, Linker CJ, Kohl C, et al. A phase 2, open-label, single-arm, phase 2 trial that evaluated the safety and efficacy of DUVE monotherapy in indolent NHL, including in patients with MZL. (Figure 2) DYNAMO Trial Design

STUDY DESIGN
• DYNAMO (NCT:14-06; NC1:308220) was an open-label, single-arm, phase 2 trial that evaluated the safety and efficacy of DUV monotherapy in indolent NHL, including in patients with MZL. (Figure 2) DYNAMO Trial Design

RESULTS
• Of 119 patients enrolled in the DYNAMO trial, 18 demonstrated MZL histology4 – Extramedullary (50%) was the most common MZL subtype, followed by splenic (28%) and nodal (22%) (Table 1)

• The median duration of DUV exposure was 6.4 months (range, 0.9-37.3 months) (Table 3) – Most patients experienced dose modifications, including dose interruptions (89%) and dose reductions (17%), similar to the overall population7

• The ORR per IRC (CR + PR + SD) was 39% (95% CI, 17.3%-64.3%), with 35% achieving partial response (PR) and 4% achieving complete response (CR) (Table 4)

• The median time to response with DUV was 3.7 months (range, 1.8-6.4 months) (Table 3)

• The median PFS per IRC assessment was 15.5 months (95% CI, 3.6-27.8 months) (Figure 4)

• 12 of 18 patients were evaluable for the change in the sum of the products of diameters (SPD) of nodal target lesions – of the 3 in PR at discontinuation, follow-up imaging was not available for 1 patient, but the other 2 had sustained responses of > 1 year as of the most recent imaging after treatment discontinuation

• The median duration of DUV exposure was 6.4 months (range, 0.9-37.3 months) (Table 3)

• Most patients experienced dose modifications, including dose interruptions (89%) and dose reductions (17%), similar to the overall population7

• The ORR with DUV was 39% (95% CI, 17.3%-64.3%), with 35% achieving partial response (PR) and 4% achieving complete response (CR) (Table 4) – The ORR was 75% for nodal subtype, 80% for splenic subtype

• Neutropenia and diarrhea were among the most common grade ≥ 3 AEs, occurring in 28% and 17% of patients, respectively

• Most AEs were mild to moderate in nature (grade ≤ 2) – Of the 3 in PR at discontinuation, follow-up imaging was not available for 1 patient, but the other 2 had sustained responses of > 1 year as of the most recent imaging after treatment discontinuation

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CONCLUSIONS
• DUV demonstrated clinical meaningful antitumor activity in patients with high-risk MZL, double-refractory to previous anticancer therapy – 67% of patients were refractory to ≥ 2 prior regimens

• The ORR with DUV was 39% (95% CI, 17.3%-64.3%), with durable responses observed (median not yet reached)

• T Fatigue

• Mucositis

• Anemia

• Neutropenia

• Myalgia

• Nausea

• Diarrhea

• Abdominal pain

• #B: One patient received a stem cell transplant (deviation from protocol). b As a single agent or in combination.

• The DCR (CR + PR + SD) was 89% – Of the 3 in PR at discontinuation, follow-up imaging was not available for 1 patient, but the other 2 had sustained responses of > 1 year as of the most recent imaging after treatment discontinuation

• The median PFS per IRC assessment was 15.5 months (95% CI, 3.6-27.8 months) (Figure 4)

• The median duration of DUV exposure was 6.4 months (range, 0.9-37.3 months) (Table 3)

FUTURE DIRECTIONS

• Most patients experienced dose modifications, including dose interruptions (89%) and dose reductions (17%), similar to the overall population7

• All patients experienced ≥ 1 adverse event (AE)

• Most AEs were mild to moderate in nature (grade ≤ 2) – Neutropenia and diarrhea were among the most common grade ≥ 3 AEs, occurring in 28% and 17% of patients, respectively

• Treatment-emergent AEs (Table 5) resulted in 33% of patients discontinuing treatment

- Causes of discontinuation: diarrhea (4 patients), pneumonitis (2 patients), pneumocytomegaly (2 patients), asepsis (2 patients), pneumonitis (2 patients), pneumocytomegaly (2 patients), asepsis (2 patients)

- One death due to peritonitis occurred and was classified as potentially related to DUV treatment

- Of the 3 in PR at discontinuation, follow-up imaging was not available for 1 patient, but the other 2 had sustained responses of > 1 year as of the most recent imaging after treatment discontinuation

Additional grade ≥ 3 treatment-emergent adverse events in ≥ 1 patient: pericardial effusion (1 patient), anemia (1 patient), hyponatremia (1 patient), paresthesia (1 patient), pleural effusion (1 patient), toxicities (1 patient), and others (4 patients).

CONCLUSIONS
• DUV demonstrated clinical meaningful antitumor activity in patients with high-risk MZL, double-refractory to previous anticancer therapy – 67% of patients were refractory to ≥ 2 prior regimens

• The ORR with DUV was 39% (95% CI, 17.3%-64.3%), with durable responses observed (median not yet reached)

• The DCR (CR + PR + SD) was 89% – The median PFS with DUV was 15.5 months (95% CI, 3.8-27.8 months)

• Based on the types of AEs observed in the study and this high-risk patient population, DUV had a manageable safety profile, consistent with previous reports in other advanced hematologic malignancies5

• These preliminary findings suggest that DUV may be a promising oral treatment for patients with double-refractory MZL for whom there are limited treatment options

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Figure 2. DYNAMO Trial Design

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