**DYNAMO: A Phase 2 Study Demonstrating the Clinical Activity of Duvelisib in Patients with Double-Refractory Small lymphocytic Lymphoma**

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**Background**

Duvelisib is a Small Molecule Inhibitor of PI3K-δ and PI3K-γ. Duvelisib targets PI3K-δ and PI3K-γ, and has a manageable safety profile.

**Key Eligibility Criteria**

- *Prior therapy*: at least 2 therapies failed
- *Progression*: within 6 months of last dose
- *Performance Status*: 0–2
- *Grades*: ≤ 1 of 4

**Study Design**

- **Trial Type**: Single-arm, open-label, single-agent study
- **Dose**: 50 mg twice daily, adjusted for toxicity
- **Duration**: Up to 12 months

**Response Assessments**

- **Objective Response Rate (ORR)**: 18 (95% CI 34.9, 15.8)
- **Progression-Free Survival (PFS)**: 12.7 (95% CI 10.1, 15.4)

**Conclusion**

- Duvelisib is an efficacious and well tolerated treatment option for patients with double refractory SLL.
- 100% of patients had a reduction in tumor burden.
- Median PFS of 12 months.
- Two-year OS for evaluable patients: 68%.
- Overall survival: 100%.

**Efficacy**

- **Overall Response Rate**
  - ORR per IRC: 18 (95% CI 34.9, 15.8)
  - Complete Response: 6 (95% CI 34.9, 15.8)
  - Partial Response: 12 (95% CI 34.9, 15.8)

- **Median Time to Response**: 2 months (range: 1.4 – 12)

- **Duration of Response Per IRC**
  - Median response duration: 12 months (95% CI 34.9, 15.8)

**Safety**

- **Most Common AEs (≥15% of SLL Patients)**
  - Hematologic: Neutropenia (n=28)
  - Nonhematologic: Fatigue (n=28)

**Demographics and Baseline Characteristics**

- **PFS**
  - FOLFOX (n=28)
  - FLAIR (n=28)
- **OS**
  - FOLFOX (n=28)
  - FLAIR (n=28)

**Key Secondaries**

- **Key Secondary Endpoints**
  - OS: 18 months (95% CI 34.9, 15.8)
  - ORR: 18 (95% CI 34.9, 15.8)

**Summary**

- Duvelisib synergistically targets both malignant B cells (PI3K-δ) and the supporting microenvironment (PI3K-γ).
- Robust clinical activity was observed in Phase 1 study in advanced B- and T-cell lymphomas (Flinn ASH 2014; O’Brien ASH 2014; Honore ASH 2014).
- Here we present the results in patients with SLL, enrolled in DYNAMO™, a Phase 2, open-label, single-arm study evaluating the safety and efficacy of duvelisib in patients with SLL.

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- 100% of patients had a reduction in tumor burden.
- Median PFS of 12 months.
- Two-year OS for evaluable patients: 68%.
- Overall survival: 100%.

**Conclusion**

- Duvelisib monotherapy is clinically active in double-refractory SLL.
- ORR of 68% per IRC, ORR of 86% per investigator assessment.
- 100% of evaluable SLL patients had tumor reduction.
- Responses were durable (median 10 months).
- Median PFS of 12 months.
- Duvelisib has a manageable safety profile.
- In long-term follow-up (median 18 months), duvelisib remains well tolerated.
- Duvelisib monotherapy has demonstrated favorable benefit/risk in double-refractory SLL, and may represent an important treatment option for these patients.