

# ABILITY-1, a phase 1/2 study of MDNA11, a next generation IL-2 agonist, alone or with pembrolizumab in advanced solid tumors: interim analysis

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

**MDNA11 - the Only "β-enhanced not-α" Albumin-fused IL-2**

- β-enhanced (30x increase in affinity): Selective CD8<sup>+</sup> T and NK cell activation and proliferation
- Not-α: Reduced Treg stimulation & improved safety
- Albumin fusion: Half-life extension (Q2W/Q3W dosing) and localization in the tumor & TdLN
- Expands 'stem-like' TCF1<sup>+</sup> CD8<sup>+</sup> T cells: Sustained self-renewal and memory potential
- Robust single agent activity: Deep & durable responses in ICI-resistant advanced solid tumors
- Clinical activity in combination with pembrolizumab: In cancers not responsive to ICI

**Superior 'β-enhanced' receptor selectivity**

**Enhanced PK properties**

Engineered IL-2 + Linker + Human Albumin

α chain binding: Abolished  
β chain binding: Enhanced

↑ Half life  
↑ Tumor and TdLN accumulation

\*Structure is an artistic render using PDB (2MAC (3J2) - 1A06 (3SA))  
TdLN, Tumor draining lymph node; ICI, immune checkpoint inhibitor; ORR, objective response rate

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

**MDNA11 Monotherapy**

**Phase 1: Dose Escalation / Evaluation** (mixed advanced tumors)

- 120 μg/kg (Q2W/Q3W)
- 90 μg/kg (Q2W RDE)
- 60 μg/kg (Q2W)
- 3-30 μg/kg (Q2W)

**Phase 2: Dose Expansion** (advanced ICI resistant tumors)

- Cutaneous Melanoma (2<sup>o</sup> ICI resistant)
- MSI-H / dMMR (tumor-agnostic)
- TMB-H (tumor-agnostic)
- Viral-Associated

**MDNA11 + Pembrolizumab**

**Phase 1: Dose Escalation / Evaluation** (mixed advanced solid tumors)

- 120 μg/kg (Q2W/Q3W)
- 90 μg/kg (Q2W eRDE)
- 60 μg/kg (Q2W)

**Phase 2: Dose Expansion** (advanced ICI resistant tumors)

- Cutaneous Melanoma (1<sup>o</sup> ICI resistant)
- MSI-H / dMMR (tumor-agnostic)
- TMB-H (tumor-agnostic)
- Gynecological

BEDR, biological effective dose range  
ABILITY-1: A Beta-only IL-2 ImmunoTherapy Study (NCT05086692)  
\*Phase 2 eligible patients\* refer to patients with cancers selected for phase 2 expansion cohorts treated with ≥60 μg/kg MDNA11 (OBD range)  
MSI-H/dMMR and TMB-H (≥ 10 mut/Mb) biomarkers based on local laboratory testing  
This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

## Patient Baseline Characteristics

Baseline Characteristics	Monotherapy (N = 61)	Combination Therapy (N = 50)
Age, median years (range)	63 (27, 85)	63 (31, 76)
Male, N (%)	35 (57.4%)	20 (40.0%)
ECOG, N (%)	0 (65.6%) 1 (34.4%)	25 (50.0%) 25 (50.0%)
Prior Lines of Therapy, N (%)	46 (75.4%) 1-3L ≥4L [range]	29 (58.0%) 1-3L [4-15]
Prior ICI, N (%)	49 (80.3%)	34 (68.0%)
Target Lesion SOD, median mm [range]	75 [10.4-306.5]	80.0 [13-345]
LDH (U/L), N (%)	19 (31.1%) > 250	21 (42.0%)
Liver Metastasis, N (%)	13 (21.3%)	16 (32.0%)
Brain Metastasis, N (%)	3 (4.9%)	1 (2.0%)

ICI, immune checkpoint inhibitor; LDH, lactate dehydrogenase

**Patients with 29 Different Advanced Stage Solid Cancers Enrolled**

Response achieved in 7 tumor types

**ABILITY-1 TRIAL**  
Monotherapy (N=61)  
Combination (N=50)

**Head & Neck:** SCC of Tongue: 1 (1.6%), Neuroendocrine: 1 (2.0%), Salivary Adenocarcinoma: 1 (2.0%)

**Lung:** NSCLC: 3 (4.9%), SCLC: 5 (10.0%), Mesothelioma: 2 (4.0%), SCLC: 1 (2.0%)

**Mammary:** TNBC: 3 (4.9%), Breast: 2 (4.0%)

**Skin and Soft Tissue:** Cutaneous Melanoma: 20 (32.8%), Adipocarcinoma: 2 (3.3%), Basal Cell Carcinoma: 1 (1.7%), Squamous Cell Carcinoma: 2 (3.3%)

**Gastrointestinal:** Colon: 4 (6.6%), Gastric: 3 (4.9%), Esophageal: 1 (2.0%), Pancreatic: 1 (2.0%), Hepatocellular: 1 (2.0%)

**Reproductive Tract:** Ovarian: 4 (6.6%), Endometrial: 1 (1.6%), Cervical: 1 (1.6%), Testicular: 1 (1.6%), Uterine: 1 (2.0%)

ICI, immune checkpoint inhibitor; LDH, lactate dehydrogenase

## Safety Profile Consistent with MoA of MDNA11

Monotherapy (N = 61) | Combination (N = 50)

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

- No DLTs in monotherapy or combination therapy up to 120 μg/kg
- >90% TRAEs grade 1-2 and transient, resolving by 48 hours
- Grade 3-4 mainly laboratory abnormalities without clinical sequelae
- Single transient Grade 4 CRS in a patient with low baseline blood pressure

TRAES in ≥ 15% of patients in monotherapy or combination therapy. Multiple events of the same TRAE in the same patient is counted once at the highest grade.

## Durable Single Agent Activity in Phase-2 Eligible Expansion Cohorts

MDNA11 ≥ 60 μg/kg

New lesions developed and stabilized; shrinkage of target lesions by >80%

Cutaneous Melanoma (ICI 2<sup>o</sup> Resistance): Off-treatment remission for >7 months

7-week treatment break, Complete Tumor Regression, Off-treatment remission for >21 months

Legend: CR (Complete Response), PR (Partial Response), SD (Stable Disease), IUPD (Incompletable/Unplanned Discontinuation), ICPD/PD (Incompletable/Planned Discontinuation), Tumor Re-stage, Roll over portion

PDAC, pancreatic ductal adenocarcinoma; CRC, colorectal cancer; NET, neuroendocrine tumor; cSCC, cutaneous squamous cell carcinoma

## Cutaneous Melanoma - secondary ICI resistance

Cutaneous Melanoma N = 8 | MSI-H/dMMR N = 9 | TMB-H N = 5

- ORR of 37.5% (1 CR + 2 PRs)
- DCR of 75% (1 CR + 2 PRs + 3 SD)
- Tumor regression in 6 of 8 (75%) patients

**MSI-H/dMMR Tumors progressed on ICI:**

- ORR of 22.2% (2 PRs)
- DCR of 77.8% (2 PRs + 5 SD)

ORR of 41.7% and DCR of 83.4% with MDNA11 as next therapy post-ICI progression

CR + PR: 16.7%, SD: 41.7%, PD: 41.7%

## Encouraging Clinical Activity in Combination Phase-2 Eligible Expansion Cohorts

MDNA11 ≥ 60 μg/kg (Q2W/Q3W) + 400 mg Pembrolizumab (Q6W)

Deepening tumor response (-36%) at week 49 (>10 wks after end of treatment)

Further deepening tumor response (-42.6%) at week 75 (>40 wks after end of treatment)

CR, colorectal cancer; SCLC, small cell lung cancer; TNBC, triple negative breast cancer; RCC, renal cell carcinoma; NSCLC, non-small cell lung cancer

## Microsatellite-stable Endometrial Cancer (ICI 2<sup>o</sup> Resistance)

MSI-H Endometrial (N = 6) | MSI-H (N = 5) | TMB-H (N = 8) | MSS Endometrial (N = 4)

- ORR of 50% (2 PRs)
- DCR of 75% (2 PRs + 1 SD)

**TMB-H (≥ 10 mut/Mb) Tumors:**

- ORR of 25% (2 PRs; CRC and breast)
- DCR of 87.5% (2 PRs + 5 SD)
- Tumor regression in 6 of 8 (75%) patients

## Monotherapy Efficacy in ICI-Resistant Cancers

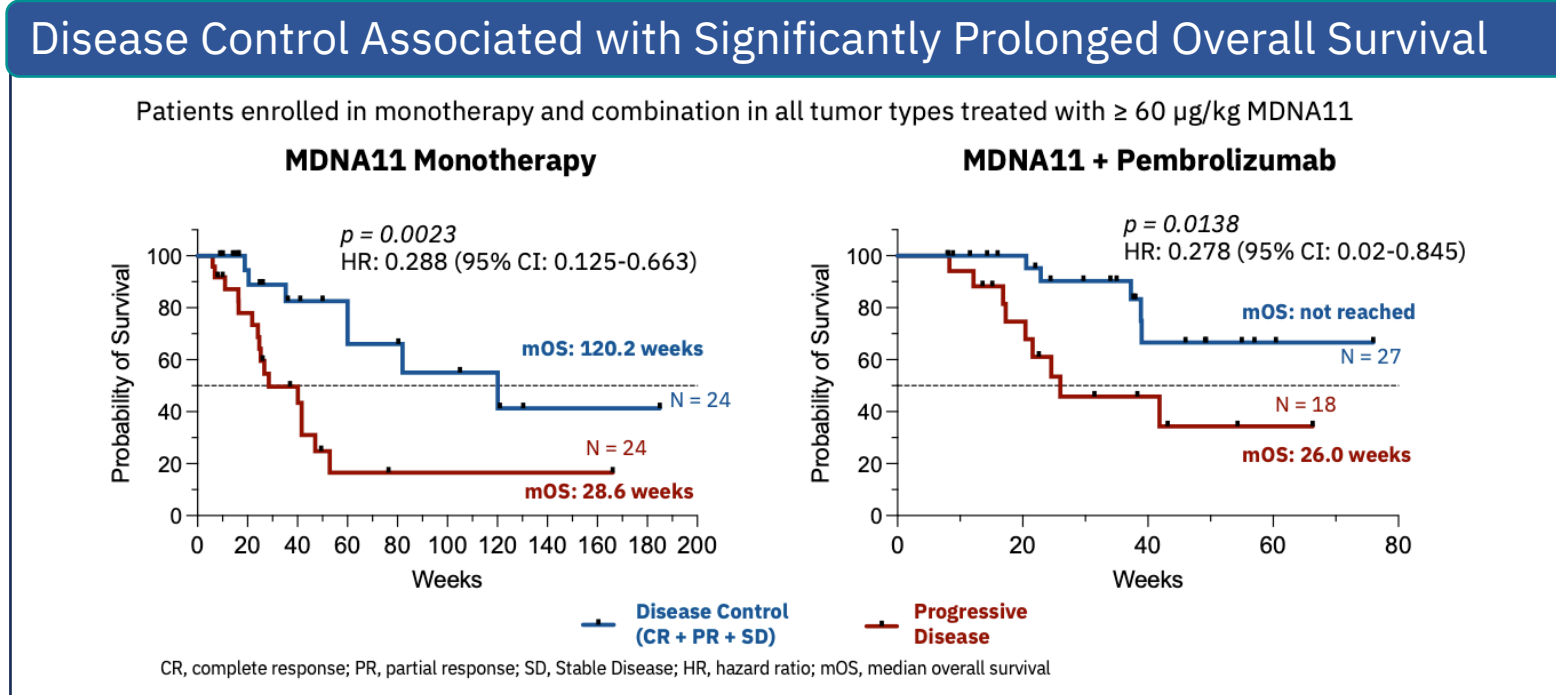
MDNA11 ≥ 60 μg/kg	Case 1	Case 2	Case 3	Case 4	Case 5
<b>Tumor</b>	Cutaneous Melanoma	Cutaneous Melanoma	Cutaneous Melanoma	MSI-H PDAC	MSI-H PDAC
<b>Age (yr)</b>	62	64	56	55	85
<b>Tumor Mutation(s)</b>	BRAF T599dup	BRAF V600K	NRAS mutation	-	-
<b>Prior ICI</b>	Nivolumab + Ipilimumab	Pembrolizumab	Nivolumab + Ipilimumab	Pembrolizumab	Pembrolizumab
<b>ICI resistance Feature</b>	Secondary	Secondary	Secondary	Primary	Secondary
<b>Response to MDNA11 Monotherapy</b>					
<b>Target lesion shrinkage</b>	-100%	-31.7%	-31.2%	-100%	-36.8%
<b>Liver Metastasis</b>	No	No	Yes	Yes	No
<b>BOR</b>	CR	PR	PR	PR	PR

BOR, best overall response

## Combination Efficacy in ICI-Resistant/Ineligible Cancers

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8 (roll-over)*
<b>Tumor</b>	TMB-H Breast (22 mut/Mb)	TMB-H CRC (67 mut/Mb)	MSS Endometrial	MSS Endometrial	MSI-H CRC	Cutaneous Melanoma	SCC anal	TMB-H NET Bladder
<b>Age (yr)</b>	60	51	63	67	75	43	70	53
<b>Prior Lines of Therapy</b>	9	2	2	3	1	1	2	4
<b>Prior ICI</b>	Not eligible	Not eligible	Pembrolizumab (+ levatinib)	Pembrolizumab	Not eligible	Nivolumab + Ipilimumab	Not eligible	Not eligible
<b>ICI resistance Feature</b>	-	-	Secondary	Secondary	-	Primary	-	-
<b>Response to MDNA11 + Pembrolizumab</b>								
<b>Target Shrinkage</b>	-76.1%	-42.6%	-100%	-36.1%	-33.4%	-30.7%	-100%	-59.3%
<b>Liver Metastasis</b>	Yes	No	No	No	No	Yes	No	No
<b>BOR</b>	PR	PR	PR	PR	PR	PR	PR	PR

\*enrolled in MDNA11 monotherapy and rolled over to MDNA11 + pembrolizumab; MSS, microsatellite stable; BOR, best overall response



## MDNA11 in Advanced Solid Tumors – Key Takeaways

- Manageable safety profile:** No DLTs observed in any cohort. >90% TRAEs were grade 1-2 and transient
- Biological Effective Dose Range (BEDR):** Preliminary recommended dose for expansion (pRDE) for monotherapy and combination arms was established at 90 μg/kg (Q2W) with the BEDR set at 60 to 120 μg/kg (Q2W or Q3W)
- Durable single-agent activity in ICI-resistant disease:** 55 efficacy evaluable patients enrolled across 18 tumor types; 48 patients treated at BEDR. Among ICI resistant/ineligible cancers in Phase 2 expansion cohorts (N = 22), ORR was 22.7% (95% CI, 10.1-43.4) and DCR was 68%  
In expansion cohorts, the response rates were:
  - Cutaneous melanoma** (secondary ICI resistance): **ORR 37.5%** (95% CI, 13.7-69.4), **DCR 75%**
    - Remission-free survival in one patient was > 7 months post MDNA11
  - MSI-H/dMMR tumors:** **ORR 22.2%** (95% CI, 6.3-54.7), **DCR 77.8%**
    - Remission free survival of one PDAC patient was > 21 months post MDNA11
- Encouraging efficacy with pembrolizumab:** 46 efficacy evaluable patients enrolled across 19 tumor types at BEDR. Among ICI resistant/ineligible cancers in Phase 2 combination expansion cohorts (N = 30), ORR was 20% (95% CI, 9.5-37.3) and DCR was 60%  
In combination expansion cohorts, the response rates were:
  - MSS endometrial cancer** with secondary ICI resistance: **ORR 50%** (95% CI, 15-85), **DCR 75%**
  - TMB-H (MSS) tumors** (breast and colon): **ORR 25%** (95%, 7.2-59.1), **DCR 87.5%**
  - 2 additional PRs in anal SCC and ICI primary resistant cutaneous melanoma

**Disease control is associated with substantially prolonged overall survival in both monotherapy & combination cohorts**

We are extremely grateful to the patients and their families for participating in this study. We acknowledge all clinical sites, principal investigators and staff for supporting this study. Information on 'Declaration of Interest' has been submitted to ESMO.

