TPS2687 Poster Session

# Phase 2 dose expansion of START-001: A phase 1/2 study of invikafusp alfa (STAR0602), a first-in-class, selective T cell receptor (TCR)-targeting, bifunctional antibody-fusion molecule, as monotherapy in patients with antigen-rich tumors resistant to anti-PD(L)-1.

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**Background:** Many patients do not respond to anti-PD(L)-1-based therapies and most responders eventually develop resistance. Thus, the development of effective therapies for anti-PD(L)-1 resistance is a significant unmet medical need. Invikafusp, a selective, dual T cell agonist targeting Vβ6/Vβ10 T cells, is being evaluated in START-001: a multicenter Phase 1/2 monotherapy trial in patients with anti-PD(L)1-resistant, antigen-rich (TMB-H, MSI-H/dMMR, or virally associated) solid tumors. The completed Phase 1 dose escalation of intravenous invikafusp, Q2W, per 3+3 design, identified a recommended Phase 2 dose (RP2D) of 0.08 mg/kg, and demonstrated clinically meaningful single-agent anti-tumor activity in patients with anti-PD(L)-1 resistant tumors, including confirmed partial responses in TMB-H, microsatellite stable, colorectal cancer (CRC) patients with one durable response lasting ~12 months. It promoted potent and selective expansion of mainly CD8+ Vβ6/ Vβ10 T cells with a novel central memory T cell phenotype, and led to ctDNA decrease and expansion of antigen-specific T cells. Based on these results, the US FDA granted Fast Track Designation for invikafusp in TMB-H CRC. **Methods:** Study design: Using an optimal Simon's 2 stage design, Phase 2 of START-001 is a dose expansion at the RP2D, to further investigate the safety and anti-tumor activity of invikafusp in 9 cohorts of patients who have the following solid tumors: 1) tissue-agnostic, TMB-H; 2) tissue-agnostic, dMMR/MSI-H; 3) CRC (both Ras wild-type and mutant) TMB-H and/or MSI-H/dMMR); 4) virally associated tumors such as Merkel cell carcinoma, cervical, oropharyngeal, anal, penile, vaginal, and vulvar cancers, or EBV-related solid tumors; 5) metastatic triple-negative breast cancer; 6) platinum-resistant epithelial ovarian cancer; 7) metastatic castration-resistant prostate cancer; 8) primary stage IV or recurrent non-small cell lung cancer; and 9) immunogenic tumors (e.g., cSCC, melanoma and RCC). Major Eligibility criteria: ≤ 3 lines of prior cancer therapies [anti-PD(L)-1s allowed] for advanced or metastatic disease; intolerance to standard therapies including anti-PD(L)-1s allowed; no liver metastases or adequately treated liver metastases either locally (e.g., by surgery, radiofrequency ablation, or chemoembolization) or systemically and stable for 3 months. Primary objective: to further evaluate anti-tumor activity of invikafusp as monotherapy in each of the above-described 9 cohorts of patients with anti-PD(L)-1-resistant, unresectable, locally advanced, or metastatic solid tumors. Primary endpoint: overall response rate (ORR) per iRECIST. The enrollment to the first three cohorts has begun. Clinical trial information: NCT05592626. Research Sponsor: Marengo Therapeutics, Inc.