INTERIM SINGLE-AGENT SAFETY AND ANTI-TUMOR ACTIVITY FROM DOSE ESCALATION PHASE OF ABILITY STUDY ON MDNA11, A LONG-ACTING BETA-ONLY IL-2 AGONIST


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Background High dose (HD) IL-2 has shown durable tumor response in a subset of metastatic melanoma and renal cell carcinoma (RCC), but its clinical utility is limited by need for frequent administration, undesirable activation of immune suppressive Tregs, and severe toxicities. MDNA11 is an albumin-fused long-acting engineered IL-2 agonist with enhanced affinity for IL-2Rbg with no binding to IL-2Ra, enabling Q2W administration, limiting Treg activation while potentiating anti-tumor CD8+ T and NK cells and reducing toxicities.

Methods The objective of the dose-escalation phase of the ABILITY (A Beta-only IL-2 ImmunotherapY) study is to determine the safety and tolerability, define the recommended phase-2 dose (RP2D), and assess preliminary tumor response of MDNA11 in patients with advanced solid tumors. In this modified 3+3 dose escalation, patients received a fixed dose of 3 (dose level 1 or DL1), 10 (DL2) or 30 (DL3) ug/kg by intravenous (IV) infusion on a Q2W schedule. Step-up dosing (SUD) is implemented starting at DL4 where patients received 2 priming doses at 30 ug/kg (Q2W) prior to escalation to the target dose (Q2W) of 60 ug/kg (DL4) or 90 ug/kg (DL5; enrolling). Primary endpoints include incidence, nature and severity of adverse events (AEs). Secondary endpoints include assessment of pharmacokinetics, pharmacodynamics and tumor response per RECISTv1.1.

Results As of July 21, 2022, 14 patients have been dosed with MDNA11 (DL1 = 1, DL2 = 3, DL3 = 4, DL4 = 6). Tumor types enrolled were melanoma (n=7), RCC (n=1), pancreatic ductal adenocarcinoma (n=2), sarcoma (n=2), squamous cell carcinoma (n=1) and gastro-esophageal adenocarcinoma (n=1). PK analysis showed dose-dependent increase in MDNA11 exposure. MDNA11 has been well tolerated with no dose-limiting toxicities observed at up to DL4. The most common drug-related AEs were infusion related reactions (71%), pyrexia (35%), diarrhea (28%) and nausea (28%), and with a majority of these being Grade 1 or 2 and lasted less than 24 hours. Tumor responses were evaluated in 10 patients and 4 patients had not reached their first assessment. Single-agent activity based on RECISTv1.1 included stable disease (SD) observed in patients with melanoma (n=1), sarcomas (n=2) and pancreatic cancer (n=1).

Conclusions MDNA11 is well tolerated with no DLTs up to target dose of 60 mg/kg (DL4) and enrolment for 90 mg/kg (DL5) has initiated. There is dose-dependent increase in plasma exposure and evidence of single-agent anti-tumor activity in 4 of 10 (SD) patients.

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Trial Registration NCT05086692

REFERENCE


Ethics Approval The study was approved by each institution’s Ethic Board.