MDX-124, a novel annexin-A1 antibody, shows significant multi-faceted activity in preclinical models of various clinically challenging cancers

Abstract #5294

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BACKGROUND

Annexin-A1 (ANXA1) is secreted from both cancer and immune cells in response to several physiological stimuli and modulates cellular functions through interactions with formyl peptide receptors (FPR1/2). Overexpression of ANXA1 has been observed in multiple cancer indications and often correlates with decreased overall survival[1-2]. ANXA1 has also been shown to promote cancer cell proliferation[3], angiogenesis[4], migration[5] and drug resistance[6], and to regulate the tumor microenvironment[7]. MDX-124 is a novel humanized antibody targeting ANXA1 and previously we have presented data demonstrating its significant anti-proliferative activity. Here we provide further confirmatory data on the mechanism of action of MDX-124, notably its impact on tumor growth, cell cycle arrest and migration in several preclinical cancer models.

METHODS

Cell Cycle Analysis: BxPC-3, A549 and MDA-MB-231 cells ($1x10^6$) incubated for 24 h with MDX-124 (10 and 25 µM). Cells were harvested and labeled with Cytophase violet dye (8 µM) before incubation at 37°C for 30 min. Flow cytometry was conducted using a CytoFLEX LX (Beckman Coulter) and analyzed with FlowJo™ (BD Life Sciences) to quantify the percentage of cells in each cell cycle phase (G1, S and G2). Statistical significance was calculated using a 2-way ANOVA with Tukey's multiple comparison correction (GraphPad Prism 9).

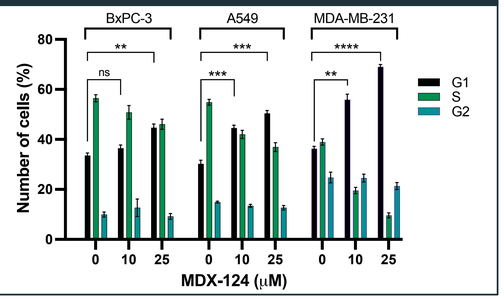
Migration: A panel of cancer cell lines ($1x10^6$ cells) were pre-treated with MDX-124 (0 µM – 50 µM) for 1 h and transferred into 8 µm pore transwell plates for 24 h incubation. Migrated and non-migrated cells were harvested and counted using flow cytometry (CytoFLEX LX). Statistical significance was calculated using a 2-way ANOVA with Tukey's multiple comparison correction (GraphPad Prism 9).

Proteomic Analysis: MDA-MB-231 cells ($5x10^6$) incubated with MDX-124 (10 µM) for 72 h. Cell lysates were obtained with levels of cancer-related proteins versus untreated control cells determined using a Proteome Profiler™ human oncology XL array kit as per manufacturer's instructions (R&D Systems).

***In-vivo* Efficacy Study:** FVB mice were inoculated via intracardiac injection with $4x10^5$ MycCap-Bo prostate cancer cells (n = 6-10 tumors). Mice randomized to treatment groups after 7 days and treated via i.p injection with isotype control (IgG2b) or a murine analog of MDX-124 (MDX-001) at 10 mg/kg, BIW for 14 days. Tumor growth was evaluated using bioluminescent imaging (BLI). Statistical significance was calculated at day 14 using an unpaired t-test (GraphPad Prism 9).

RESULTS

Figure 1. Incubation of MDX-124 with pancreatic (BxPC-3), lung (A549) or triple-negative breast (MDA-MB-231) cancer cells significantly decreased the proportion of cells in S-phase and increased the frequency of G1 phase versus untreated controls in a dose-dependent manner (ns = not significant, **p<0.01, ***p<0.001 and ****p<0.0001).



KEY FINDINGS

In several preclinical models of cancer MDX-124:

- **Significantly inhibited cancer cell proliferation via cell cycle arrest**
- **Significantly decreased cancer cell migration**
- **Reduced the expression of several key proteins involved in cancer cell migration, invasion and metastasis**
- **Significantly decreased prostate tumor growth *in-vivo* by 52%**

Medannex will generate initial clinical data in 2022 from a First-in-Human study evaluating MDX-124 in patients with locally advanced, unresectable or metastatic solid malignancies.

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RESULTS (Continued)

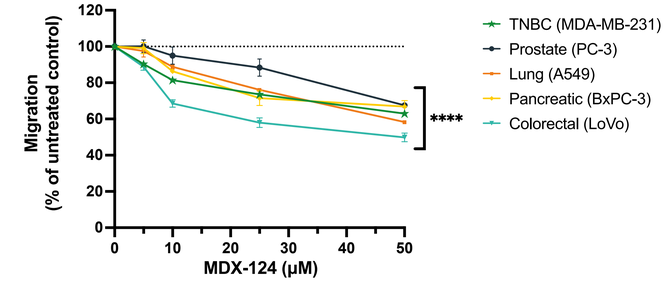

Figure 2. MDX-124 significantly decreased cancer cell migration in a panel of cancer cell lines versus untreated control cells (****p<0.0001 MDX-124 versus untreated control).

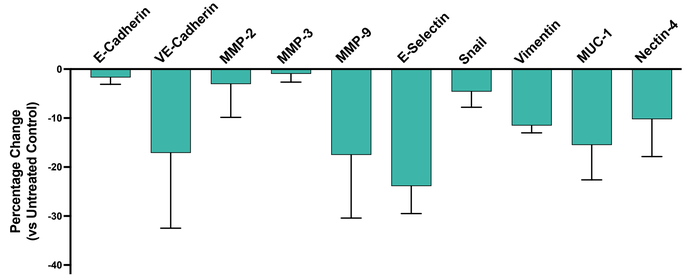

Figure 3. In MDA-MB-231 cells MDX-124 reduced the expression of several proteins involved in cancer cell migration, invasion and metastasis.

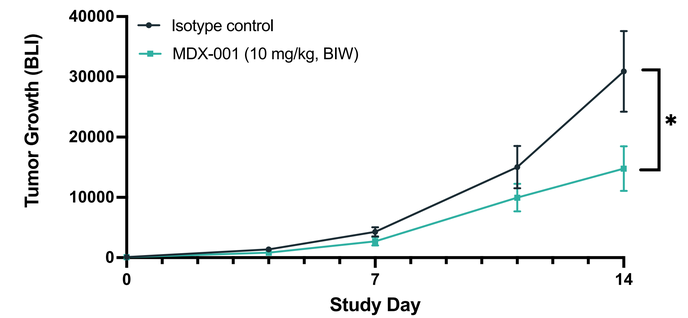

Figure 4. The murine analog of MDX-124 (MDX-001) significantly decreased MycCap-Bo prostate tumor growth versus mice treated with an isotype control (*p<0.05).

References:

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Presented at the American Association for Cancer Research (AACR) Annual Meeting. April 8–13, 2022