Efficacy and safety of entinostat (ENT) and pembrolizumab (PEMBRO) in patients with melanoma progressing on or after a PD-1/L1 blocking antibody.

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**BACKGROUND**

Tumor-related immune checkpoints (TCs) have improved prognosis for patients with advanced melanoma, but there is a latent need for patients who progress after ICI. Clinical trials have shown entinostat (ENT) and pembrolizumab (PEMBRO) to be active in patients progressing on other ICI. This phase I trial evaluated the efficacy and safety of the combination of ENT and PEMBRO in patients with melanoma progressing on or after a PD-1/L1 blocking antibody.

**METHODS**

**Patients**

Eligible patients were those with measurable disease per RECIST 1.1, and willingness to have fresh tumor samples collected during screening and at other time points as necessary.

**Treatment**

ENT (150 mg/m² on days 1 and 8) and PEMBRO (200 mg on days 1, 8, 15, and 22) were administered on a 21-day cycle. A total of 34 patients were enrolled, 18 of whom were Black or African American.

**Samples**

Samples were collected C1D1, C1D15, and C2D15. Data from the original 34 patients are reported here. The study was approved by the institutional review board for all sites.

**Efficacy**

No clinical benefit was observed in 14/34 patients (41%). Median duration of response was 3 months (95% CI: 0-14.3 months).

**Safety**

No unexpected toxicities were observed. Several Grade 3 adverse events included liver enzyme increase, mucosal inflammation, colitis, and autoimmune hepatitis.

**Correlates**

NanoString is a registered trademark of NanoString Technologies, Inc., in the United States and abroad. Additional analyses are ongoing to identify biomarkers that can predict clinical benefit in this population.

**CONCLUSIONS**

ENT + PEMBRO continues to demonstrate promising activity and safety profile in melanoma patients who have progressed on ICI. Preliminary biomarker analysis supports the hypothesis that the addition of ENT reprograms differential immune landscape in patients that have progressed on an anti–PD-(L)1. Additional analyses are ongoing to identify biomarkers that can predict clinical benefit in this population.

**References:**


**Aims:**

- Determine clinical benefit rate, defined as complete or partial response or stable disease for 24 weeks or more from initiation of treatment.
- Evaluate responses in melanoma patients who progressed on or after PD-1/L1 ICI.
- Evaluate the safety profile of ENT + PEMBRO.

**Endpoints:**

- Clinical benefit rate
- Median duration of response
- Safety

**METHODS (continued)**

**PATIENT DEMOGRAPHICS**

Demographics

- 34 patients were enrolled, 18 of whom were Black or African American.

**EFFICACY**

Fifteen patients were treated in 19/34 patients as shown in Figure 2. A partial response was confirmed, resulting in a CR of 18% (6/34 patients).

**Correlates**

NanoString Tumor Inflammation Signature Score

- The mean signature score was -2.4 (SD 1.4, median 0.0).

**SAFETY**

- The most common adverse events were rash, fatigue, and nausea.

**Figure 5.**

- Pearson correlation coefficients for the correlation of tumor expression-level changes and microarray expression changes.

**Tables**

- Table 1: Patient characteristics and tumor stage at baseline.
- Table 2: Additional biomarker analyses.

**Figure 1.**

- Change in tumor size from baseline over time in patients treated with Pembrolizumab (blue) and Pembrolizumab + entinostat (red).

**Figure 2.**

- Change in tumor size from baseline over time in patients treated with Pembrolizumab (blue) and Pembrolizumab + entinostat (red).

**Figure 3.**

- Change in tumor size from baseline over time in patients treated with Pembrolizumab (blue) and Pembrolizumab + entinostat (red).

**Figure 4.**

- Change in tumor size from baseline over time in patients treated with Pembrolizumab (blue) and Pembrolizumab + entinostat (red).

**Figure 5.**

- Change in tumor size from baseline over time in patients treated with Pembrolizumab (blue) and Pembrolizumab + entinostat (red).