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

Daniel H Palmer[1], Stefan N Symeonides[2], Alan Christie[2], Emily Spiers[2], Chiara Braconi[3], Mairéad G. McNamara[4], Debashis Sarker[5], Fiona C Dempsey[6], Scott J Crichton[6], Colin Tennant[6], Christopher B Wood[6], Lisa C Yule[6] and Sarah P Blagden[7]

[1]Liverpool ECMC, University of Liverpool and Clatterbridge Cancer Centre, Liverpool, UK; [2]Edinburgh ECMC, University of Edinburgh and Edinburgh Cancer Centre, Edinburgh, UK; [3]University of Glasgow and Beatson West of Scotland Cancer Centre, Glasgow, UK; [4]University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [5]King's College London and Guy's Hospital, London, UK; [6]Medannex, Edinburgh, UK; [7]Early Phase Clinical Trials Unit, Churchill Hospital, University of Oxford, Oxford, UK

KEY FINDINGS

- Preliminary data indicate very encouraging safety, tolerability, and anti-tumor 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.

BACKGROUND

Annexin-A1 released by tumor and immune cells under diverse stimuli, engages formyl-peptide receptors (FPR1/2) to rewire cell behavior fuelling tumor growth[1], angiogenesis[2], migration[3], and drug resistance[4] while reshaping the tumor 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 humanized IgG1 monoclonal antibody that specifically targets annexin-A1[8] to inhibit tumor growth, reduce metastasis and induce ADCC activity[9-11] (Figure 1).

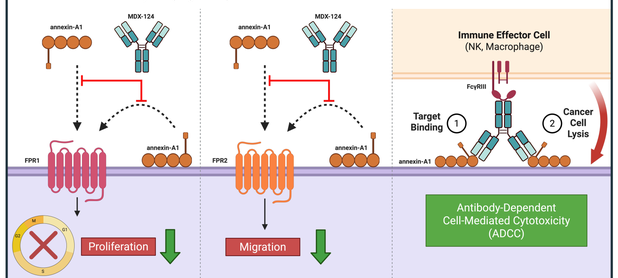

Figure 1. Mechanism of action of MDX-124.

METHODS

This modular, multi-arm phase 1b study of MDX-124 is enrolling adult patients with advanced solid tumors 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-tumor activity. Efficacy is assessed per RECIST v1.1 and adverse events are graded according to CTCAE v5.0. Tumor and immunological biomarkers are exploratory endpoints.

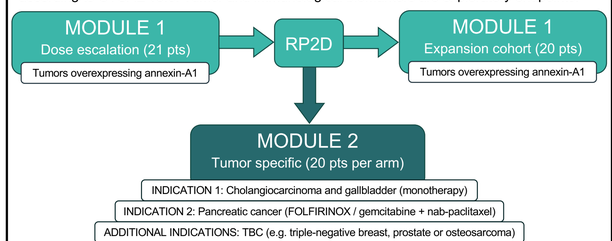

Figure 2. Study schema for the ATTAINMENT trial.

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
Diarrhea	4 (19%)	0
Vomiting	3 (13%)	0
ALP increase	3 (14%)	0
Peripheral edema	3 (14%)	0
Anemia	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

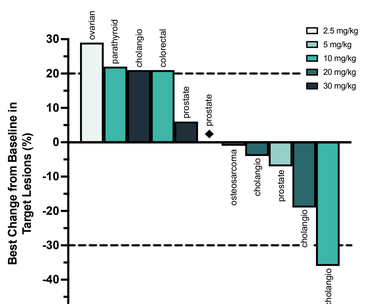

Figure 3. Best change of target lesion size from baseline in evaluable patients receiving MDX-124 monotherapy (n = 11). ◆ Patient evaluable, but not measurable per RECIST.

Cholangiocarcinoma

Module 1

- Tumor 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.

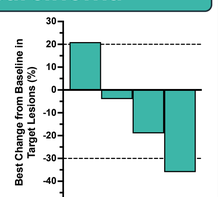

Figure 4. Best target lesion change in evaluable cholangiocarcinoma patients.

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

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 recognized 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 tumor types including cholangiocarcinoma

CCF 13th Annual Conference | Salt Lake City May 1-3 2026

Corresponding Author: Professor Daniel Palmer
Contact Email: attainment@liverpool.ac.uk

REFERENCES

(1) Vecchi *et al.*, (2018). *BBA Mol. Cell Research*, **1865**(9): 1368–1382. **(2)** Yi and Schnitzer (2009). *PNAS*, **106**(42): 17886–17891. **(3)** Belvedere *et al.*, (2014). *BMC Cancer*, **14**(1): 1-15. **(4)** Onozawa *et al.*, (2017). *Oncology Reports*, **37**(1): 235-240. **(5)** Araujo *et al.*, (2021). *Cells*, **10**: 2245. **(6)** Gong *et al.*, (2025). *J Exp Clin Cancer Res*, **44:** 151. **(7)** Bai *et al.*, (2020). *JITC*, **8**(1): 1–9. **(8)** Gramlich *et al.*, (2021). *Antibodies*, **10**(1): 11. **(9)** Al-Ali *et al.*, (2024). *Oncogene*, **43**: 608-614. **(10)** Dempsey *et al.*, (2022). *J. Clinical Oncology*, **40**: 590. **(11)** Dempsey *et al.*, (2021). *Cancer Research*, **81** (13 supplement): 1874.