Epacadostat plus pembrolizumab in patients with advanced melanoma: Phase 1 and 2 efficacy and safety results from ECHO-202/KEYNOTE-037

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Background: Tumors can evade immunosurveillance through upregulation of indoleamine 2,3-dioxygenase 1 (IDO1). Epacadostat (E) is a potent, selective inhibitor of the IDO1 enzyme. The combination of E + the PD-1 inhibitor pembrolizumab (P) is being evaluated in an open-label, phase 1/2 study in multiple tumor types (ECHO-202/KEYNOTE-037). We report phase 1 and 2 efficacy and safety data for patients (pts) with advanced melanoma (27Feb2017 data cutoff).

Methods: Pts previously treated with checkpoint inhibitors were excluded. Pts received E (25, 50, 100, or 300 mg PO BID) + P (2 mg/kg or 200 mg IV Q3W) during phase 1.
MTD was not exceeded. E (100 mg BID) + P (200 mg Q3W) was selected for phase 2. Responses were assessed in RECIST 1.1 evaluable pts.

**Results:** 64 pts enrolled (phase 1, n = 22; phase 2, n = 42). Median age, 65; male, 70%; BRAF+, 30%; M1c disease, 52%. Median duration of follow-up was 253+ days (range, 5 to 904+ days). Among 54 efficacy evaluable pts, ORR was 56% (30/54; 8 CR, 22 PR) and DCR (CR + PR + SD) was 78% (42/54). In treatment-naive pts (n = 45), ORR was 56% (25/45; 6 CR, 19 PR) and DCR was 78% (35/45). Among treatment-naive pts receiving E 100 mg BID (n = 30), ORR was 60% (18/30; 2 CR, 16 PR). Responses were observed regardless of PD-L1 and BRAF mutation status. At data cutoff, 28/30 responses in the melanoma cohort were ongoing (median duration of response = 287.5+ days, range 1+ to 763+ days). Median PFS was 12.4 mo; PFS rates at 6, 12, and 18 mo were 70%, 54%, and 50%, respectively. In treatment-naive pts, median PFS has not been reached; PFS rates at 6, 12, and 18 mo were 68%, 52%, and 52%. The most common (>15%) all-grade treatment-related AEs (TRAEs) were fatigue (39.1%), rash (32.8%), pruritus (26.6%), and arthralgia (15.6%). Grade ≥3 TRAEs were observed in 17.2% of pts (most common: lipase increased, n = 4; rash, n = 3; and amylase increased, n = 2). 3 pts discontinued due to TRAEs (lipase increased, n = 1; arthralgia, n = 2). No treatment-related deaths occurred. Biomarker evaluation is ongoing.

**Conclusions:** Consistent with the phase 1 results, E + P continues to be well tolerated and showed promising clinical activity. A phase 3 study in pts who are treatment-naive for advanced melanoma is ongoing (NCT02752074).

**Clinical trial identification:** NCT02178722

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