Pharmacokinetics and Pharmacodynamics of MDNA11, a Long-acting IL-2 Superkine, as Single Agent and in Combination with Pembrolizumab in Patients with Advanced Solid Tumors

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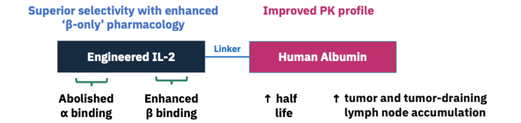
MEDICENNA

Key Findings

- MDNA11 is a next-generation, long-acting, 'β-enhanced not-α' IL-2 superkine
- MDNA11 shows compelling single-agent activity in CPI-resistant tumors
- MDNA11 in combination with pembrolizumab demonstrated clinical activity in tumor types that do not typically respond to CPI
- Serum exposure of MDNA11 is consistent across repeated dosing cycles in combination with pembrolizumab
- Consistent with its design, MDNA11 induces dose-dependent, sustained expansion of CD8⁺ T and NK cells with minimal Treg expansion, as monotherapy & combined with pembrolizumab
- MDNA11 promotes increases in effector and memory CD8⁺ T cells subsets, providing the potential for enhanced tumor killing and durable anti-tumor responses
- Increase in stem-like CD8⁺ T cells is associated with clinical benefit

MDNA11: A Long-acting 'β-enhanced Not-α' IL-2 Superkine

Engineered to overcome key limitations of high dose IL-2



Enhanced β-binding + **Non-α binder** + **Albumin-fusion** → **Superior Anti-cancer Response**

Potentiate activation of CD8⁺ T & NK cells | *Reduce* stimulation of Tregs & improve safety | *Half-life extension and increase tumor exposure*

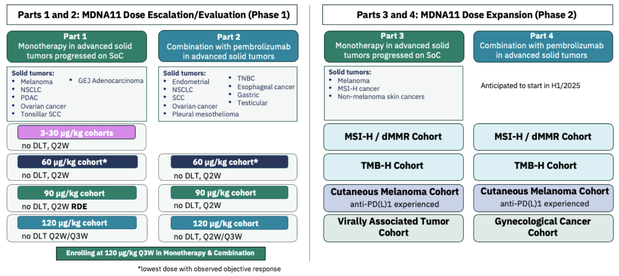
MDNA11 demonstrated a favorable safety profile and promising anti-tumor activity as a single agent and in combination with pembrolizumab

(Yavari et al., Melanoma Bridge 2024; To et al., SITC 2024)

Study Design

ABILITY-1: FIH Trial of MDNA11 in Advanced Solid Tumors

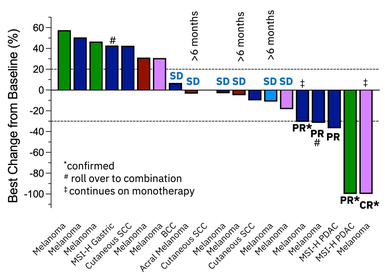
ABILITY-1: **A B**eta-only **IL-2 I**mmuno**T**herap**Y** Study (NCT05086692)



MSI-H, microsatellite instability-high; MSS, microsatellite stable; dMMR, mismatch repair deficient; TMB-H, tumor mutational burden-high; GEJ, gastroesophageal junction; HNSCC, head and neck squamous cell carcinoma; NMSC, non-melanoma skin cancer; BCC, basal cell carcinoma; SCC, squamous cell carcinoma; MCC, Merkel cell carcinoma; NSCLC, non-small cell lung cancer; ccRCC, renal cell carcinoma, clear cell; TNBC, triple-negative breast cancer; mCRC, metastatic colorectal cancer; DLT, dose-limiting toxicity; RDE, recommended dose for expansion; CPI, immune checkpoint inhibitor, CR, complete response; PR, partial response; SD, stable disease

MDNA11 Shows Monotherapy Clinical Activity in Patients Refractory to CPI

Best response on Phase 2 eligible, CPI resistant patients treated with MDNA11 ≥ 60ug/kg



Objective Response Rate (ORR):

- 5/20 (25%) [95% CI: 6-44]
  - 1 Complete Response
  - 4 Partial Responses

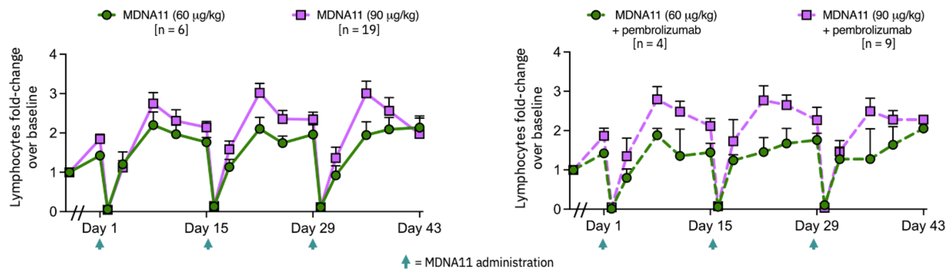
Clinical Benefit Rate:

- 8/20 (40%)
  - 1 Complete Response
  - 4 Partial Responses
  - 6 Stable Disease, including 3 for > 6 months

Monotherapy expansion (90 µg/kg)
120 µg/kg
90 µg/kg
60 µg/kg
10, 30, 60 ,90 µg/kg (intra-patient dose escalation)

Data cut-off: November 18, 2024

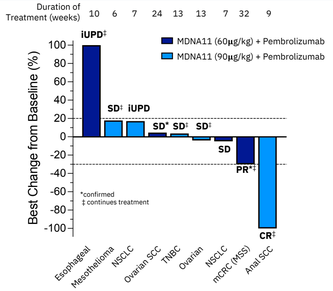
Dose-dependent Lymphocyte Expansion Sustained with Repeat Dosing



Lymphocyte counts elevated above baseline for >14 d after each MDNA11 dose whether given as single agent or in combination with pembrolizumab

MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W. Data represents mean ± SEM

MDNA11 + Pembrolizumab Shows Clinical Activity in Less Immunologically Responsive Tumor Types



CR in 70 yr M with anal SCC

- Progressed on 2 prior lines of treatment (1L capecitabine/mitomycin + radiation; 2L carboplatin/paclitaxel)

Confirmed PR in 52 yr F with MSS mCRC

- Progressed on 2 prior lines of chemotherapy (1L folinate/fluorouracil/oxaliplatin; 2L capecitabine)

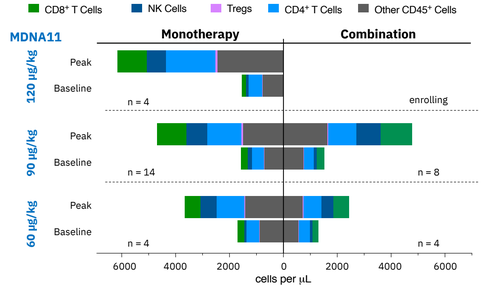
Combination dose escalation continues

MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W

Data cut-off: November 18, 2024

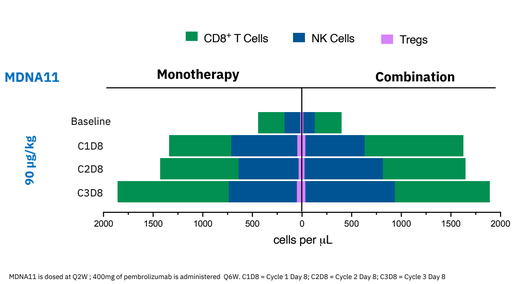
This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Dose-Dependent Expansion of CD8⁺ T and NK Cells



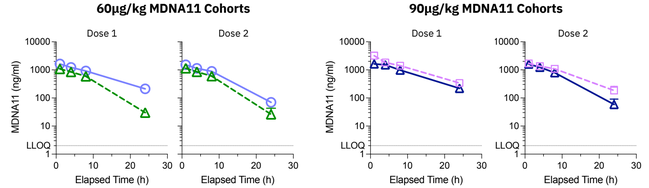
MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W

Sustained Expansion of CD8⁺ T and NK Cells Over Multiple Cycles



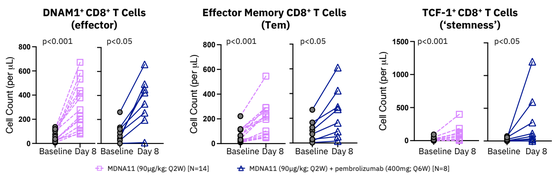
MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W. C1D8 = Cycle 1 Day 8; C2D8 = Cycle 2 Day 8; C3D8 = Cycle 3 Day 8
Monotherapy: Baseline (n = 12), C1D8 (n = 12), C2D8 (n = 8), C3D8 (n = 6). Combination: Baseline (n = 8), C1D8 (n = 8), C2D8 (n = 7), C3D8 (n = 5)

MDNA11 PK Profiles Are Consistent Across Repeated Dosing



Data shown for MDNA11 target Dose cycle 1&2 and represents Mean ± SEM; MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W

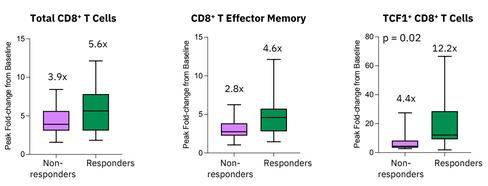
MDNA11 Expands Effector, Memory and 'Stem-like' CD8⁺ T Cells



MDNA11, both as single agent and combined with pembrolizumab, promotes expansion of CD8⁺ T cell subsets which have been associated with durable anti-tumor immunity

p-values based on paired non-parametric Wilcoxon test

Clinical Benefit is Associated with Increase in CD8⁺ T Cell 'Stemness'



Efficacy evaluable patients in MDNA11 monotherapy and combination cohorts (60 and 90 µg/kg). Responders: CR + PR + SD > 6 months (n = 9); Non-responders: PD (n = 14)
Median peak-fold change indicated; p-value by Mann-Whitney test

Acknowledgements:
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