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HAEMATOLOGICAL MALIGNANCIES

1006O Copanlisib monotherapy activity in relapsed or refractory indolent B-cell lymphoma: Combined analysis from phase I and II studies

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Background: Copanlisib, a pan-class I phosphatidylinositol 3-kinase (PI3K) inhibitor with potent PI3K-α and PI3K-δ activity, has been explored as monotherapy in four phase I or II studies in patients with relapsed or refractory (r/r) indolent B-cell lymphoma having progressed on two or more prior lines of therapy. Because of similar entry criteria for all four studies, we therefore conducted a combined safety and efficacy analysis.

Methods: Patients with indolent B-cell non-Hodgkin lymphoma and r/r to ≥ 2 prior lines of treatment were eligible. Previous treatment included rituximab and an

alkylating agent. Copanlisib was administered intravenously intermittently on days 1, 8 and 15 of a 28-day cycle at either 0.8 mg/kg (studies NCT00962611, NCT02155582, and NCT01660451-A) or as a flat 60 mg dose (NCT01660451-B). The primary efficacy endpoint was objective response rate (ORR) using Cheson criteria based on central independent review and/or investigator assessment.

Results: The full analysis set comprised 168 patients, with follicular (n = 126) and marginal zone (n = 26), being the most common lymphoma sub-types. The median age was 64 (range 25-82), with ECOG status 0/1 being 56%/40%. The most common grade (G) 3/4 treatment emergent adverse events (AEs) were transient hyperglycemia (32%/6%, respectively) and transient hypertension (27%/0, respectively). Other all-grade AEs (all-grade%/G3%/G4%) occurring in > 25% of patients included diarrhea (36/5/0), fatigue (29/3/0), and nausea (26/1/0). Serious AEs of interest included pneumonia (10/7/1), pneumonitis (6/3/0) and one case of colitis (G4). The ORR for the entire dataset was 60%, with 21 (12%) patients with complete responses (CR; 1 uCR), 79 (47%) with partial responses (PR), and 51 (30%) with stable disease (SD). Based on investigator assessments, the ORR was 54%, with 9 (5%) CR, 81 (48%) PR, and 54 (32%) SD.

Conclusions: Treatment of indolent B-cell lymphoma patients with copanlisib administered intermittently and intravenously resulted in a manageable and predictable safety profile, with a low incidence of severe GI-related toxicities. The ORR for indolent lymphoma patients treated with copanlisib was robust by both independent and investigator analysis.

Clinical trial identification: NCT00962611, NCT02155582, NCT01660451.

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