Interim PK/PD, Safety and Efficacy Data of Monotherapy Dose Escalation of a Phase 1/2 Trial With MDNA11 in Patients With Advanced Solid Tumors

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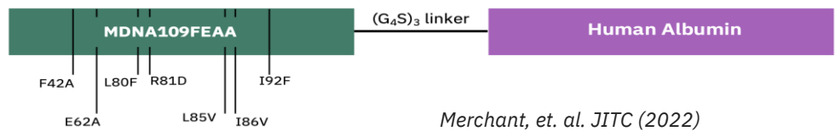
Overview of MDNA11

- Long-acting IL-2 super-agonist
- Strong activation of CD8⁺ T and NK cells
- Minimal impact on Treg cells
- Reduced toxicity

MDNA11 is engineered with targeted mutations to increase IL-2Rβ affinity and eliminate IL-2Rα binding.

Fusion to human albumin extends half-life, overcoming need for frequent dosing, and promotes MDNA11 accumulation in tumors.



Merchant, et. al. JITC (2022)

ABILITY (A Beta-only IL-2 ImmunoTherapY) Study (NCT05086692)

ABILITY-1 is a Phase 1/2 study assessing MDNA11's safety, pharmacokinetics, pharmacodynamics, and preliminary efficacy in patients with advanced solid tumors, as monotherapy and in combination with Pembrolizumab.

Study Design

MDNA11 Monotherapy Dose Escalation (IV Q2W)

- Modified 3+3
- Intra-patient dose escalation allowed
- Parallel backfill
- Select monotherapy RDE

3 µg/kg → 10 µg/kg → 30 µg/kg → 60* µg/kg → 90* µg/kg → 120* µg/kg

* Step-up dosing (SUD) implemented

MDNA11 (Q2W) + Pembrolizumab (Q6W) Dose Escalation

Select PD1/L1 relapsed and CPI naive indications

Identify combination RDE (cRDE) for MDNA11

Assess safety, tolerability and anti-tumor activity

Dose Evaluation in Monotherapy

Optimize SUD schedule

MDNA11 Monotherapy Dose Expansion

- Melanoma
- Non-melanoma skin cancer (CSCC, BCC, and MCC)
- MSI-H/dMMR tumors

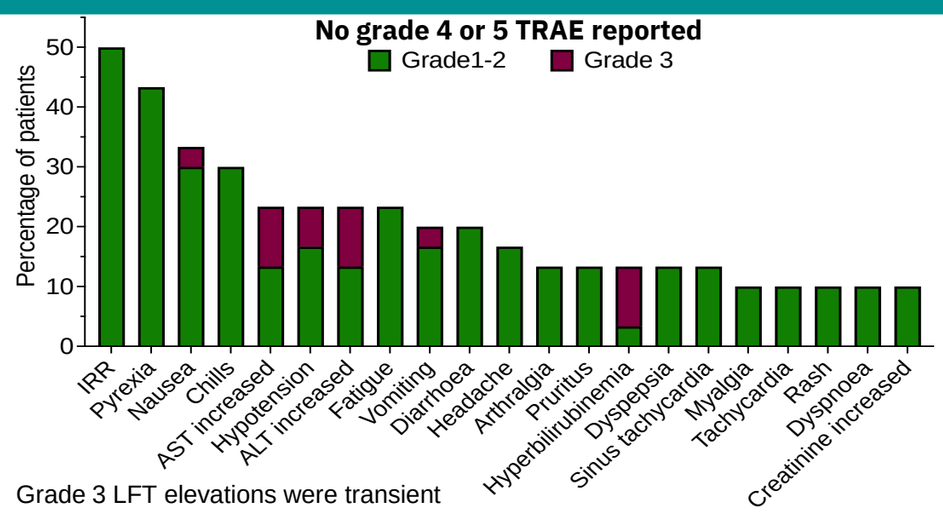
MDNA11 + Pembrolizumab Dose Expansion

MDNA11(Q2W, cRDE) + Pembrolizumab (Q6W, 400mg)

Assess safety, tolerability and anti-tumor activity

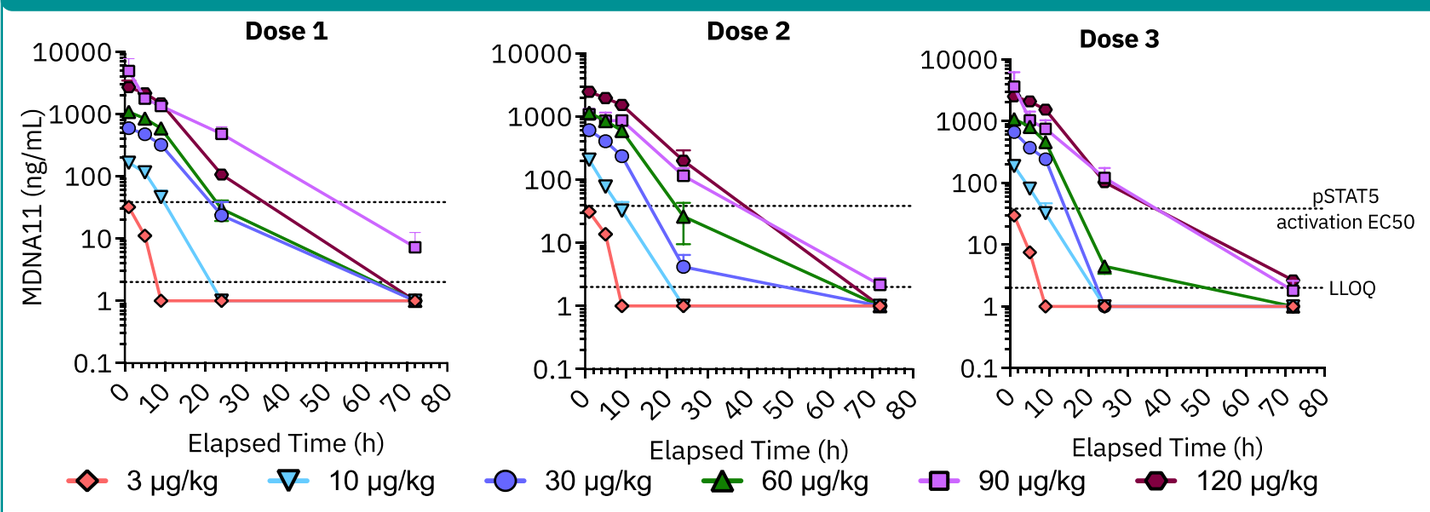
Baseline characteristics	N=30
Age, median years (range)	63 (27-78)
Male, N (%)	22 (73.3%)
Baseline ECOG = 0, N (%)	19 (63.3%)
Baseline ECOG = 1, N (%)	11 (36.6%)
Primary Tumor Type	**N (%)**
Melanoma (14 Cutaneous, 1 Mucosal and 1 Acral)	16 (53.3 %)
Non-small Cell Lung Cancer (NSCLC)	3 (10%)
Pancreatic Ductal Adenocarcinoma (PDAC)	3 (10%)
Renal Cell Carcinoma	2 (6.6%)
Sarcoma (1 Pleiomorphic sarcoma and 1 Leiomyosarcoma)	2 (6.6%)
Ovarian Cancer	2(6.6%)
Tonsillar Squamous Cell Carcinoma	1 (3.3%)
Gastro-esophageal Adenocarcinoma	1 (3.3S%)
Prior Anti-cancer Systemic Therapies	**N (%)**
Prior Lines of Therapy: 1-2	22 (73.3%)
Prior Lines of Therapy: 3-4	8 (26.6%)
Immunotherapy	22 (73.3%)
Targeted Therapy	5 (16.6%)
Chemotherapy	15 (50 %)

Treatment Related Adverse Events (TRAE) in ≥10% of Patients

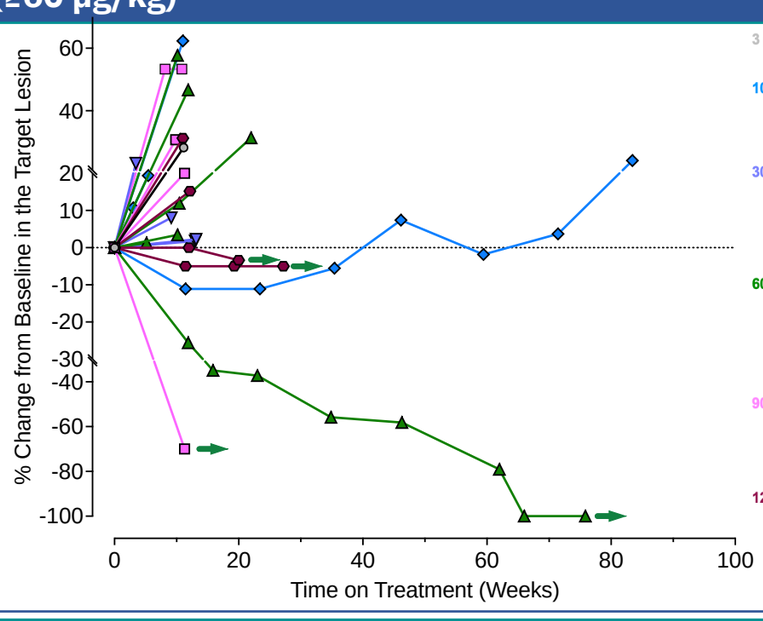


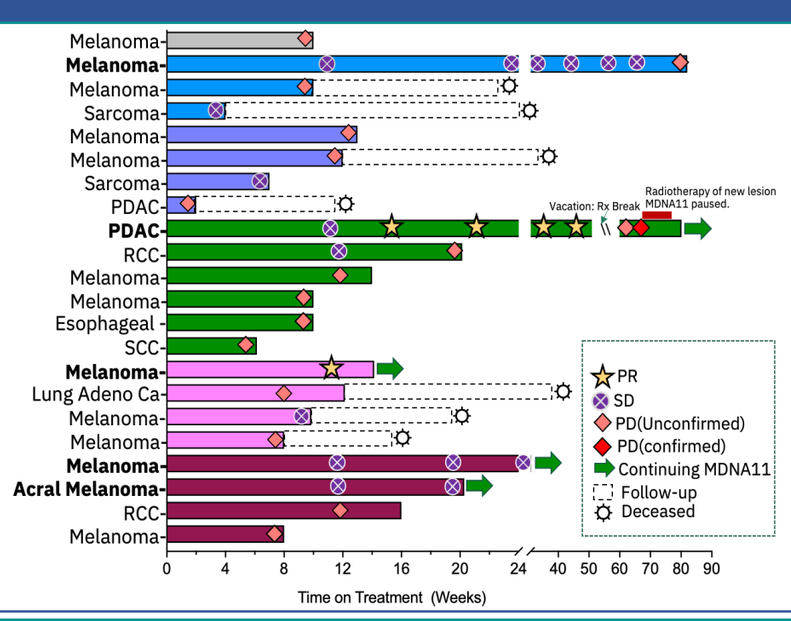
Grade 3 LFT elevations were transient

PK Profile Shows Dose Dependent Increase of MDNA11 Serum Levels

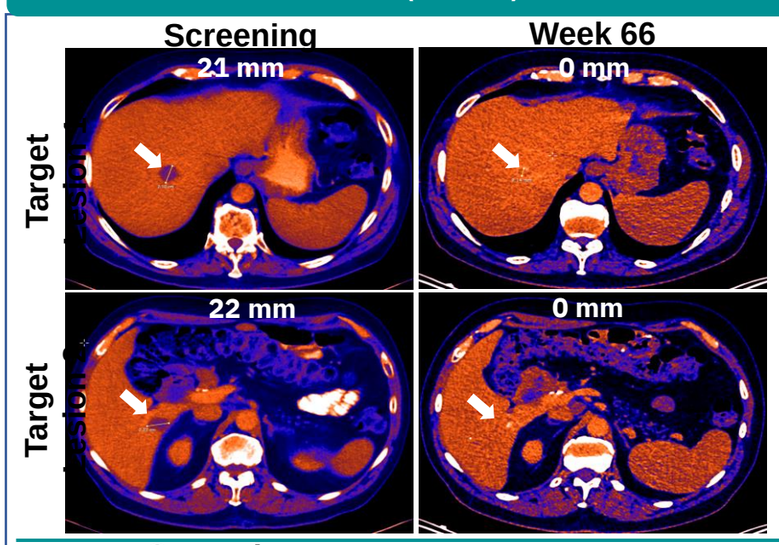


Disease Control Rate of 33.3% (PR=2 and Durable SD=3) in Patients Receiving Higher Doses of MDNA11 (≥60 µg/kg)





PR Achieved in 2 of 15 (13.3%) Patients Receiving Higher Dose of MDNA11 (≥60 µg/kg)



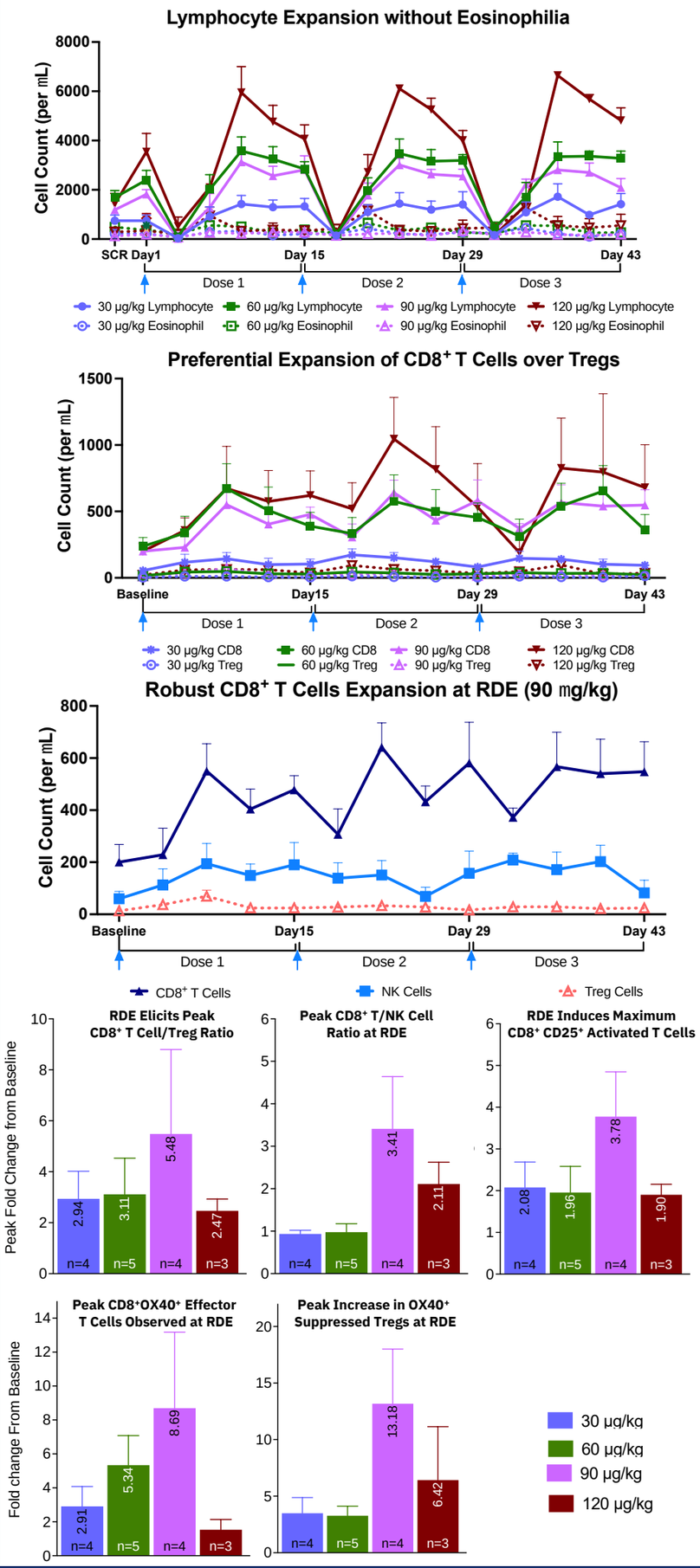
PR at 60 µg/kg :

- Pancreatic ductal adenocarcinoma (PDAC, MSI-H) treated with two prior lines.
  - Whipple procedure + Adj FOLFIRINOX
  - 1L: Gemcitabine + nab-Paclitaxel
  - 2L: Pembrolizumab (PD-primary resistant)
- PR first observed at week 16.
- **100% reduction of target and non-target lesion at week 66 on MDNA11 alone.**
- Patient developed a single new lesion while on treatment break (vacation) and continues to receive MDNA11

PR at 90 µg/kg :

- Cutaneous melanoma progressed on prior line of dual checkpoint inhibitors
- 70% reduction of the target lesion at week 12.

Optimal Immune Response at 90 µg/kg , Monotherapy Recommended Dose for Expansion



Conclusions

- No dose limiting toxicity reported.
- 95.6% of TRAE were of grade 1-2 severity; no grade 4 or 5 events reported.
- 90 µg/kg declared as monotherapy RDE.
- MDNA11 shows dose-dependent increase in PD parameters with activation markers peaking at 90 µg/kg.
- PR in 2 patients (60 and 90 µg/kg), SD in 7 patients.
- Monotherapy dose-expansion arm is currently enrolling patients.
- MDNA11 combination therapy with Pembrolizumab to begin in Q4 of 2023.