MDX-124, a first-in-class annexin-A1 targeting antibody, in patients with locally advanced or metastatic solid malignancies: Preliminary safety and activity from a first-in-human phase I trial

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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.

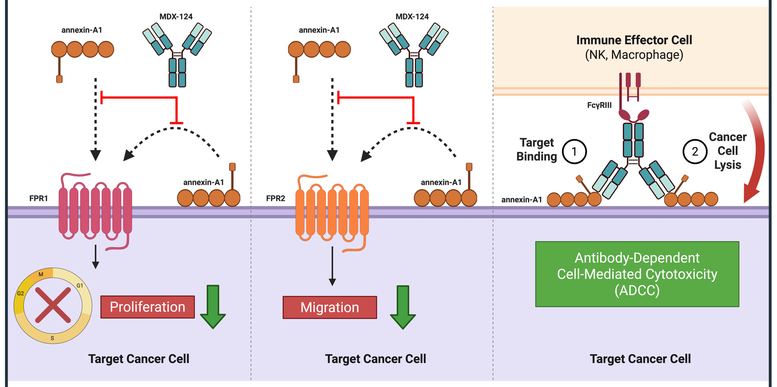

Figure 1. Mechanism of action of MDX-124.

METHODS

This modular, multi-arm phase 1 dose escalation study of MDX-124 is enrolling adult patients with solid tumours likely to overexpress annexin-A1 (Figure 2). Module 1 is a single agent dose escalation using a BOIN design with an expansion cohort. Module 2 will assess MDX-124 as monotherapy and in combination with standard of care therapies in indication-specific arms. MDX-124 is administered Q2W at doses ranging from 1–30 mg/kg, with a 21-day DLT period. The primary objective is to determine the RP2D of MDX-124 as monotherapy and in combination. Secondary objectives include safety, tolerability, pharmacokinetics and anti-tumour activity. Efficacy is assessed per RECIST v1.1 and adverse events are graded according to CTCAE v5.0. Tumour and immunological biomarkers are exploratory endpoints.

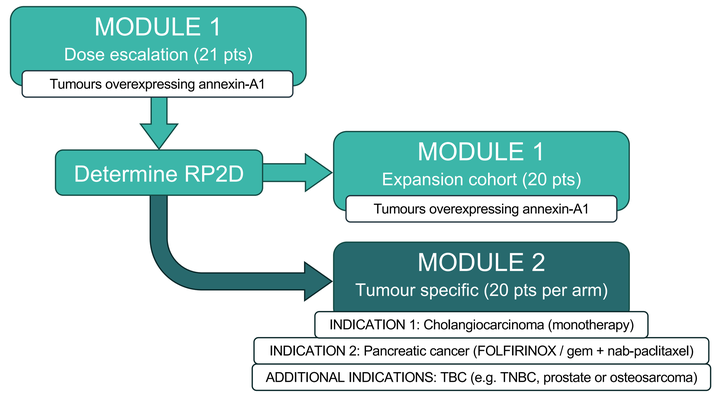

Figure 2. Study schema for the ATTAINMENT trial.

☑ KEY FINDINGS

- Preliminary data indicate very encouraging safety, tolerability, and anti-tumour activity of MDX-124, at doses up to and including 30 mg/kg Q2W.
- Disease control rate in evaluable patients of **55%** at data cut-off with 1 confirmed partial response.
- **No** grade 3–4 treatment-related adverse events or dose limiting toxicities observed to date.
- Module 2 evaluating MDX-124 as monotherapy and in combination with standard of care therapies across selected tumour types will begin enrolment in Q4 2025. Clinical trial information: ISRCTN78740398.

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RESULTS

Participant Characteristics

Table 1. Demographic and baseline characteristics

Number of patients	21
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 62% of patients (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 (13%)	0
ALP increase	3 (14%)	0
Peripheral oedema	3 (14%)	0
Anaemia	2 (10%)	0
Anorexia	2 (10%)	0
AST increase	2 (10%)	0

Anti-Tumour Activity

- Overall disease control rate of 35% (6/17, CT scan results pending for 4 patients), with 55% (6/11) in evaluable patients at data cut-off (Figure 3)
  - 1 confirmed partial response (cholangiocarcinoma), 4 stable disease and 1 non-CR / non-PD
  - Evaluable patients are defined as receiving 4 cycles of MDX-124 and a post-baseline CT scan

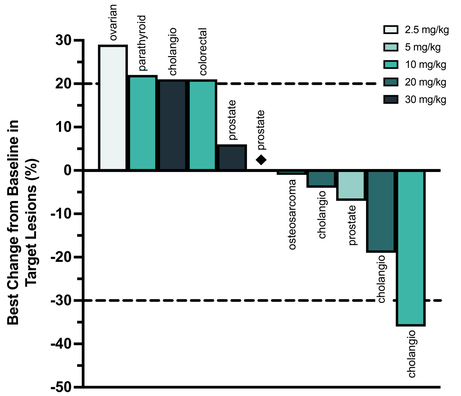

Figure 3. Best change of target lesion size from baseline in evaluable patients receiving MDX-124 monotherapy (n = 11). ◆ Patient evaluable, but not measurable per RECIST.

Pharmacokinetics

- Dose proportional increase in serum concentration of MDX-124 observed across 1-30 mg/kg cohorts (n = 17 patients) (Figure 4)
- PK data show accumulation of MDX-124 at cycle 4 suggesting less frequent scheduling should be investigated in Module 1 expansion cohort (e.g. Q3W)

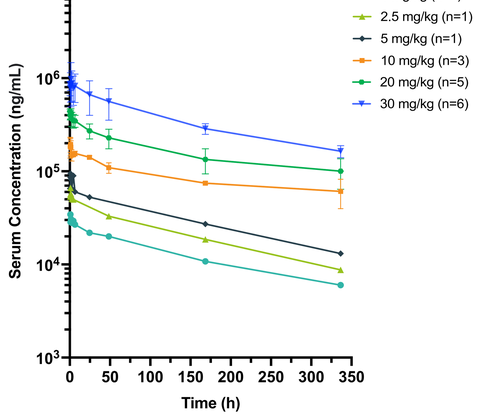

Figure 4. Pharmacokinetic profile of MDX-124 in serum obtained during cycle 1 from all dose cohorts (1-30 mg/kg).

Patient 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 lesion size** observed (Figure 5)
- ✓ **No** DLTs or treatment related SAEs observed to date

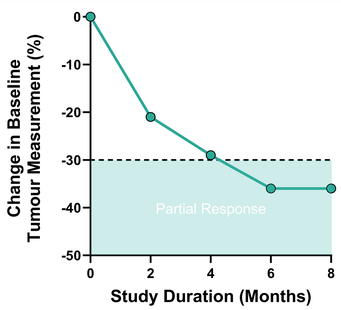

Figure 5. Change in size of target lesions.

Next Steps

Module 1

- RP2D will be determined in Q4 2025
- Expansion cohort to further evaluate dosing and scheduling to be initiated

Module 2

- Cholangiocarcinoma monotherapy arm in 2nd line population selected based on disease control rate (3/4 pts) observed to date (Figure 6)
- Pancreatic cancer arm in combination with FOLFIRINOX and/or gem + nab-paclitaxel as 1st line
- Enrolment to commence Q4 2025

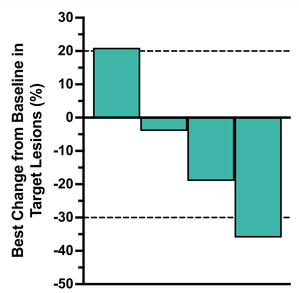

Figure 6. Best change in target lesions of evaluable cholangiocarcinoma patients.

References

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