Intratumoral delivery of tavokinogene telseplasmid (plasmid IL-12) and electroporation induces local and systemic enhancement of CD8 T cells and sensitizes to anti-PD1 therapy

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**Background**

- Sustained disease control and prolonged survival in patients with TNBC is uncommon, highlighting the need for improved immune-based strategies particularly in poorly immunogenic tumors.
- Interleukin-12 (IL-12) is involved in the generation of innate and adaptive immune responses, an inflammatory tumor microenvironment and is critical in eliciting a productive anti-tumor immune response.
- Intratumoral injection of plasmid IL-12 (tavokinogene telseplasmid; TAVO™) followed by electroporation (EP) (TAVO-EP; collectively designated TAVO) is a gene therapy approach that drives local and immunologically relevant exposure of IL-12 with minimal systemic immune-related toxicity.*

**Methods**

- Murine TNBC (JC-HER3) cells were orthotopically implanted into mice and allowed to establish prior to treatment with TAVO or control plasmid.
- On days 0, 4, and 7, the mice underwent IT administration of plasmid, followed by in vivo electroporation.
- Tumors were digested and CD45+ cells sorted for flow cytometry.
- Flow cytometry for activated T cell populations and MDSCs and IHC summary were harvested on day 14.
- Tumor-bearing mice (n=7 for each group) underwent interventions described in A, and the tumors were measured every other day and shown by Mean ± SEM.

**Results**

- **Figure 2. TAVO Treatment Expands an Effector CD8 T cell Population Both Locally and in Murine TNBC Model**
- **Figure 3. Systemic Response to TAVO in TNBC Patients**
- **Figure 4. TAVO Treatment Enhances Survival of Tumor-Bearing Mice When Combined With Anti-PD1**
- **Figure 5. Clinical Data Demonstrates That TAVO Treatment Converts a Previous ICB Non-Responder**

**Summary & Conclusions**

- TAVO treatment overcomes an immunologically "cold" tumor microenvironment by expanding T cells locally and systemically and by minimizing the infiltration of potentially suppressive granulocytic cells in both preclinical models and TNBC patients.
- There is an increase in expression of PD-1/PD-L1 following TAVO therapy that may sensitize a patient to subsequent checkpoint inhibitor therapy.
- Combined treatment of TAVO and PD-1/PD-L1 blockade enhanced anti-tumor efficacy and prolonged survival in preclinical models of TNBC.
- These data are supportive of ongoing trial OMS-I141 (KEYNOTE-890), a phase 2, multi-cohort, open-label, multicenter study.

- Cohort 1 will be a single-arm study of intratumoral TAVO-EP plus pembrolizumab therapy.
- Cohort 2 will be a single-arm study of intratumoral TAVO-EP plus pembrolizumab with nab-paclitaxel (Abraxane®) chemotherapy.
- Patients with TNBC and EP accessible cutaneous/subcutaneous disease will be enrolled.

**References**


*Abbreviations: BC, breast cancer; EOS, end of study; ICB, immune checkpoint blockade; IHC, immunohistochemistry; IL-12, interleukin-12; IT, intratumoral; PD-1, programmed death-1; PD-L1, programmed death ligand 1; TNBC, triple-negative breast cancer; TAVO, tavokinogene telseplasmid; TAVO™, tavokinogene telseplasmid; MDSC, myeloid-derived suppressor cell.