

ATTAINMENT: A modular phase Ib trial of MDX-124, a first-in-class annexin-A1 targeting antibody in patients with advanced solid tumours including cholangiocarcinoma

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KEY FINDINGS

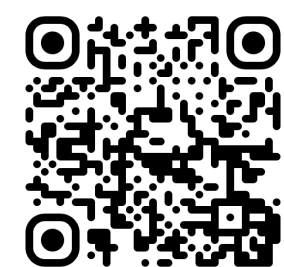
- Preliminary data indicate very encouraging safety, tolerability, and anti-tumour activity of MDX-124, at doses up to and including 30 mg/kg Q2W.
- Disease control rate in evaluable cholangiocarcinoma patients of **75%** with 1 confirmed partial response.
- No** grade 3–4 treatment-related adverse events or dose limiting toxicities observed to date.
- Module 2 evaluating MDX-124 as monotherapy in cholangiocarcinoma patients 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 tumor growth¹, angiogenesis², migration³, and drug resistance⁴ while reshaping the tumour microenvironment⁵. 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-A1⁸ to inhibit tumour growth, reduce metastasis and induce ADCC activity^{9–11} (Figure 1).

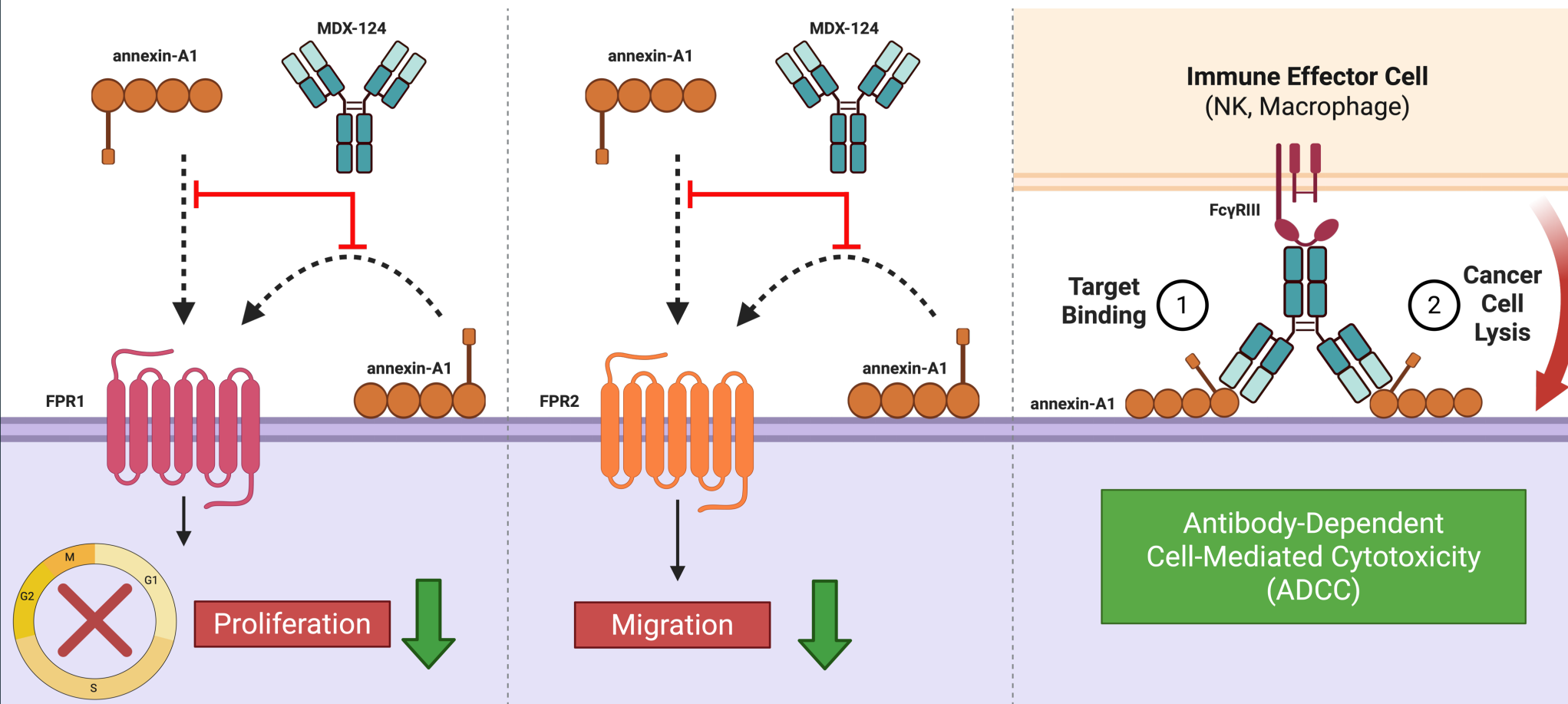


Figure 1. Mechanism of action of MDX-124.

METHODS

This modular, multi-arm phase 1b study of MDX-124 is enrolling adult patients with advanced 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 is assessing 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. Primary objectives are to determine the RP2D of MDX-124 (module 1) and safety as monotherapy or in combination (module 2). Secondary objectives include safety, PK 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.

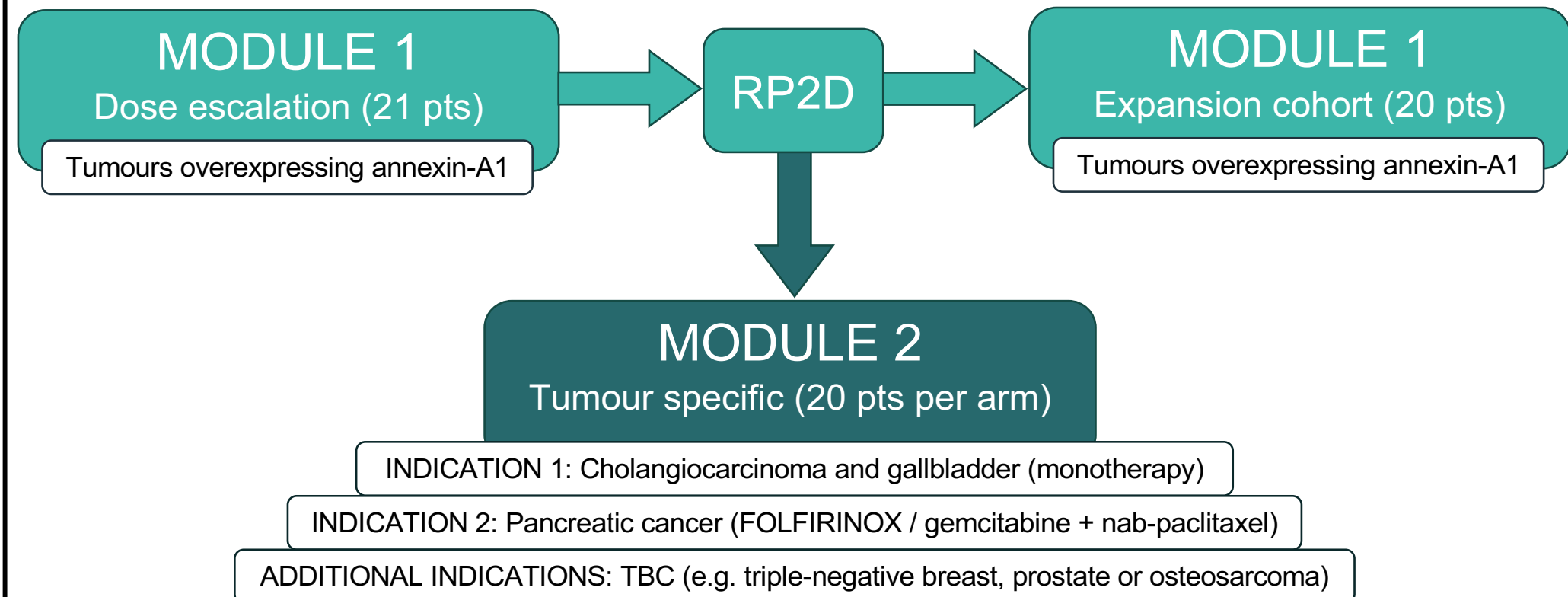


Figure 2. Study schema for the ATTAINMENT trial.

RESULTS (MODULE 1 DOSE ESCALATION)

Participant Characteristics

Table 1. Demographics and baseline characteristics

Number of patients	21
Median age (years) (range)	60 (28–80)
Median prior treatment regimens (range)	3 (1–9)
Primary cancer types*	10

* Prostate, ovarian, parathyroid, cholangiocarcinoma, colorectal, ampullary, pancreatic, osteosarcoma, gallbladder and chondrosarcoma

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 edema	3 (14%)	0
Anaemia	2 (10%)	0
Anorexia	2 (10%)	0
AST increase	2 (10%)	0

Anti-Tumor 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

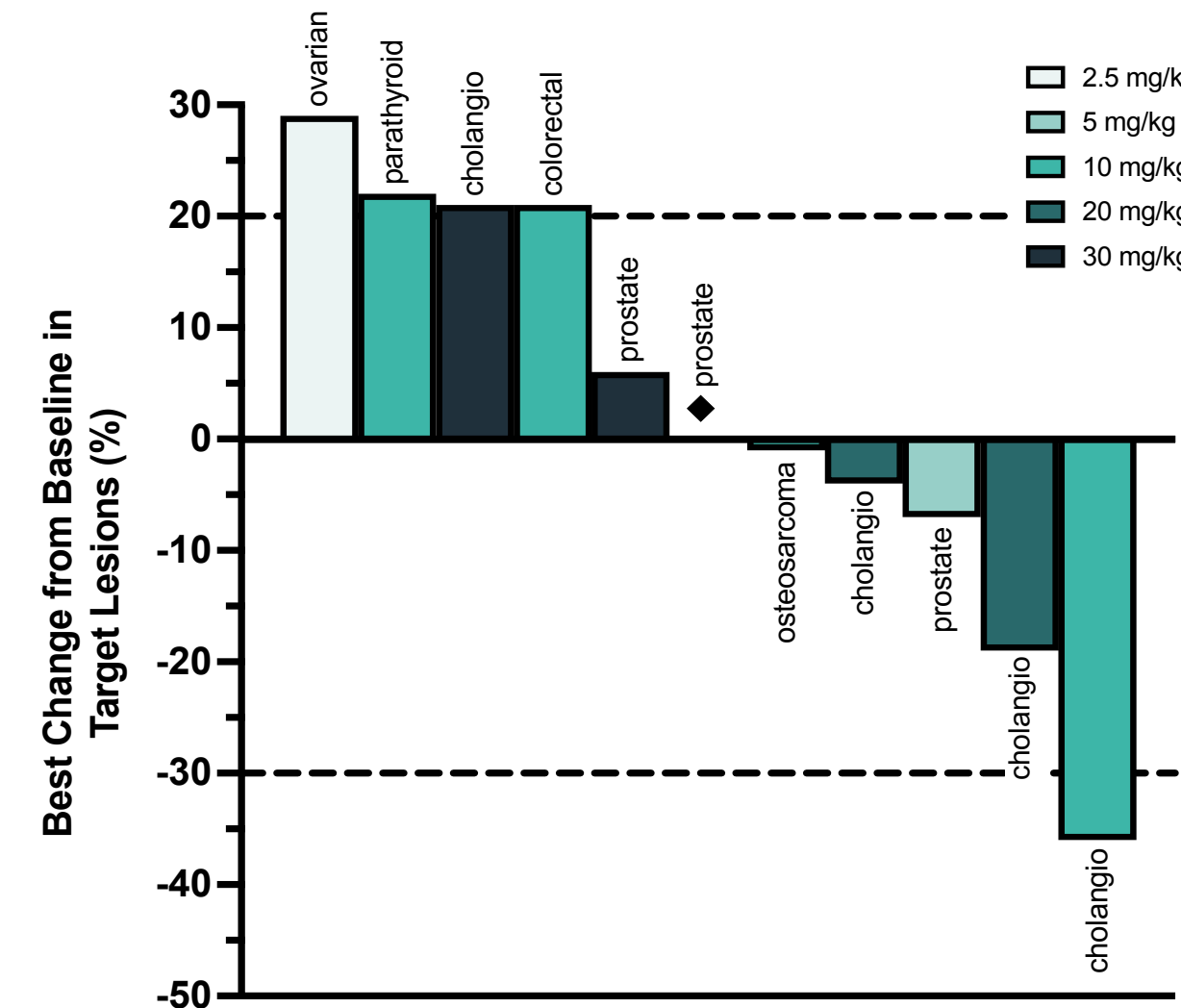


Figure 3. Best change of target lesion size from baseline in evaluable patients receiving MDX-124 monotherapy (n = 11). ♦ Patient evaluable, but not measurable per RECIST.

Cholangiocarcinoma

Module 1

- Tumour shrinkage in 3/4 evaluable patients (Figure 4).

Module 2

- MDX-124 monotherapy in 2nd line cholangiocarcinoma population.
- Inclusion:** Patients must have received and have documented disease progression following GemCis (+/- durvalumab).
- Exclusion:** Patient has received more than 1 line of prior systemic therapy with chemotherapy in advanced setting. Prior adjuvant / neoadjuvant treatment or treatment with a targeted therapy (e.g. IDH1 / FGFR2 inhibitors) is not exclusionary.

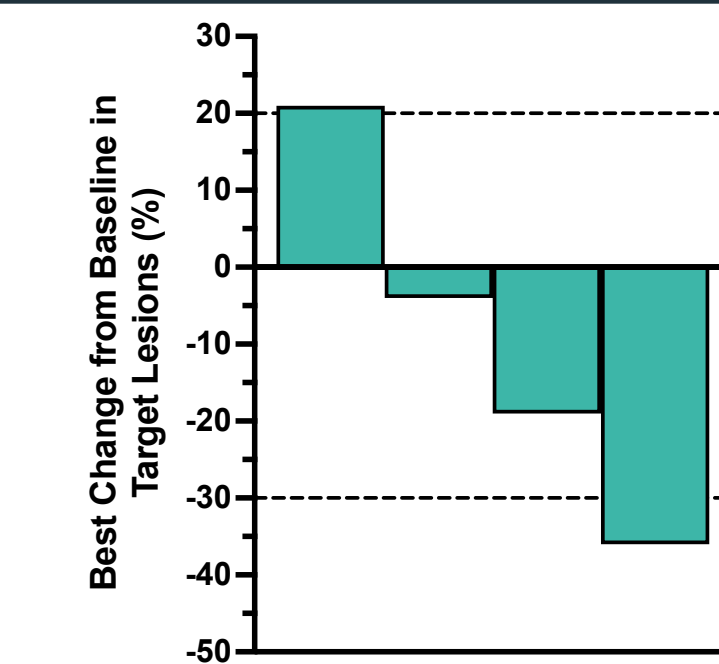


Figure 4. Best target lesion change in evaluable cholangiocarcinoma patients.

Patient Case Study

- Male, 52 years old, metastatic cholangiocarcinoma
- Prior lines of treatment include gemcitabine + cisplatin (neoadjuvant), capecitabine and radiotherapy
- Started 28th February 2024 and remained on study for ~12 months
- ✓ **Confirmed partial response** on MDX-124 monotherapy with **36% reduction** in target lesion size observed
- ✓ **No DLTs** or treatment-related serious adverse events observed



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PATIENT FRIENDLY SUMMARY

- Annexin-A1 is a protein found in higher than normal levels in many types of cancer including cholangiocarcinoma.
- Annexin-A1 allows cancer cells to grow, spread and avoid being recognised by the immune system.
- MDX-124 is a targeted monoclonal antibody treatment that attaches to annexin-A1 preventing it from fuelling cancer development.
- There are 2 parts to this trial:
 - Part 1 is looking at the best dose of MDX-124 to give
 - Part 2 is looking at how MDX-124 works in specific cancers including cholangiocarcinoma
- Results from part 1 of the trial suggest MDX-124 has:
 - A **good safety profile** with minimal side effects
 - **Anti-cancer effects** in multiple patients with tumour types including cholangiocarcinoma