MDX-124, a first-in-class annexin-A1 targeting antibody, in patients with locally advanced or metastatic solid malignancies: Data supporting RP2D from the dose escalation stage of a first-in-human phase Ib trial

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☑ KEY FINDINGS

- Preliminary data indicate good safety, tolerability, and anti-tumour activity. The RP2D for MDX-124 monotherapy was determined to be 20 mg/kg Q2W.
- Disease control rate of **60%** in evaluable participants at data cut-off with 1 confirmed partial response.
- **No** grade ≥3 treatment-related adverse events or dose limiting toxicities observed.
- Module 2 evaluating MDX-124 as monotherapy and in combination with standard of care therapies across selected tumour types is currently enrolling. Clinical trial information: ISRCTN78740398.

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BACKGROUND

Annexin-A1 released by tumour and immune cells under diverse stimuli engages formyl-peptide receptors (FPR1/2) to rewire cell behaviour - fuelling tumour growth[1], angiogenesis[2], migration[3], and drug resistance[4] while reshaping the tumour microenvironment[5]. Annexin-A1 overexpression correlates with poor prognosis in various malignancies[6-7], making it a novel target for anti-cancer therapy. MDX-124 is a first-in-class humanised IgG1 monoclonal antibody that specifically targets annexin-A1[8]. MDX-124 targets secreted forms of annexin-A1, blocking their interaction with FPR1/2 which inhibits tumour growth, reduces metastasis and induces ADCC activity[9-11] (Figure 1). Additionally, MDX-124 has demonstrated synergistic activity when combined with other anti-cancer therapies[10,12]. Here we report preliminary data from a first-in-human phase I study of MDX-124 in advanced or metastatic solid malignancies.

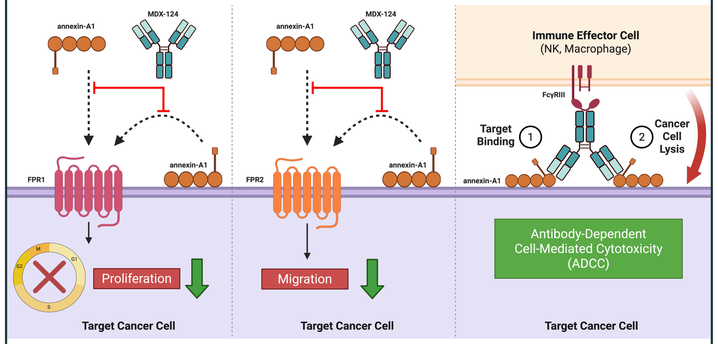

Figure 1. Mechanism of action of MDX-124.

STUDY DESIGN

This modular, multi-arm phase 1b dose escalation study of MDX-124 enrolled adult patients with solid tumours likely to overexpress annexin-A1 (Figure 2). Module 1 was a monotherapy dose escalation using a Bayesian Optimal Interval design. MDX-124 was administered Q2W at doses ranging from 1–30 mg/kg, with a 21-day DLT period. The primary objective was to determine the recommended phase 2 dose (RP2D) of MDX-124. Secondary objectives were to evaluate safety, tolerability, pharmacokinetics, and preliminary anti-tumour activity. Responses were evaluated according to RECIST v1.1. Adverse events were graded using CTCAE v5.0. Tumour and immunological biomarkers were exploratory endpoints. Module 2 is assessing MDX-124 as monotherapy and in combination with standard of care therapies in indication-specific arms.

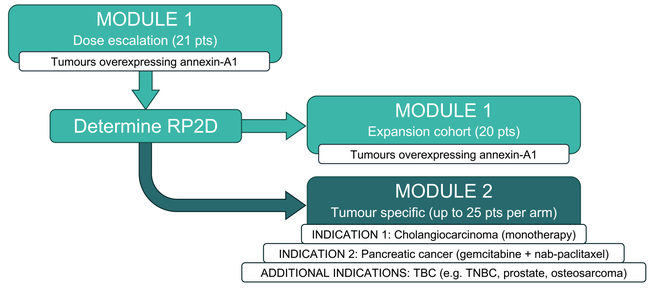

Figure 2. Study schema for the ATTAINMENT trial.

NEXT STEPS

Module 2 has been initiated and is currently enrolling. This will assess safety, tolerability and signs of efficacy of MDX-124 as monotherapy and in combination with standard of care therapies across selected tumour types:

Arm 1 (Pancreatic Cancer)

- Combination with gemcitabine / nab-paclitaxel in 1st line population
- Selected based on non-clinical data and preliminary efficacy data observed in Module 1
- Enrolment to commence Q4 2026

Arm 2 (Biliary Tract Cancer)

- Cholangiocarcinoma and gallbladder as monotherapy in 2nd line population
- Selected based on disease control rate (3/4 evaluable patients) observed in Module 1
- Enrolment commenced Q1 2026

RESULTS

Participant Characteristics

Table 1. Demographic and baseline characteristics.

Number of participants (male:female)	21 (11:10)
Median age (range)	60 (28-80)
Median prior treatment regimens (range)	3 (1-9)
Primary cancer types	10

Safety Summary

- Treatment related adverse events (TRAE) observed in 57% of participants (n = 21) at data cut-off with fatigue and nausea being most common (Table 2)

Table 2. Summary of TRAEs observed in ≥10% of patients.

TRAE	Grade 1-2 (%)	Grade ≥3 (%)
Fatigue	7 (33%)	0
Nausea	7 (33%)	0
Diarrhoea	4 (19%)	0
Vomiting	3 (14%)	0
ALP increase	3 (14%)	0
Peripheral oedema	3 (14%)	0
Anaemia	2 (10%)	0
Anorexia	2 (10%)	0
AST increase	2 (10%)	0

Participant Case Study

Background and Treatment History

- Male, 52 years old
- Cholangiocarcinoma (liver and lymph node metastasis)
- Prior lines of treatment include gemcitabine + cisplatin (neoadjuvant), capecitabine and radiotherapy

Dosing and Clinical Activity

- ✓ Started on 28th February 2024 and remained on study for ~12 months receiving 10 mg/kg (19 cycles)
- ✓ **Confirmed partial response** achieved with MDX-124 monotherapy
- ✓ **36% reduction in target lesions** observed (Figure 3)
- ✓ **No** grade ≥3 TRAEs observed during time on study

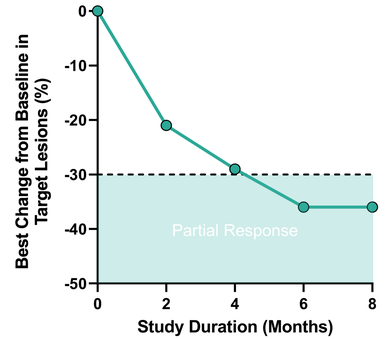

Figure 3. Best change of target lesion size from baseline in participant receiving MDX-124 monotherapy over 8-month period.

Anti-Tumour Activity

- Overall disease control rate of 48% (10/21) with 60% (9/15) in evaluable participants at cut-off (26th September 2026) (Figure 4)
  - 1 confirmed partial response (cholangiocarcinoma), 8 stable disease and 1 non-CR/non-PD observed out of 21 participants
  - Evaluable participants are defined as receiving 4 cycles (8 weeks) of MDX-124 and a post-baseline CT scan

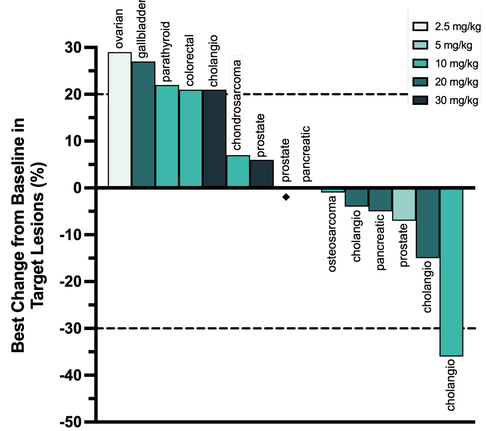

Figure 4. Best change of target lesion size from baseline in evaluable participants receiving MDX-124 monotherapy (n = 15). ◆ Participant evaluable, but not measurable per RECIST.

Pharmacokinetics

- Dose proportional increase in serum concentration of MDX-124 observed across 1-30 mg/kg cohorts (n = 21 patients) (Figure 5)
- Pharmacokinetic data show accumulation of MDX-124 at cycle 4 (data not presented) suggesting less frequent scheduling can be investigated in Module 1 expansion cohort (e.g. Q3W)

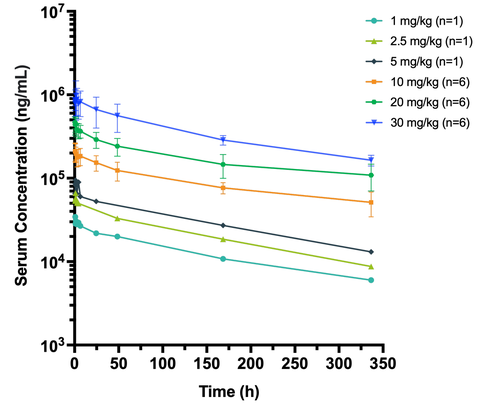

Figure 5. Pharmacokinetic profile of MDX-124 in serum obtained during cycle 1 from all dose cohorts (1-30 mg/kg).

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