Interim Single-Agent Safety and Anti-Tumor Activity During Dose Escalation in Phase 1/2 ABILITY Study of MDNA11, a Long-Acting 'Beta-Only' IL-2 Agonist

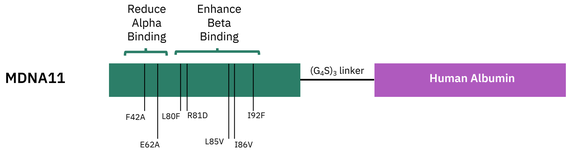
Fahar Merchant[1], Victoria G. Atkinson[2], Martin Bexon[1], Jim Coward[3], Jenny Lee[4], Charlotte R. Lemech[5], Jesus F. Antras[6], Peter Lloyd[7], Arash Yavari[8], Melissa Coello[1], Rosemina Merchant[1], Minh D. To[1]

[1]Medicenna Therapeutics Inc., Toronto, ON, Canada; [2]Gallipoli Medical Research Foundation, Greenslopes, QLD; [3]ICON Cancer Centre, South Brisbane, QLD; [4]Chris O'Brien Lifehouse, Camperdown, NSW; [5]Scientia Clinical Research, Randwick, NSW; [6]Princess Margaret Hospital, Toronto, ON, Canada; [7]KinDyn Consulting Ltd., Warnham, West Sussex, UK; [8]Oxford University, Oxford, UK

Background

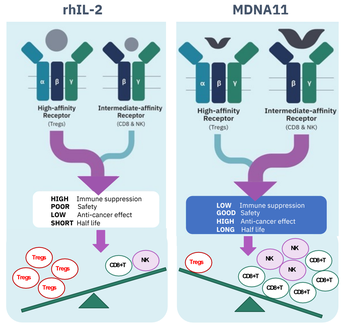
- High dose IL-2 has shown durable tumor response in a subset of metastatic melanoma and renal cell carcinoma (RCC)
- IL-2 undergoes rapid clearance due to its small size, therefore requiring frequent dosing at a high dose, resulting in severe toxicities
- Therapeutic activity of IL-2 is hindered by its preferential stimulation of immune-suppressive Tregs, diminishing the anti-tumor response driven by effector immune cells (i.e., CD8+ T and NK cells)

Overview of MDNA11



- Albumin fusion increases half-life and promotes tumor accumulation
- Superior receptor selectivity
  - Increased affinity to IL-2Rβ
  - No binding to IL-2Rα
- Potentiates activation of effector immune cells
- Reduces Treg stimulation and toxicities

Merchant et al., JITC 2022



Trial Design and Objectives

- The ABILITY (A Beta-only IL-2 ImmunoTherapY) study (NCT05086692) evaluates the safety and tolerability of MDNA11 in patients with advanced solid tumors
- The objectives of the dose-escalation phase are to determine the RP2D, study the pharmacokinetic and pharmacodynamic profile of MDNA11, and assess preliminary tumor response.

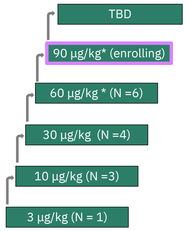
Schema of MDNA11 Phase 1/2 ABILITY Study

Basket, Accelerated Sequential Dose Escalation and Expansion Study of MDNA11 +/- Pembrolizumab

MDNA11 Monotherapy Dose Escalation

N ~ 20: Select tumors
IV Infusion, Q2W

- Modified, accelerated 3+3 design
- Intra-patient dose escalation permitted
- Safety and tolerability
- DLT assessment
- Identify RP2D
- Preliminary tumor response



*Step-up dosing utilized: two priming doses of 30 µg/kg (Q2W) prior to the indicated target dose

MDNA11 Monotherapy Dose Expansion

N~ 40
(Melanoma, up to N = 20)

MDNA11 administered alone at RP2D via IV infusion Q2W or Q3W

Signals of anti-tumor activity

MDNA11 + Pembrolizumab Dose Expansion

N~ 40
(Melanoma, up to N = 20)

Safety run-in (21 days)

MDNA11 administered at RP2D in combination with CPI via IV infusion Q3W (planned)

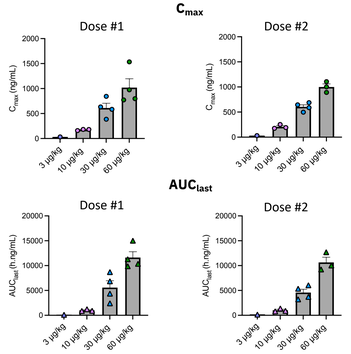
Signals of anti-tumor activity

Patient Characteristics

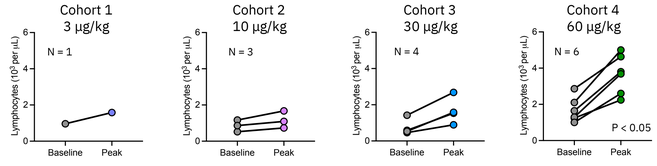
Demographics/Performance	
Median age (range), years	63 (27-78)
Male (%)	11/14 (79%)
Baseline ECOG = 0	10/14 (71%)
Baseline ECOG = 1	4/14 (29%)
Primary Cancer Diagnosis	
Melanoma	7/14 (50%)
Renal Cell Carcinoma (non-clear cell)	1/14 (7%)
Pancreatic Ductal Adenocarcinoma (PDAC)	2/14 (14%)
Sarcoma	2/14 (14%)
Squamous Cell Carcinoma	1/14 (7%)
Gastro-esophageal Adenocarcinoma	1/14 (7%)
Prior Systemic Therapies	
Prior Lines of Therapy: 1-2	9/14 (64%)
Prior Lines of Therapy: 3-4	5/14 (36%)
Prior use of immunotherapy	11/14 (79%)
Prior use of targeted therapy	4/14 (28%)
Prior use of chemotherapy	7/14 (50%)

MDNA11 PK Profile in Patients

Sustained Dose-Dependent Increase in Exposure Following Multiple Dosing Cycles



MDNA11 Elicited Increase in Lymphocytes



- Results are consistent with the anticipated pharmacological effects of MDNA11

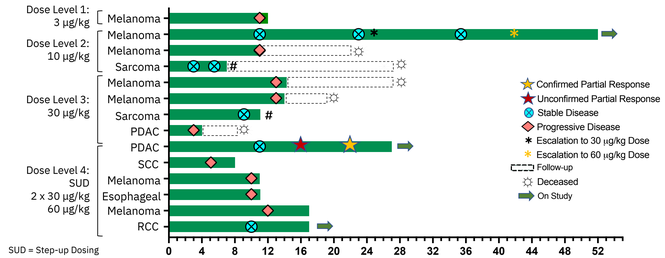
Summary of MDNA11 Related Adverse Events (AEs)

Preferred Term	Cohort 1 (3 µg/kg) N = 1	Cohort 2 (10 µg/kg) N = 3	Cohort 3 (30 µg/kg) N = 4	Cohort 4 (60 µg/kg) N = 6	Total N = 14
All Grades (> 20%)					
Infusion related reaction##	1 (100%)	2 (66.6%)	3 (75%)	5 (83.3%)	11 (78.6%)
Nausea		2 (66.6%)		5 (83.3%)	8 (57.1%)
Pyrexia		1 (33.3%)	2 (50%)	4 (66.6%)	7 (50%)
Fatigue		2 (66.6%)	2 (50%)	1 (16.6%)	5 (35.7%)
Diarrhea		1 (33.3%)	1 (25%)	2 (33.3%)	4 (28.6%)
Chills		1 (33.3%)	1 (25%)	1 (16.6%)	3 (21.4%)
Headache			1 (25%)	2 (33.3%)	3 (21.4%)
Grade 3-4 (> 5%)					
Alanine aminotransferase increase				1 (16.6%)*	1 (7.1%)
Blood bilirubin increase				1 (16.6%)*	1 (7.1%)
Hypotension			1 (25%)#		1 (7.1%)
Lymphocyte count decrease		1 (33.3%)$	1 (25%)$		2 (14.2%)

*Transient elevations and resolved within 3-4 days # Seen in patient with adrenal insufficiency $ Transient decrease in lymphocyte immediately after MDNA11 administration is expected
**Infusion related reaction mainly constituted fever, tachycardia and chills

Data cut off: October 19, 2022

Duration of Treatment and Summary of Tumor Response

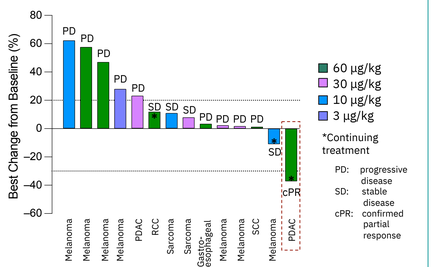


SUD = Step-up Dosing
# Target lesions exhibit SD; PD due to clinical progression or patient withdrawal

- Tumor control in 5 of 14 evaluable patients (including 1 confirmed PR in PDAC) despite low dose levels and heavily pre-treated patients

Data cut off: October 21, 2022

Summary of Tumor Response



Conclusions

- Dose-dependent increase in MDNA11 exposure sustained with repeat dosing
- MDNA11 induces lymphocyte expansion as anticipated
- Majority of MDNA11 related AEs are grade 1-2 (92%), transient and resolved within 1-2 days
- No dose-limiting toxicity, no dose de-escalation, and no dose dis-continuations to date
- Tumor control in 5 of 14 patients:
  - 1 confirmed PR in PDAC in Cohort 4 (60 µg/kg target dose)
  - 4 SD (2 sarcomas, 1 melanoma and 1 RCC)
- Currently enrolling patients in Cohort 5 (90 µg/kg target dose)