TPS2670 **Poster Session**

A phase 1/2a, multicenter, first-in-human, open-label clinical trial evaluating MDX2001, a tetraspecific T cell engager-expander in patients with advanced solid tumors.

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Background: MDX2001 is a multispecific antibody recognizing CD3 and CD28 on T cells, and c-MET and TROP2 on tumors. Anti-CD3 provides the primary signal for T cell activation; anti-CD28 delivers the secondary signal for enhanced T cell activation, survival, and proliferation. Combinatorial targeting of c-MET and TROP2 by MDX2001, either on the same or different cancer cells, provides more effective engagement on tumor cells, and may better address tumor heterogenicity and the development of resistance due to antigen downregulation. *In vitro* and *in vivo* studies with MDX2001 demonstrate potent antitumor activity with no CD28-superagonist activity and minimal T cell activation in the absence of tumor cells. **Methods:** This Phase 1/2a, multicenter, first-in-human, open-label clinical trial explores intravenous MDX2001 in patients with advanced solid tumors (NCT06239194). The study design consists of Phase 1a dose escalation guided by a Bayesian Optimal Interval design with a target maximum tolerated dose toxicity rate of 30%, Phase 1b dose expansion, and Phase 2a indication expansion. Patients with non-small cell lung, renal cell, prostate, breast cancer and 10 other selected tumors known to have significant levels of TROP2 or c-MET expression are eligible for Phase 1a. In Phase 1b, patients will be randomized into 2 dose cohorts using a Bayesian Optimal Phase 2 (BOP2) design. Once a recommended Phase 2 dose (RP2D) is determined, Phase 2a will enroll patients in search of initial efficacy signals using a BOP2 design. The primary objectives of this study are to characterize the safety, tolerability, and anti-tumor activity of MDX2001 in patients with advanced solid tumors. Secondary endpoints include time to response, disease control rate, duration of response, pharmacokinetics, immunogenicity and evaluation of the relationship between baseline tumor target protein expression and clinical benefit. Patients will have radiologic tumor assessments every 8 weeks and will continue to receive treatment until disease progression per RECIST v1.1 (as assessed by the investigator), unacceptable toxicity, withdrawal of consent, another protocol-defined discontinuation criterion is met, or the sponsor terminates the study, whichever occurs first. The study will be conducted in United States, Europe, and Asia. Recruitment is ongoing. Clinical trial information: NCT06239194. Research Sponsor: None.