Efficacy and Safety of Duvelisib Following Disease Progression on Ofatumumab in Patients with Relapsed/Refractory CLL or SLL: Updated Results from the DUO™ Crossover Extension Study

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**BACKGROUND**

- Duvelisib (DUO) is a first-in-class, oral dual inhibitor of PI3K-δ and PI3K-γ approved by the US FDA for treatment of relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) or lymphocytic leukemia (SLL) in patients who have received 2 or more prior therapies.
- The Phase 3 DUO Study (NCT02004532) in R/R CLL/SLL showed favorable benefit-risk in patients who had received 2 or more prior therapies.
- Grade 3+ hematologic adverse events (AEs) included neutropenia (36%), anemia (13%), and thrombocytopenia (8%); the most common Grade 3+ non-hematologic AEs were diarrhea (10%), pneumonia (1%), and colitis (1%).

**EFFICACY**

**Patient Enrollment and Disposition**

- 90 of 101 patients treated with ofatumumab with confirmed disease progression on DUO elected to enroll in Study IP-145-12.
- The median duration of exposure to duvelisib was 8.8 months (max 39 months), with a median total follow-up of 12.5 months.
- As of 15 June 2018, 73 patients have discontinued duvelisib, 39 due to AEs, 19 due to PFS 6, due to death, and 9 for other reasons (e.g. voluntary withdrawal).

**Study Enrollment by Country**

- **US**
  - (n = 7; 8%)
  - Hungary
  - New Zealand
  - France

- **Australia**
  - (n = 6; 7%)
  - Italy
  - Spain

- **Europe**
  - (n = 15; 17%)
  - Belgium
  - UK
  - Australia
  - Germany

**Overall Response Rate (Investigator Assessment per IWCLL/IWG Criteria)**

- **All Trained Patients**
  - N = 90
  - N = 28
  - N = 30
  - N = 32

- **ORR**
  - 99%
  - 29
  - 15
  - 77
  - 80

- **PR**
  - 35.4
  - 35.3
  - 35.3
  - 50

- **CR**
  - 0
  - 0
  - 0
  - 0

- **CR + Vi**
  - 0
  - 0
  - 0
  - 0

- **All Trained Patients (90) vs.安慰剂 (2) vs.安慰剂 (1) vs.安慰剂 (n = 30)**
  - ORR: 99% vs. 33% vs. 6% vs. 3%
  - PR: 35.4% vs. 1% vs. 3% vs. 3%

**Safety**

- Severe opportunistic infections were reported in 3 patients.
- No pneumocytomegaly was seen.
- 1 patient was found to have a PFS 6.

**CONCLUSIONS**

- Duvelisib achieved an ORR of 77% and a median PFS of 15 months in patients with R/R CLL/SLL who had disease progression on ofatumumab monotherapy pre-crossover, in the subset of patients with del(17p) the ORR was 80%.
- Disease previously refractory to ofatumumab responded to duvelisib (ORR 73%).
- The safety profile of duvelisib monotherapy in this study was manageable and consistent with the known safety profile in CLL/SLL.
- These data further support the clinical benefit of duvelisib monotherapy in patients with R/R CLL/SLL.


**Study Design**

- Study IP-145-12 (NCT02004532) is an open-label, optional crossover extension study of DUO.
- Patients with radiologically confirmed disease progression were permitted to crossover and receive the opposite therapy.
- Eligible patients enrolled within 3 months of radiologically confirmed disease progression on the DUO study (excluding Richter’s transformation or polycythemia vera).
- Duvelisib 25 mg BID was administered until progressive disease (PD), intolerance, death, or study withdrawal.
- Pneumocystis prophylaxis was required for all patients.
- Herein we present efficacy and safety data for the 90 patients who received ofatumumab on DUO who crossed over to receive duvelisib on Study IP-145-12 following disease progression.

**Overall Response Rate (Investigator Assessment per IWCLL/IWG Criteria)**

- **All Trained Patients**
  - ORR = 99%
  - PR = 35.4%
  - CR = 0%
  - CR + Vi = 0%

- **All Trained Patients (90) vs.安慰剂 (2) vs.安慰剂 (1) vs.安慰剂 (n = 30)**
  - ORR: 99% vs. 33% vs. 6% vs. 3%
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