Prognostic and Immune-Related Factors Associated with Response to Duvelisib in the Phase 2 DYNAMO™ Clinical Trial in Patients with Indolent Non-Hodgkin Lymphoma

Pier Luigi Zinzani1, Ian W. Flihn2, Carole B. Miller3, Scott A. Tetreault4, Kirili M. Ardesheva5, Jonathan A. Pachter4, Kam Sprott6, Stephanie Lustgarten7, David T. Weaver8, Nina D. Wagner-Johnston9

1Institute of Hematology Seronigoli, University of Bologna, Bologna, Italy; 2Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; 3Saint Agnes Cancer Institute, Baltimore, MD; 4Florida Cancer Specialists, Tallahassee, FL; 5Department of Haematology, University College Hospital, London, UK; 6Varanet Oncology, Neshoba, MA; 7Slelman Cancer Center, Washington University, St Louis, MO

BACKGROUND
- Duvelisib is a small, dual PI3K-δ/Υ inhibitor that is FDA-approved for the treatment of chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), and follicular lymphoma (FL).
- The inhibition of PI3K-δ directly targets malignant cells, while PI3K-Υ inhibition disrupts the suppressive tumor microenvironment.
- In the Phase 2 DYNAMO™ trial of duvelisib monotherapy for relapsed/refractory (r/r) indolent FL (r/r IFL), the FL subgroup (n = 85) had a median progression-free survival (PFS) of 8.5 months (m) and an overall response rate (ORR) of 43%.
- An analysis of prognostic factors and immune-related variables (IRVs) undertaken was to identify subsets of DUVELISIB FL patients responsive to duvelisib.

OBJECTIVES
To identify FL risk subgroups, clinical parameters as well as according to the FL prognostic Index (FPI)1,2. Incidences of adverse events (AEs) per combined preferred term: neutropenia, diarrhea, colitis, pneumonia, pneumonitis, transaminitis, rash, and infections were also assessed in association with clinical responses. Blood collected at baseline (Cycle 1 Day 1) was analyzed by a central laboratory for a 7 gene expression signature to generate the combined MET-FLPI1, and topotecan were evaluated at screening for del(17p) cytogenetics. In addition, baseline immune cell counts by flow cytometry (subgrouped by the median values as low [L] or high [H]) were centrally assessed. Multivariate regression models were developed using a stepwise procedure from a selection of these parameters identified by individual univariate analysis for the efficacy endpoints of mPFS and ORR.

RESULTS

Table 1. Clinical Responses in Low- and High-Risk Subgroups According to Prognostic Indices

Table 2. Baseline Factor Combinations that Significantly Impact ORR

CONCLUSIONS
- In the Phase 2 DYNAMO study, mPFS and ORR were similar for duvelisib-treated FL pts regardless of poor prognostic indicators, including FPI, MET-FLPI, and chromosomal copy deletions.
- Multivariate LASSO (Cox or GLM) regressions with 84 variables revealed baseline characteristics including the number of prior therapies (1 vs 2 or more), as well as a biomarker profile of NK cell, IL17 + CD8+ T cells, [IL23RA]CCR19 that correlated with improved ORR; a biomarker profile of NK cell, IL17 + CD8+ T cells, C3+ [IL23RA]CCR19 that correlated with improved ORR
- Patients experiencing AEs (including potentially immune-related events) demonstrated generally similar PFS to those patients who did not experience AEs, after adjusting for time.

REFERENCES