ABSTRACT

Background: Intratumoral/inflammation is a requirement for response to anti-PD-1 therapy. Previously, we demonstrated that intratumoral IL-12 administration via injection of plasmid IL-12 plus electroporation (TAVO) can increase the ratio of CD8+ T cell suppressive immune subsets, and IFN-gamma gene signatures, converting weakly immunogenic tumors into highly infiltrated, immunologically active lesions that regress with anti-PD-1 antibody therapy. Here, we present updated summary safety and evidence of systemic immune modulation from our two KEYNOTE trials in TNBC and melanomas.

Methods: Melanomas (KEYNOTE-695) and TNBC (KEYNOTE-890) patients treated every 6 weeks with TAVO plus pembrolizumab; RECIST, Response Evaluation Criteria in Solid Tumors; TAVO™, intratumoral administration of interleukin-12 plasmid followed by electroporation; ER, estrogen receptor; TNBC, triple-negative breast cancer.

Results: 17 patients (TNBCs and melanomas) were assessed including 44 patients with anti-PD-1 antibody-refractory disease who were treated using the TAVO™ regimen. A total of 57 patients (TNBCs and melanomas) were treated every 6 weeks with TAVO plus pembrolizumab; RECIST, Response Evaluation Criteria in Solid Tumors; TAVO™, intratumoral administration of interleukin-12 plasmid followed by electroporation; ER, estrogen receptor; TNBC, triple-negative breast cancer. Grade 3/4 adverse events were reported as ‘unlikely’, ‘possibly’, ‘probably’ or ‘definitely’ related to study drug. Patients were assessed for treatment-related immunological changes in the frequency of CD8+ TIL and other key IL-12-driven proliferative T-cell subsets. Peripheral blood samples were interrogated for treatment-related immunological changes in the frequency of CD8+ TIL and other key IL-12-driven peripheral immune-cell populations.

Conclusion: Updated cumulative safety data demonstrates that TAVO + pembrolizumab is well-tolerated in patients with advanced solid tumors. In multiple tumor settings, peripheral/blood analyses demonstrate both local and most importantly, systemic signals of IL-12-mediated anti-tumor immunity in the absence of systemic IL-12 exposure. Thus, TAVO acts as an in situ vaccine to further potentiate the anti-tumor activity of pembrolizumab with a favorable toxicity profile.

SUMMARY AND CONCLUSIONS

- This interim analysis was limited to pre- and post-treatment matched samples (unless otherwise noted).
- Early analysis of peripheral blood and intratumoral biomarker data reveal that:
  - Increases in intratumoral CD8+ T cells may correlate with improved clinical outcome in multiple solid tumor types.
  - Decreased peripheral PMN-MDSCs may be associated with clinical response, both in melanoma and TNBC patients.
- TAVO + pembrolizumab continues to be well-tolerated in patients with advanced solid tumors.
- Across multiple indications, TAVO acts as an in situ vaccine to potentiate the anti-tumor activity of pembrolizumab.
- Enrollment in both KEYNOTE-695 and -890 is ongoing.

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