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POSTER ABSTRACTS

625.T CELL, NK CELL, OR NK/T CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Duvelisib in Patients with Relapsed/Refractory Peripheral T-Cell Lymphoma: Final Results from the Phase 2 PRIMO Trial

Neha Mehta-Shah, MD MSCI[1], Pier Luigi Zinzani, MD PhD[2], Eric D. Jacobsen, MD[3], Jasmine Zain, MD[4], Monica Mead, MD[5], Carla Casulo, MD[6], Giuseppe Gritti, MD PhD[7], Lauren C. Pinter-Brown, MD FACP[8], Koji Izutsu, MD PhD[9], Ohad S Bentur, MD[10], David Sidransky, MD[11], Jonathan E. Brammer[12], Barbara Pro, MD[13], Christopher P. Fox, MBChB(Hons), PhD FRCP[14,15], Steven Horwitz, MD[16]

[1] Washington University School of Medicine in St. Louis, St Louis, MO
[2] Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy
[3] Dana Farber Cancer Institute, Boston, MA
[4] City of Hope, Duarte, CA
[5] Department of Medicine/Division of Hematology and Oncology, UCLA Medical Center, Los Angeles, CA
[6] University of Rochester Medical Center, Rochester, NY
[7] Hematology and Bone Marrow Transplant Unit, Ospedale Papa Giovanni XXIII, Bergamo, Italy
[8] University of California Irvine, Irvine, CA
[9] National Cancer Center Hospital, Tokyo, Japan
[10] Secura Bio, Inc., Las Vegas, NV
[11] Johns Hopkins University, Baltimore, MD
[12] Department of Internal Medicine, Division of Hematology, The Ohio State University, Columbus, OH
[13] Division of Hematology & Oncology, Columbia University Irving Medical Center, New York
[14] Department of Haematology, Nottingham City Hospital, Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom
[15] School of Medicine, University of Nottingham, Nottingham, United Kingdom
[16] Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Introduction
Peripheral T-cell lymphoma (PTCL) is a heterogeneous group of aggressive lymphomas, with poor prognosis and historically median overall survival (mOS) <6 months (mo) for relapsed or refractory (R/R) disease. In North America and Europe, the 3 most common subtypes are PTCL-NOS (not otherwise specified), angioimmunoblastic T-cell lymphoma (AITL), and anaplastic large-cell lymphoma (ALCL).
Current single agent therapies for R/R PTCL have modest overall response rates (ORR) of <30% (with the exception of brentuximab vedotin for CD30+ ALCL). Duvelisib is an oral inhibitor of phosphatidylinositol 3-kinase (PI3K)-δ and PI3K-γ isoforms. PRIMO (NCT03372057) was an open-label, single-arm trial that evaluated the safety and efficacy of duvelisib monotherapy in R/R PTCL in patients from the US, EU, UK, and Japan.
Methods
Eligibility criteria included adults with pathologically confirmed R/R PTCL. *Pneumocystis jirovecii* prophylaxis (PJP) was required. After the dose optimization phase, optimal dose was determined as duvelisib 75 mg BID for 2 cycles (to maximize disease control), followed by 25 mg BID (to mitigate late toxicities), until progressive disease (PD) or unacceptable toxicity. The primary endpoint was ORR by Independent Review Committee (IRC) assessment (Lugano 2014 criteria). Here we report final results of the PRIMO dose expansion phase (EP).
Results
The PRIMO-EP included 123 patients with R/R PTCL (data cutoff: Feb 2, 2024). Baseline characteristics: median age: 65 (range 21-92) years, male sex: 54.5%, median prior lines of therapy: 2 (range 1-9), most common baseline histologies: PTCL-NOS (n=53), AITL (n=37), and ALCL (n=20). Common reasons for duvelisib discontinuation included: PD: 41%, adverse events (AEs): 22%, stem cell transplant (SCT): 10%, and death: 8%. The median follow-up for PFS was 6.24 mo. Efficacy outcomes: ORR: 48%, complete response rate (CRR): 33%, median progression-free survival (mPFS): 3.45 mo, median duration of response

(DOR): 7.89 mo, and mOS: 12.35 mo. Outcomes stratified by baseline histology: ORR: 49.1% (PTCL-NOS), 62.2% (AITL), 15.0% (ALCL); mPFS: 3.45 mo (PTCL-NOS), 8.34 mo (AITL), 1.64 mo (ALCL); mOS: 11.04 mo (PTCL-NOS), 18.07 mo (AITL), 6.34 mo (ALCL); mDOR: 7.39 mo (PTCL-NOS), 11.70 mo (AITL), 1.97 mo (ALCL). Nineteen patients (15%) received SCT after PRIMO (11/12 with planned SCT at time of duvelisib treatment discontinuation plus 8 additional patients).
There were 4 (3.3%) fatal treatment-related AEs (cryptococcosis, Epstein-Barr virus associated lymphoproliferative disorder, pneumonitis, and sepsis) and 6 (4.9%) fatal AEs other than PD which were unrelated or unlikely related to duvelisib. AEs of special interest (Grade ≥3) included: ALT/AST elevation: 24.4%, neutropenia: 17.9%, infections: 13.0%, cutaneous reactions: 10.6%, diarrhea: 9.8%, pneumonia: 4.1%, pneumonitis: 0.8%, and colitis: 0.8%. There were no cases of PJP. AEs leading to dose hold or dose reduction occurred in 44.7% and 9.8% of patients, respectively. The median relative dose intensity was 97.7%.
Conclusions
The final analysis of the PRIMO-EP demonstrated an ORR of 48% and a CRR of 33%, with 15% of patients continuing to SCT; these results compare favorably to currently available single-agent options. AEs were generally manageable with per-protocol dose modifications and were consistent with those observed previously. PRIMO-EP results confirm duvelisib to be a promising agent for this disease with a high unmet need, poor prognosis, and limited effective treatment options. Based on these results, the sponsor is initiating a randomized phase 3 study in the EU/UK to investigate duvelisib in R/R nodal T follicular helper cell lymphoma (TERZO™).

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Off Label Disclosure: Duvelisib (DUV), an oral inhibitor of phosphatidylinositol 3-kinase (PI3K)-Î´Â and PI3K-Î³ isoforms, is approved in the US, EU, and UK for treatment of adult patients with R/R CLL (and for SLL in the US) after â‰¥2 prior systemic therapies (and for refractory follicular lymphoma after â‰¥2 prior systemic therapies in the EU and UK).Â The use of duvelisib in T cell lymphoma is investigational.

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