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• Interleukin-12 (IL-12) is a potent immunoregulatory cytokine that plays a key role in the crosstalk between the innate immune response (dendritic, macrophage, and natural killer cells) and the adaptive immune response (T cells and B cells). Through this activity, IL-12 promotes tumor-immune responses.1

• DNA plasmid-based IL-12, tavoquinogene teleplasmid (TAVO™), delivered to accessible tumors by intratumoral injection and combined with electroporation (TAVO-EP) has been shown to induce activation of innate and adaptive tumor-infiltrating and peripheral immune cells, regression of treated and distant untreated lesions (abscopal effect), and expression of PD-L1 in patients with melanoma or TNBC, without the systemic toxicity that has historically limited therapeutic use of IL-12.2

The combination of TAVO-EP and pembrolizumab has demonstrated durable responses in melanoma patients with immunologically “cold” tumors or with prior progression on anti-programmed cell death protein 1 (anti-PD1) therapy.3

• A phase 1 study demonstrated the safety and tolerability of TAVO-EP in patients with locally advanced or recurrent TNBC cutaneous and subcutaneous tumors.4

• Combining TAVO-EP with an anti-PD-1 antibody, such as pembrolizumab, is thought to further improve responses in patients with mTNBC by converting poorly-immunogenic/low TIL tumors into immune-responsive/high TIL tumors.

• KEYNOTE-890/OMS-I141 is a phase 2, open-label, multicenter study.

• Patients in Cohort 2 will receive the following treatments:
  - TAVO-EP: days 1, 5, and 8, every 6 weeks, for up to 18 cycles.
  - TAVO dose is 0.5 mg/mL at dose volume of ~1/4 lesion volume, injected intratumorally.
  - Pembrolizumab: 200 mg IV, every 3 weeks, for up to 35 cycles.
  - Nab-paclitaxel: 100 mg/m² IV on days 1, 8, and 15 every 4 weeks, for up to 25 cycles.

• ORR by blinded independent central review (BICR) based on RECIST v1.1

• The planned sample size of Cohort 2 is 40 patients and is based on the ability to determine statistically significant and clinically meaningful improvement in PFS and OS vs chemotherapy alone for the treatment of 1st-line PD-L1 positive mTNBC.6

• Imaging for tumor assessment will be completed every 12 weeks.

Mechanism of Action of TAVO-EP

• IL-12 is a potent proinflammatory cytokine with the following antitumor mechanisms:
  - Increasing MHC I antigen presentation
  - Attracting additional TNF, TNF-α, and CD8+ T cells into TNBC
  - Reversing tumor-induced immunosuppression

Clinical translation of IL-12 immunotherapies experienced setbacks in 1990s-2000s due to severe toxicities associated with systemic IL-12 injections. Intratumoral delivery of plasmid IL-12 (TAVO) followed by electroporation yields sustained expression of IL-12 and stimulates a systemic proinflammatory immune response, without systemic immune-related toxicities.

References

7. Phillips Gilmore Oncology Communications Inc, for professional assistance with poster preparation.

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