A phase 1/2a, multicenter, first-in-human, open-label clinical trial evaluating monotherapy with MDX2004, a trispecific antibody-fusion protein in patients with advanced tumors

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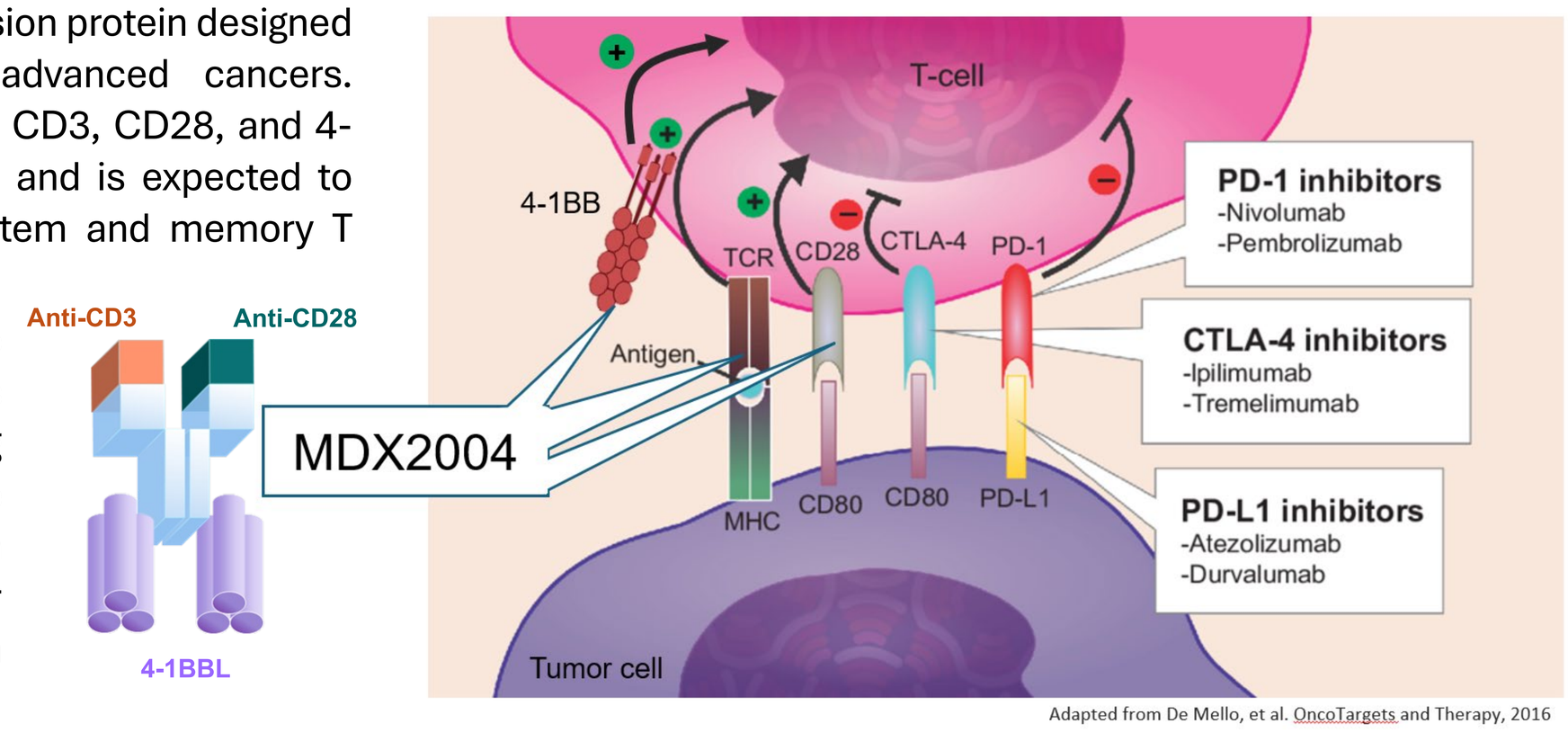
Background

MDX2004 is a trispecific antibody-fusion protein designed as an immunotherapy to treat advanced cancers. MDX2004 stimulates T cells through CD3, CD28, and 4-1BB, to enhance immune activation and is expected to activate T lymphocytes, including stem and memory T cells (Figure 1 and 2)[1].

Collectively, both in vitro and in vivo data demonstrate that MDX2004 is effective in activating T cells resulting in tumor cell killing (Figure 3). The efficacy of MDX2004 was tested in vivo in humanized mouse tumor models and demonstrated efficacy in tumor growth inhibition.



Adapted from De Mello, et al. OncoTargets and Therapy, 2016

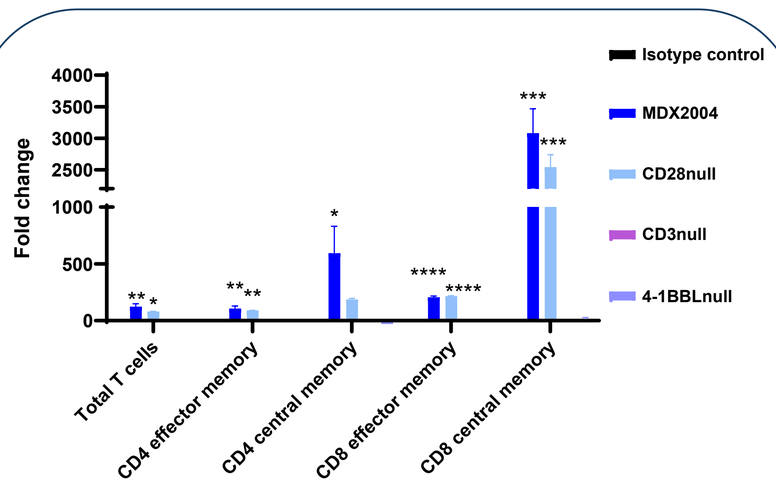


Figure 1. MDX2004 Expands Memory T cells, especially CD8

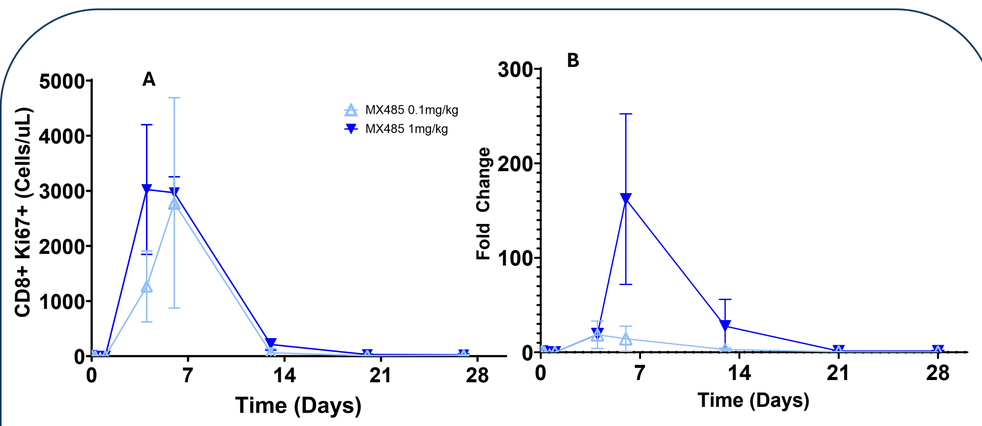


Figure 2. In Vivo Increase in CD8 T cell Proliferation (A) and Memory T cells (B) in NHP Treated with MDX2004 Surrogate

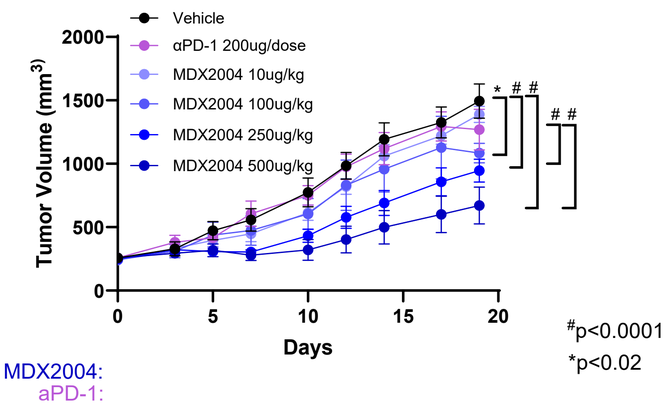
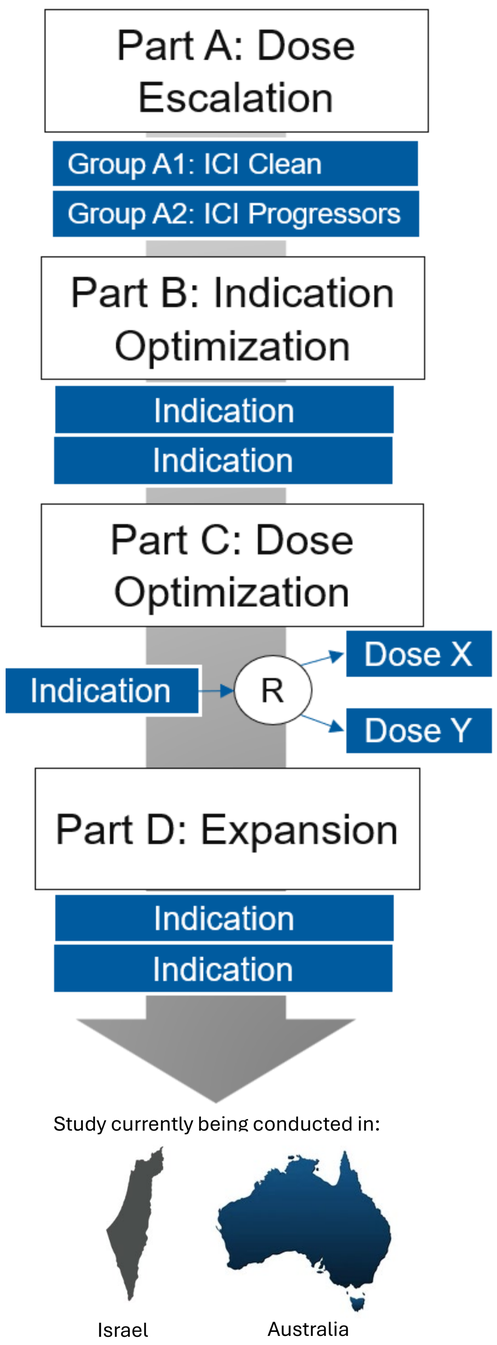


Figure 3. MDX2004 Inhibits Tumor Growth in Humanized Mouse Models

MDX-2004-101 Study Design



Key Inclusion Criteria

- For Part A - Group A1 only: Participant is naïve to ICI therapy or has received an ICI alone or in combination >16 weeks prior to Cycle 1 Day 1 dosing (ICI clean).
- For Part A - Group A2 only: Participant has achieved SD or better (or lack of disease progression) for at least 16 weeks while on treatment with an ICI alone or in combination then subsequently progressed (ICI progressors). The last dose of ICI must have occurred <16 weeks prior to Cycle 1 Day 1 dosing.
- Capable of giving signed informed consent
- Patients must be ≥ 18 years of age
- Histologically or cytologically confirmed diagnosis of metastatic solid tumors
- Eastern Cooperative Oncology Group (ECOG) performance status 0-1
- All patients should have at least 1 measurable disease per RECIST v1.1. Adequate hematologic, hepatic and renal function and appropriate contraceptive use for clinical trial participation.
- Adequate organ function
- Undergo adequate washout period

Key Exclusion Criteria

- Participant had a previous immune-related Grade 3 or 4 AE that led to discontinuation of treatment of immuno-oncology agents within 6 months of Cycle 1 Day 1.
- Unresolved toxicities from previous anticancer therapy
- Known untreated, active, or uncontrolled brain metastases
- Any clinically significant cardiac disease
- Prior solid organ or hematologic transplant
- Known positivity with human immunodeficiency virus (HIV), known active hepatitis B or C, or uncontrolled chronic or ongoing infectious requiring intravenous treatment.
- Receipt of a live-virus vaccination within 28 days of planned treatment start
- Participation in a concurrent clinical study in the treatment period.
- Known hypersensitivity to MDX2004 or any of its ingredients

Study Objectives

Primary

- Safety and tolerability in participants with advanced solid tumor malignancies
- Part A only: Identify a maximum tolerated dose or recommended dose for further development
- Part B, C and D: Assess the anti-tumor efficacy in participants with advanced solid tumor malignancies

Secondary

- Characterize the pharmacodynamics of MDX2004
- Characterize the pharmacokinetics of MDX2004
- Characterize the immunogenicity of MDX2004
- Further characterize anti-tumor efficacy and clinical benefit

Exploratory

- Evaluate potential biomarkers in blood and tumors pre- and post-treatment that may predict or correlate with response to MDX2001

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1. Seung, E et al. MDX2004, a novel immune rejuvenator targeting CD3, CD28 and 4-1BB, augments tumor immunity in preclinical animal models. Presented at SITC, November 2025, Abstract 1156.

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