INTERIM PK/PD, SAFETY AND EFFICACY DATA OF MONOTHERAPY DOSE ESCALATION OF A PHASE 1/2 STUDY WITH MDNA11 IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background MDNA11 is an albumin-fused long-acting IL-2 agonist with enhanced affinity for IL-2Rb and no binding to IL-2Ra, resulting in potent CD8+ T and NK cell activation, limited Treg increase and reduced toxicities. 1 ABILITY (A Beta-only IL-2 ImmunoTherapy) is a Phase 1/2 study evaluating the safety, pharmacokinetic (PK), pharmacodynamic (PD) and preliminary clinical activity of MDNA11 as monotherapy and in combination with Prembrolizumab in pre-treated patients with advanced solid tumors.

Methods The dose-escalation phase of ABILITY uses a modified 3+3 design to determine the recommended dose for expansion (RDE). Patients received a fixed dose of 3, 10 or 30 μg/kg (dose levels 1–3; DL1–3) by intravenous infusion on a Q2W schedule. Step-up dosing was implemented starting at DL4 where patients received 2 or 3 priming doses prior to the target dose of 60 μg/kg (DL4), 90 μg/kg (DL5) or 120 μg/kg (DL6). Primary endpoints include incidence and severity of adverse events (AEs). Secondary endpoints include assessment of PK, PD and tumor response per RECISTv1.1 and iRECIST

Results As of June 22, 2023, twenty dose limiting toxicity (DLT)-evaluable patients have been dosed with MDNA11 during monotherapy dose escalation (3–120 μg/kg). Tumor types enrolled included melanoma (n=11), renal cell carcinoma (n=2), pancreatic ductal adenocarcinoma (PDAC; n=2), sarcoma (n=2), tonsillar squamous cell carcinoma (n=1), gastroesophageal adenocarcinoma (n=1) and lung adenocarcinoma (n=1). PK analysis showed dose-dependent increase in MDNA11 exposure. Immune profiling showed robust lymphocyte expansion, including increase in CD8+ T and NK cells and limited change in Tregs. There were no DLTs observed. The most common AEs were infusion related reaction (65%) comprising pyrexia (50%), nausea (45%), chills (35%), fatigue (30%) and diarrhea (25%), with the majority being grade 1–2 and resolved within 48–72 hours. Transient (~1week duration) transaminases increase was seen in 25% of patients. Tumor response was evaluated in 19 patients. Single-agent activity included stable disease (SD) observed in 6 patients, including a melanoma patient with SD beyond 1.5 year, and an ongoing partial response (PR) in a PDAC patient who had previously progressed on immune checkpoint inhibitor and is currently continuing on MDNA11 for >1 year.

Conclusions MDNA11 is well tolerated with no DLTs up to target dose of 120 μg/kg on a Q2W schedule. Evidence of clinical activity includes SD in 6 of 19 patients in addition to a durable PR in a PDAC patient. Data analysis is ongoing to inform RDE selection.

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Trial Registration NCT: 05086692

REFERENCE

Ethics Approval The study was conducted with approval from institutional ethics committee and informed consent from participants.

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