Interim results from the phase 1/2 ABILITY-1 study of a long-acting 'beta-enhanced not-alpha' IL-2 superkine in patients with advanced solid tumors

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MEDICENNA

CT047

Summary

Mechanism: MDNA11 is a 'beta enhanced not alpha' albumin-fused next generation IL-2 agonist which preferentially expands CD8⁺ T cells and NK cells while minimizing Treg activation

Safety profile: No DLT up to 120 µg/kg MDNA11 across both monotherapy & combined with pembrolizumab. Majority (>90%) of TRAEs were Grade 1-2 and transient

Efficacy: 10 objective responses in monotherapy and in combination dose escalation with pembrolizumab

MDNA11 monotherapy: Durable single-agent activity in heavily pre-treated, ICI resistant patients
- ORR 29.4% (95% CI: 13.3-53.1%) in 17 P2 monotherapy expansion eligible/primary ICI resistant melanoma patients treated with ≥60 µg/kg MDNA11 Q2W: 1 CR (confirmed) + 4 PRs (2 confirmed)
- 2 PRs in 4 (50%) MSI-H/dMMR cancers
- 2 patients with ongoing remission after stopping MDNA11 single-agent therapy (>6 wks and >1 yr)

***MDNA11 combination with pembrolizumab*:** 5 objective responses (1 CR + 4 PRs) in ongoing dose escalation
- ORR of 30.8% (4 of 13) in P2 combination dose expansion eligible patients
- 2 PRs in 4 (50%) endometrial cancers
- Clinical activity in historically low IO responders: 1 CR in anal SCC + 1 PR in MSS CRC (TMB-H)

Pharmacodynamics: Robust expansion of immune effector cells in monotherapy and combined with pembrolizumab, including increases in effector (DNAM), 'stem-like' (TCF-1) and memory CD8⁺ T cells

MDNA11: A Unique 'β-enhanced Not-α' IL-2 Albumin-fused Superkine

Beta-enhanced (30x): preferential CD8⁺ T cell expansion

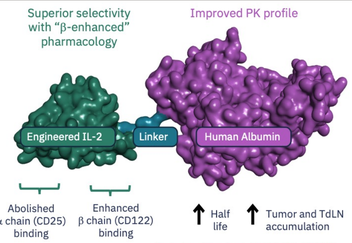
Not-alpha: reduced Treg stimulation and improved safety

Albumin fusion: half-life extension (Q2W dosing) and enhanced retention in TME & TdLN

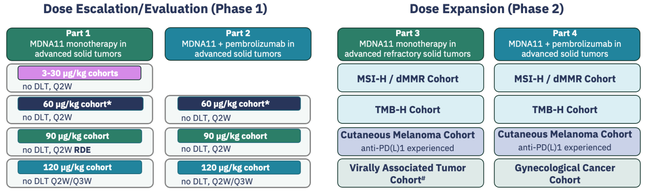
Expands 'stem-like' TCF1⁺ CD8⁺ T cells with self-renewal and memory potential

Robust single agent activity – deep & durable responses in ICI-resistant advanced solid tumors

Clinical activity in immunologically less responsive tumors combined with pembrolizumab



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



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

#replaced non-melanoma skin cancer cohort

'Phase 2 expansion eligible patients' refer to patients with cancers planned for phase 2 expansion cohorts, treated with ≥60 µg/kg MDNA11 Q2W.

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

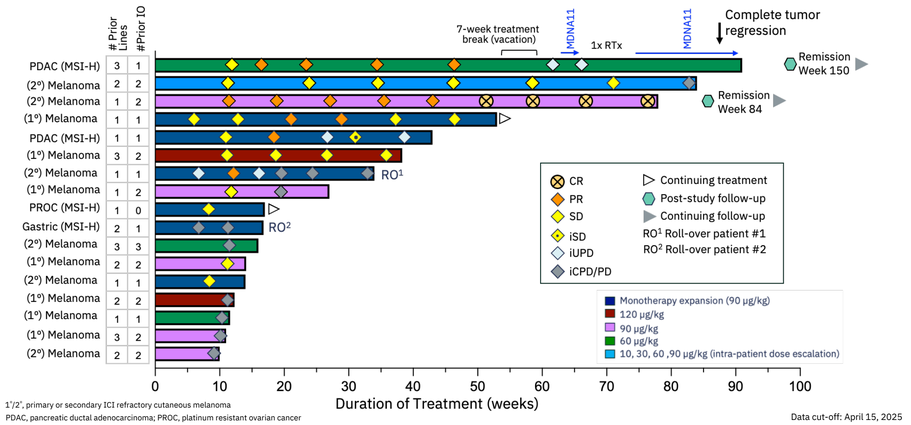
Demographics and Clinical Characteristics

Baseline Characteristics	Monotherapy (N = 47)	Combination (N = 33)
Age, median years (range)	63 (27-85)	54.5 (42-70)
Male, N (%)	32 (68.1%)	12 (36.3%)
Baseline ECOG = 0, N (%)	27 (57.4%)	13 (39.4%)
Baseline ECOG = 1, N (%)	20 (42.6%)	20 (60.6%)
Prior Systemic Therapies	**N (%)**	**N (%)***
Prior Line of Therapy: 1	15 (31.9%)	8 (25%)
Prior Line of Therapy: ≥2	32 (68.1%) [range: 2-7]	24 (75%) [range: 2-15]
Prior Immunotherapy	40 (85.1%)	18 (56.2%)
Targeted Therapy	22 (46.8%)	21 (65.6%)
Chemotherapy	21 (44.7%)	27 (84.4%)
Primary Tumor Type	**N (%)**	**N (%)**
Melanoma	20 (42.6%)	2 (6.1%)
MSI-H/dMMR (tumor agnostic)	9 (19.1%)	4 (12.1%)
Gynecological	2 (4.3%)	10 (30%)
TMB-H (tissue agnostic)	0	5 (15%)
Squamous cell carcinoma (SCC)	5 (10.6%)	2 (6.1%)
Lung cancer	2 (4.3%)	2 (6.1%)
Mesothelioma	0	2 (6.1%)
PDAC	2 (6.4%)	0
RCC	2 (4.3%)	0
Sarcoma	2 (4.3%)	0
BCC	2 (4.3%)	0
Others	1 (2.1%)	6 (18%)
Metastatic Site	**N (%)**	**N (%)**
Liver	11 (27.7%)	11 (32.3%)
Brain	4 (8.5%)	1 (3.1%)

*information not available for 1 patient

MDNA11 Monotherapy: Durable Single Agent Activity

Phase 2 Expansion Eligible and Primary ICI Resistant Melanoma Patients Treated with ≥ 60µg/kg MDNA11



1'/2', primary or secondary ICI refractory cutaneous melanoma

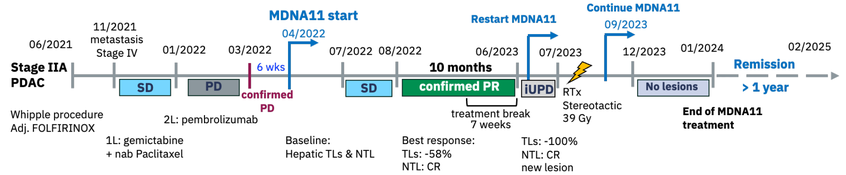
PDAC, pancreatic ductal adenocarcinoma; PROC, platinum resistant ovarian cancer

Data cut-off: April 15, 2025

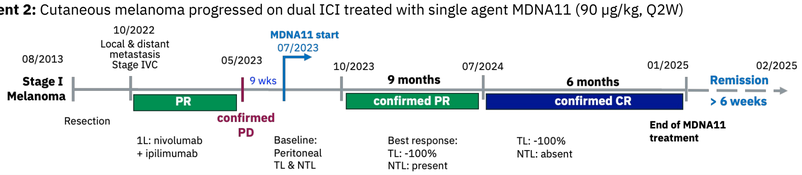
MDNA11 Monotherapy: Case Highlights with Complete Regression

2 patients continuing in post-treatment remission following complete regression of all tumor lesions

Patient 1: ICI-progressed MSI-H PDAC treated with single agent MDNA11 (60 µg/kg, Q2W)

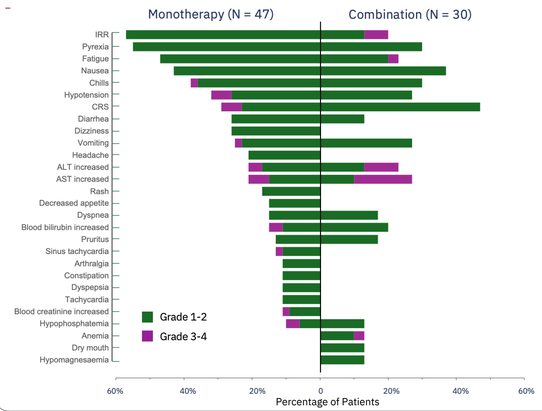


Patient 2: Cutaneous melanoma progressed on dual ICI treated with single agent MDNA11 (90 µg/kg, Q2W)



TRAEs in ≥ 10% of Patients in MDNA11 Monotherapy and Combination Cohorts

No Dose Limiting Toxicity in Either Monotherapy or Combination Dose Escalation Cohorts



Monotherapy
- Majority (92%) of TRAEs were grade 1-2, resolving within 48 hours
- Grade 3 liver function test elevations (ALT/AST) were transient and asymptomatic
- Grade 3 hypotension in patients with baseline adrenal insufficiency
- No non-laboratory grade 4 TRAE

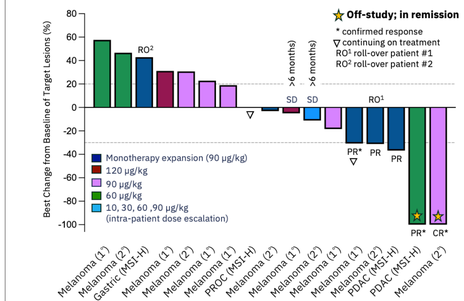
Combination Therapy
- Majority (90%) of TRAEs were grade 1-2, resolving within 48 hours
- Grade 3 liver function test elevations (ALT/AST) were transient and asymptomatic
- No non-laboratory grade 4 TRAE

IRR, immune related reaction; CRS, cytokine release syndrome; ALT, alanine aminotransferase; AST, aspartate aminotransferase

Data cut-off: April 14, 2025

Compelling Single Agent Activity in ICI Resistant Patients

Best Response in ICI Resistant Patients Treated with MDNA11 ≥ 60 µg/kg



Monotherapy ORR

29.4% (1 CR, 4 PRs)
P2 eligible patients + 1º ICI-resistant melanoma (n = 17)
95% CI: 13.3-53.1%

40% (1 CR, 3 PRs)
P2 eligible patients (n = 10)
95% CI: 16.8-68.7%

Tumor-Specific ORR

50% (2 PRs)
MSI-H/dMMR tumors (n = 4)

33% (1 CR, 1 PR)
2º ICI-resistant melanoma (n = 6)

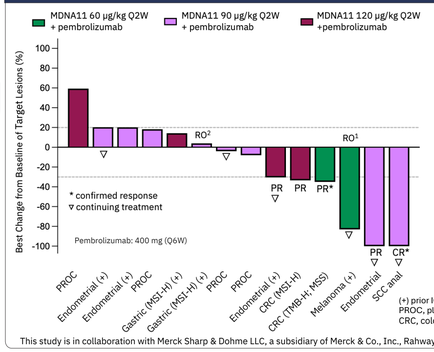
Disease Control Rate: 64.7%
1 CR, 4 PRs, 6 SDs (11/17)

Clinical Benefit Rate: 41.2%
1 CR, 4 PRs, 2 SD >6months (7/17)

1'/2', primary or secondary ICI refractory cutaneous melanoma; PDAC, pancreatic ductal adenocarcinoma; PROC, platinum resistant ovarian cancer

Data cut-off: April 15, 2025

Combination Dose Escalation: Clinical Activity Across Multiple Tumor Types



Combination ORR

35.7% (1 CR, 4 PRs)
P2 eligible patients + virally associated tumors (n = 14)
95% CI: 16.4-61.3%

30.8% (4 PRs)
P2 eligible patients (n = 13)*
95% CI: 12.7-57.6%

*excludes CR in SCC anal

Tumor-Specific ORR

50% (2 PRs)
Endometrial tumors (n = 4)

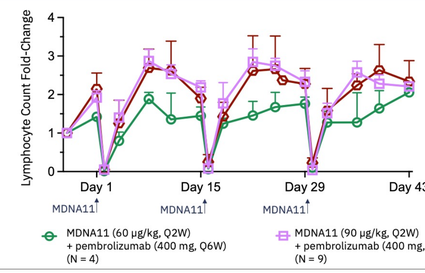
Disease Control Rate: 57.1%
1 CR, 4 PRs, 3 SDs (8/14)

(+) prior ICI exposure
PROC, platinum resistant ovarian cancer
CRC, colorectal cancer; SCC, squamous cell carcinoma

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

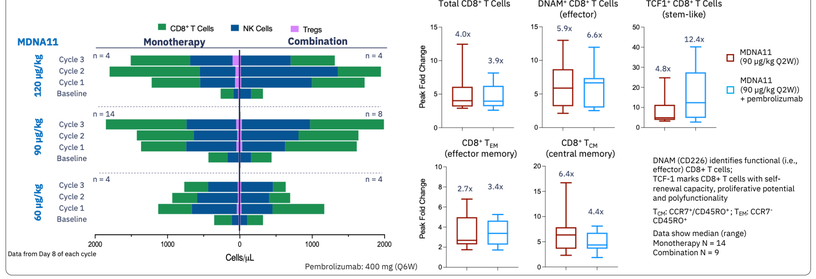
Data cut-off: April 15, 2025

Robust Lymphocyte Expansion with MDNA11 + Pembrolizumab Combination Therapy



MDNA11 Induces a Sustained Expansion of CD8⁺ T and NK Cells

MDNA11 Induces Expansion of Effector, Stem-like and Memory CD8⁺ T Cells



DNAM (CD226) identifies functional (i.e., effector) CD8+ T cells; TCF-1 marks CD8+ T cells with self-renewal capacity, proliferative potential and polyfunctionality

T_{EM}: $CCR7^{-}/CD45RO^{+}$; T_{EM}: $CCR7^{-}$ $CD45RO^{+}$

Data show median (range)
Monotherapy N = 14
Combination N = 9