Abstract TPS2670: 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 TUMOR (NCT06239194)

BACKGROUND

MDX2001 is a multispecific antibody recognizing CD3 and CD28 on T cells, and c-MET and TROP2 on tumor cells. 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, can **provide more effective engagement on tumor cells,** and may better address **tumor heterogenicity** and the development of retreatment **resistance** due to antigen downregulation. Preclinical studies with MDX2001 (Figures 1 and 2) demonstrate potent antitumor activity with no CD28-superagonist activity and minimal T cell activation in the absence of tumor cells [1].

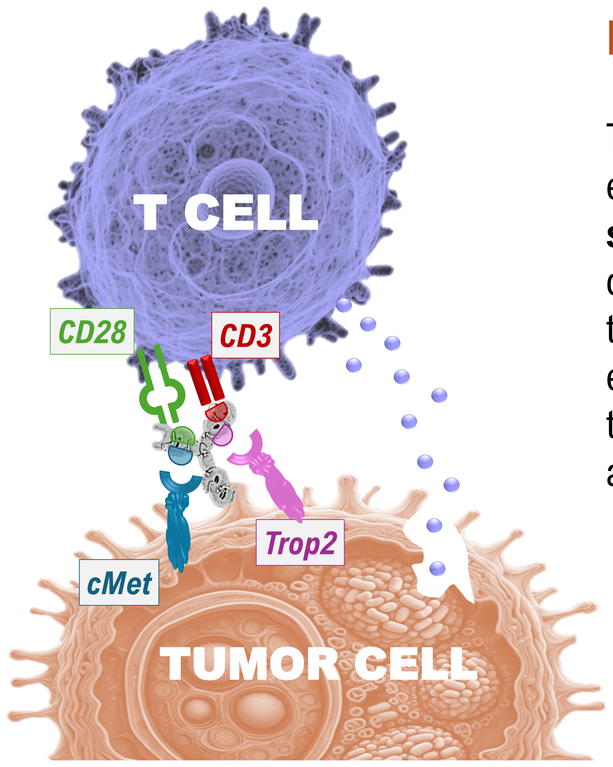


Figure 1. MDX2001 induces potent T cell activation in the presence of target tumor cells

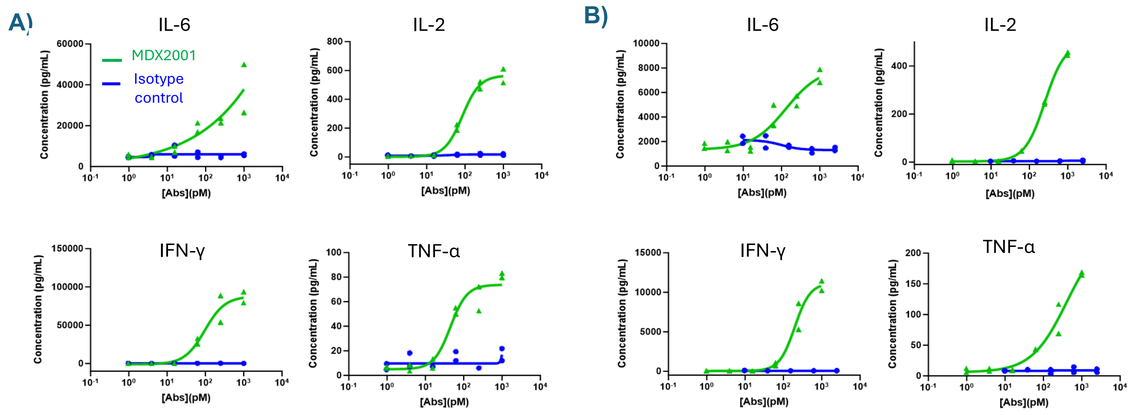


Figure 1. Human PBMC were co-cultured with a non-small cell lung carcinoma cell line H1975 (A) or a triple-negative breast cancer cell line HCC1143 (B) tumor cell lines in the presence of MDX2001 (green lines) or isotype control (blue lines). Cytokine concentrations in the supernatants were measured using Luminex-based multiplex assay.

Figure 2. MDX2001 triggers robust *in vitro* tumor cytolytic activity when added to co-cultures of PBMCs and tumor cells

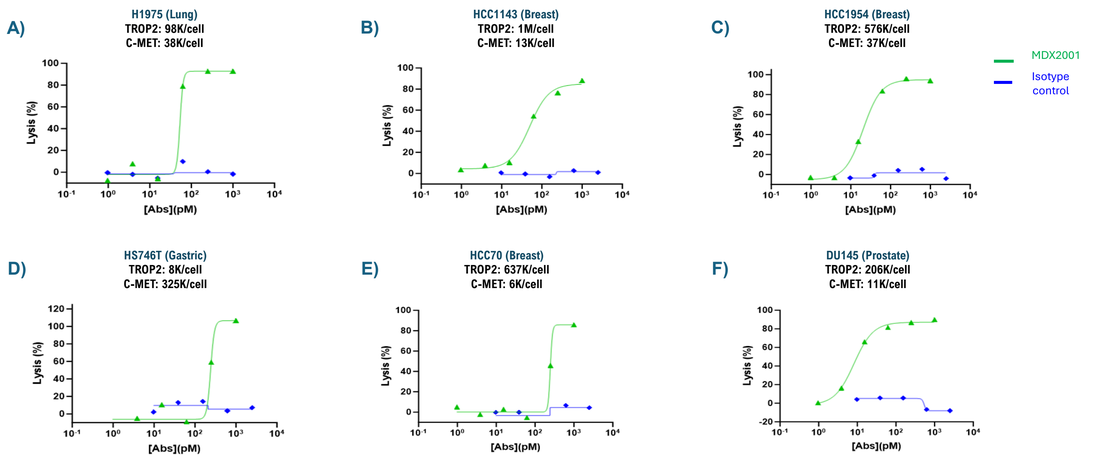
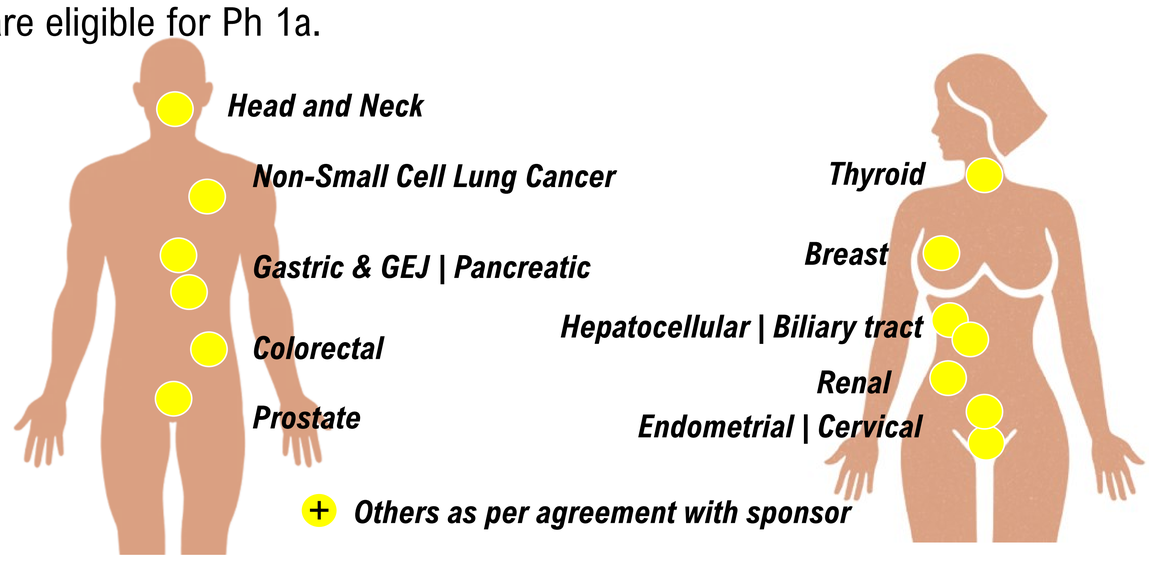


Figure 2. Human PBMC were co-cultured with H1975 (A), HCC1143 (B), HCC1954 (C), Hs746T (D), HCC70 (E), DU145 (F) tumor cell lines in the presence of MDX2001 (green lines) or isotype control (blue lines). Expression of TROP2 and c-MET (molecules per cell) indicated on the top of each graph.

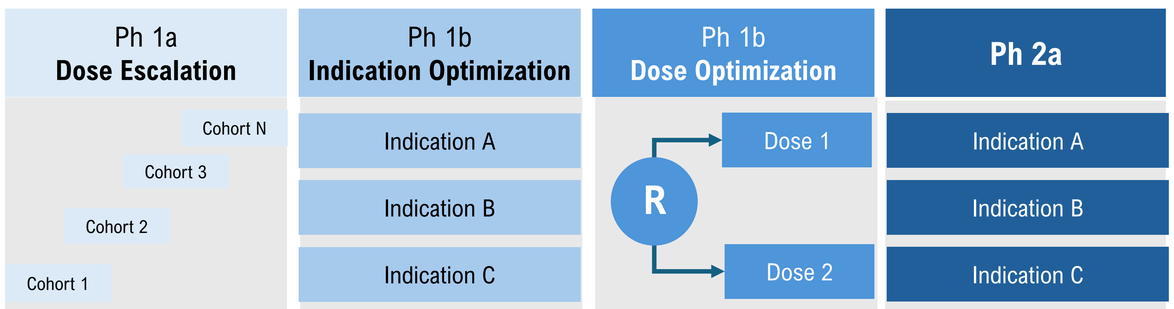
METHODS

This Phase 1/2a, multicenter, **first-in-human**, open-label clinical trial explores intravenous dosing of **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 selected tumors known to have significant levels of TROP2 or c-MET expression are eligible for Ph 1a.



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.

CLINICAL TRIAL SCHEMA



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.

1. Ling Xu et al. Beyond bispecifics: MDX2001, a novel tetraspecific antibody targeting T lymphocyte activation and survival enhancing receptors (LASER) directed to TROP2 and C-MET in solid tumor malignancies. Presented at SITC, November 2024, Abstract 1287.

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