

**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**

10 December 2025

ESMO-IO Congress 2025



MEDICENNA

Authorship and Affiliations

Andre Mansinho¹, Victoria Atkinson², Jacqueline T. Brown³, Luiz Cabezon-Gutierrez⁴, Sara Coelho⁵, Cinta Hierro⁶, Austin Duffy⁷, Pablo Gajate Borau⁸, Irene Moreno⁹, Hong Shue¹⁰, Michael J. Chisamore¹¹, Amy Prawira¹², Fahar Merchant¹³, Melissa Coello¹³, Minh D. To¹³, Arash Yavari¹³, Nina Merchant¹³, Paolo A. Ascierto¹⁴

¹START Lisbon Centro de Ensaaios Clínicos, ULS Sta Maria, Lisbon, Portugal

²Greenslopes Private Hospital, Gallipoli Research Foundation University of Queensland, Australia

³Emory Winship Cancer Institute, Atlanta, GA, USA

⁴Hospital Universitario de Torrejon, Torrejon de Ardoz (Madrid), Spain

⁵Instituto Português de Oncologia do Porto, Porto, Portugal

⁶Institut Català d'Oncologia, Badalona, Spain

⁷START Dublin, Mater Misericordiae University Hospital, Dublin, Ireland

⁸Hospital Universitario Ramon y Cajal, Madrid, Spain

⁹START Madrid – Centro Oncologico Clara Campal CIOCC HM Hospital, Madrid, Spain

¹⁰Sunshine Coast Haematology and Oncology Clinic, Buderim, Australia

¹¹Merck & Co., Inc., Rahway, NJ, USA

¹²Obatica Pty Ltd, Sydney, Australia

¹³Medicenna Therapeutics, Toronto, ON, Canada

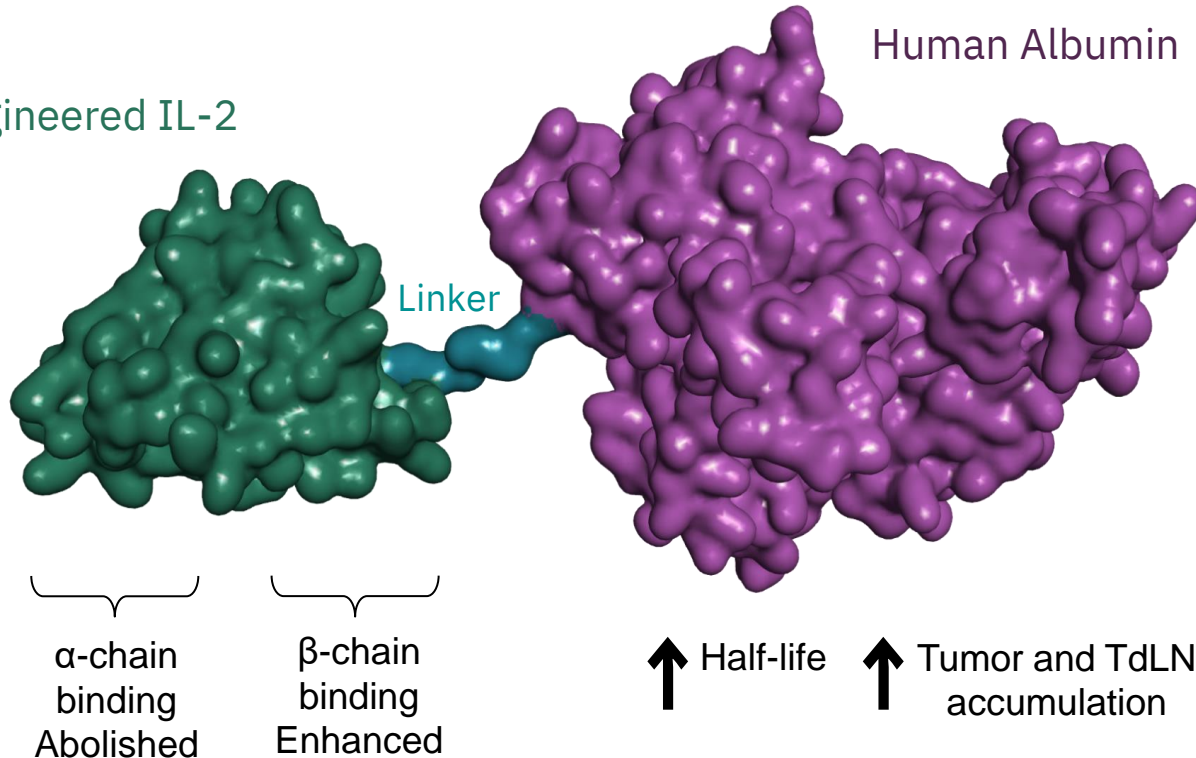
¹⁴Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli, Italy

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

Superior 'β-enhanced' receptor selectivity

Enhanced PK properties

Engineered IL-2



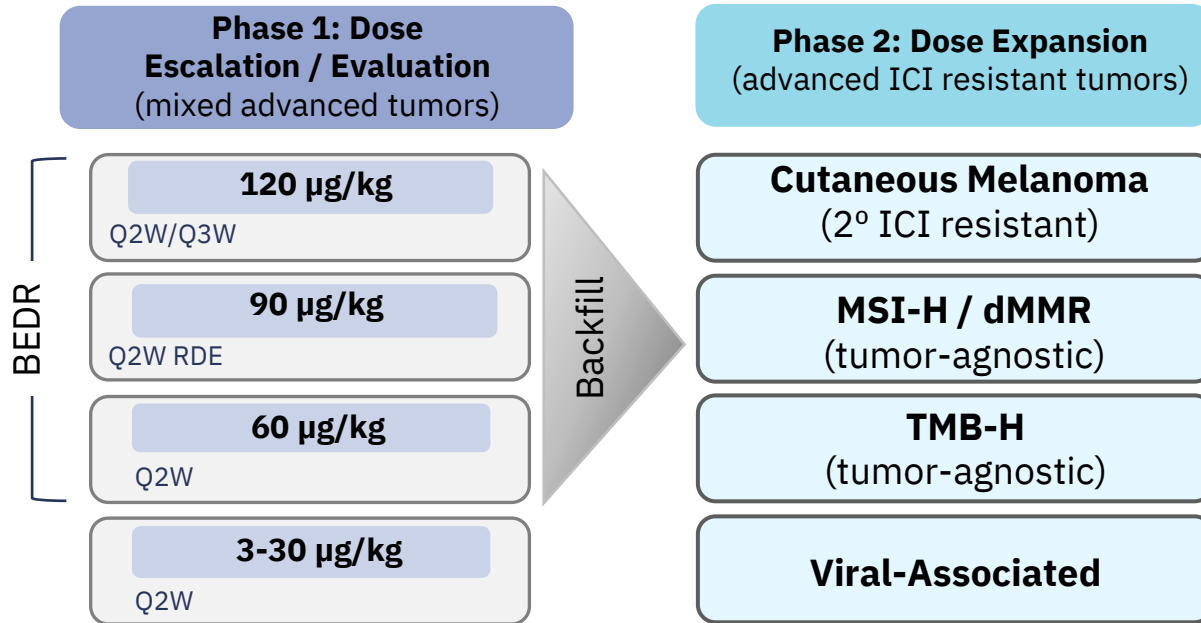
MDNA11, the Only "β-enhanced not-α" Albumin-fused IL-2

- β-enhanced (30× increase in affinity): Selective CD8⁺ 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⁺ CD8⁺ 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

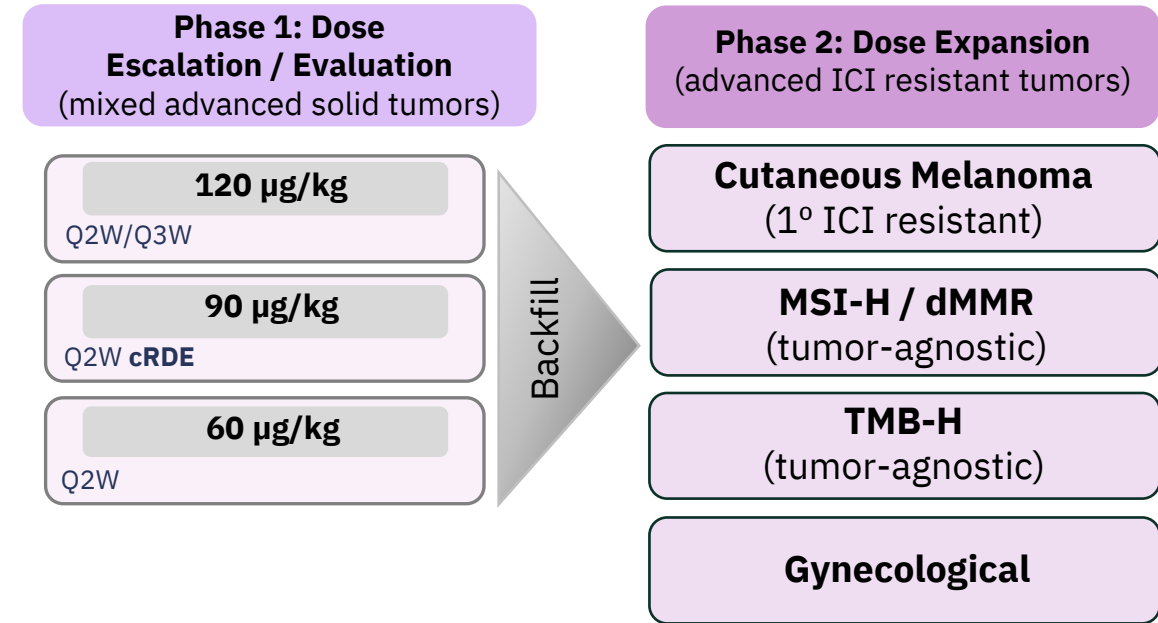
*Structure is an artistic render using PDB (1M4C (hIL2) – 1A06 (HSA))

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

MDNA11 Monotherapy



MDNA11 + Pembrolizumab



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
Mechanical fixes only:

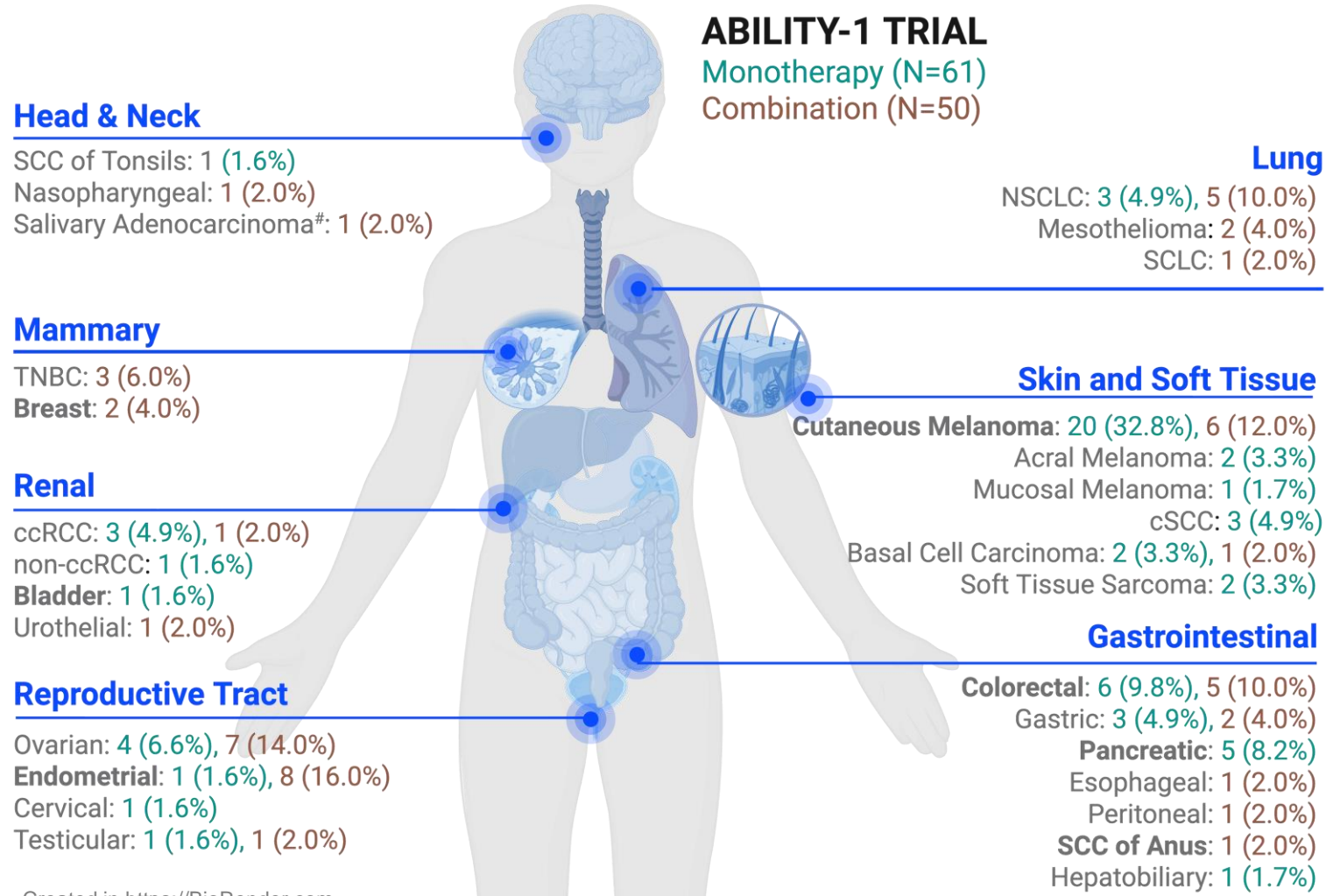
This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

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 1	40 (65.6%) 21 (34.4%)	25 (50.0%) 25 (50.0%)
Prior Lines of Therapy, N (%)	1-3L ≥4L [range]	46 (75.4%) 15 (24.6%) [4-7]	29 (58.0%) 21 (42.0%) [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 (%)	> 250	19 (31.1%)	21 (42.0%)
Liver Metastasis, N (%)		13 (21.3%)	16 (32.0%)
Brain Metastasis, N (%)		3 (4.9%)	1 (2.0%)

Patients with 29 Different Advanced Stage Solid Cancers Enrolled

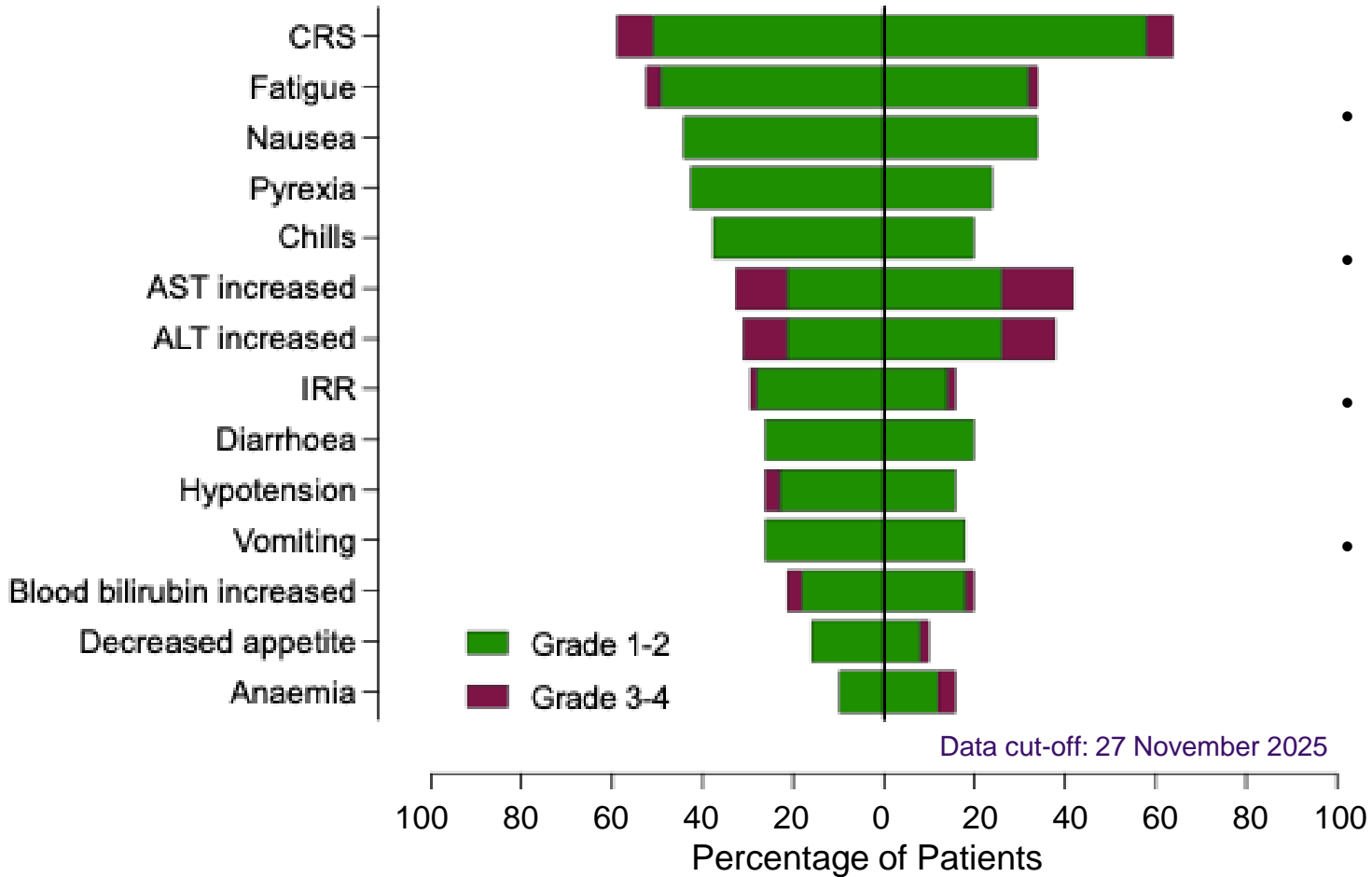
Response achieved in 7 tumor types



cSCC, cutaneous squamous cell carcinoma; TNBC, triple-negative breast cancer; ccRCC, clear cell renal cell carcinoma; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer

Summary of Monotherapy and Combination Therapy Safety

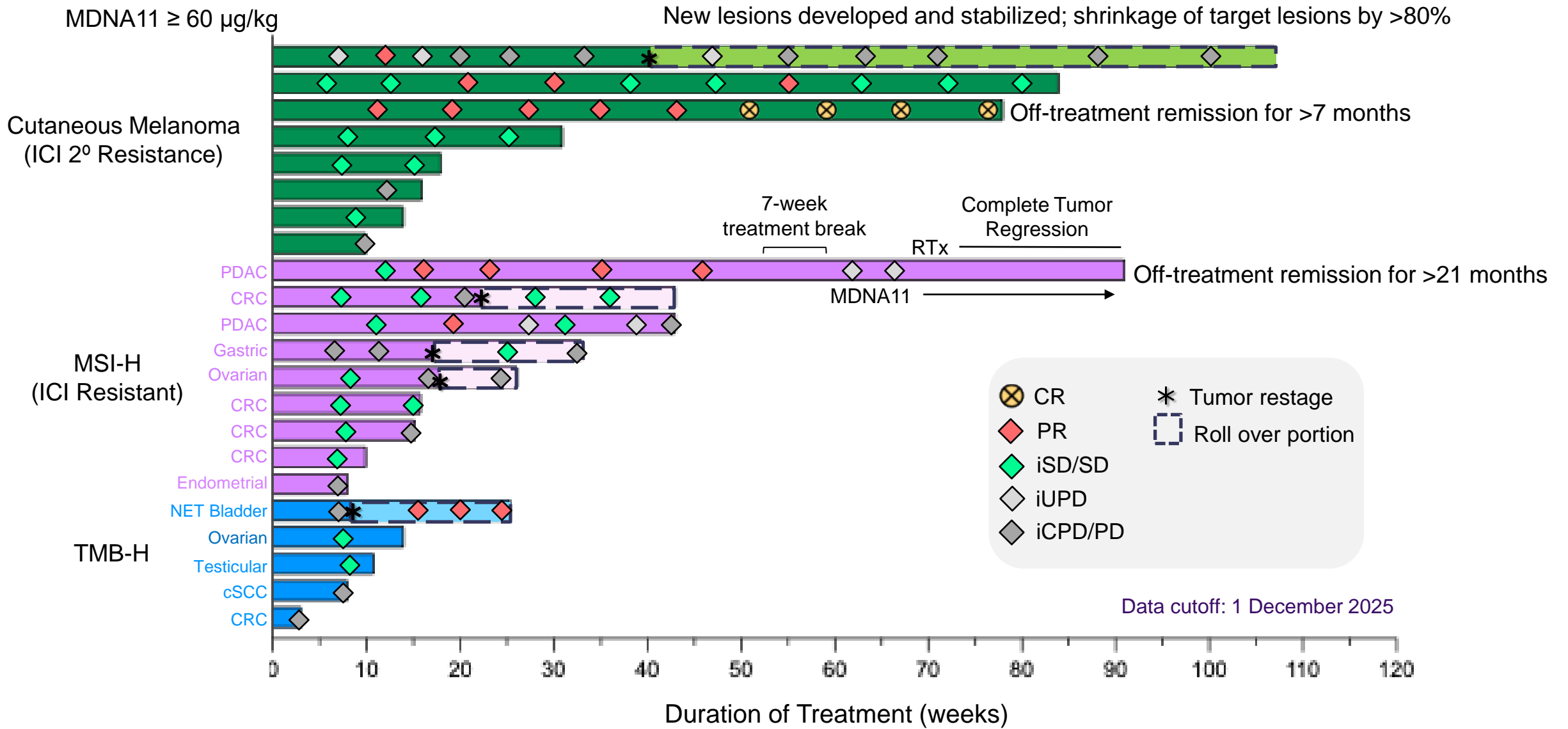
Monotherapy (N = 61) Combination (N = 50)



- **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

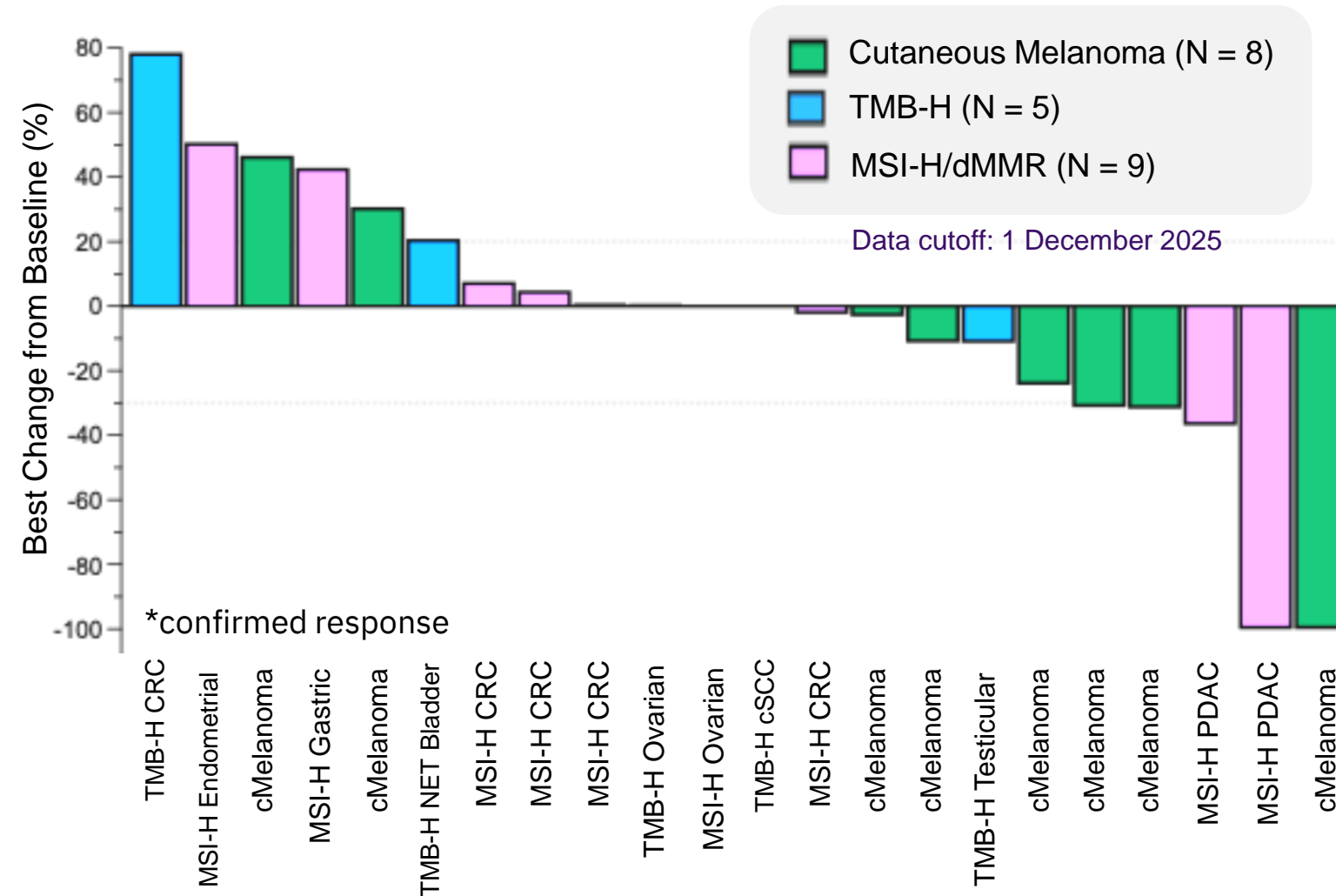
TRAEs in ≥15% of patients in monotherapy or combination therapy. Multiple events of the same TRAE in the same patient are counted once at the highest grade.

Durable Single Agent Activity in Phase-2 Eligible Expansion Cohorts



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

Single-agent activity in Phase 2–eligible expansion cohorts



Cutaneous melanoma

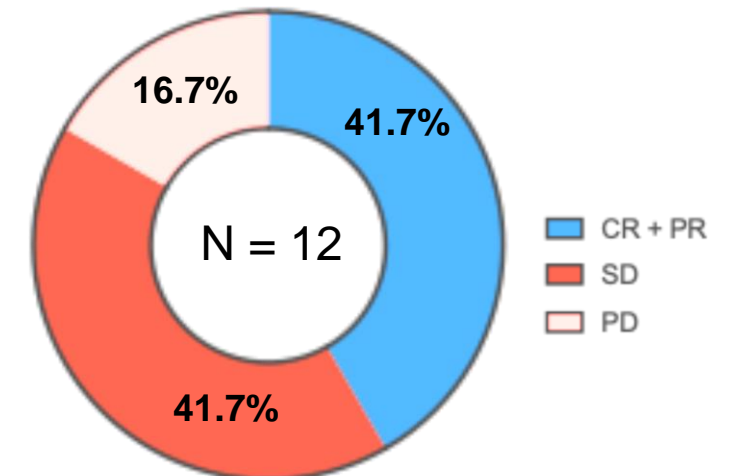
Secondary ICI resistance:

- 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



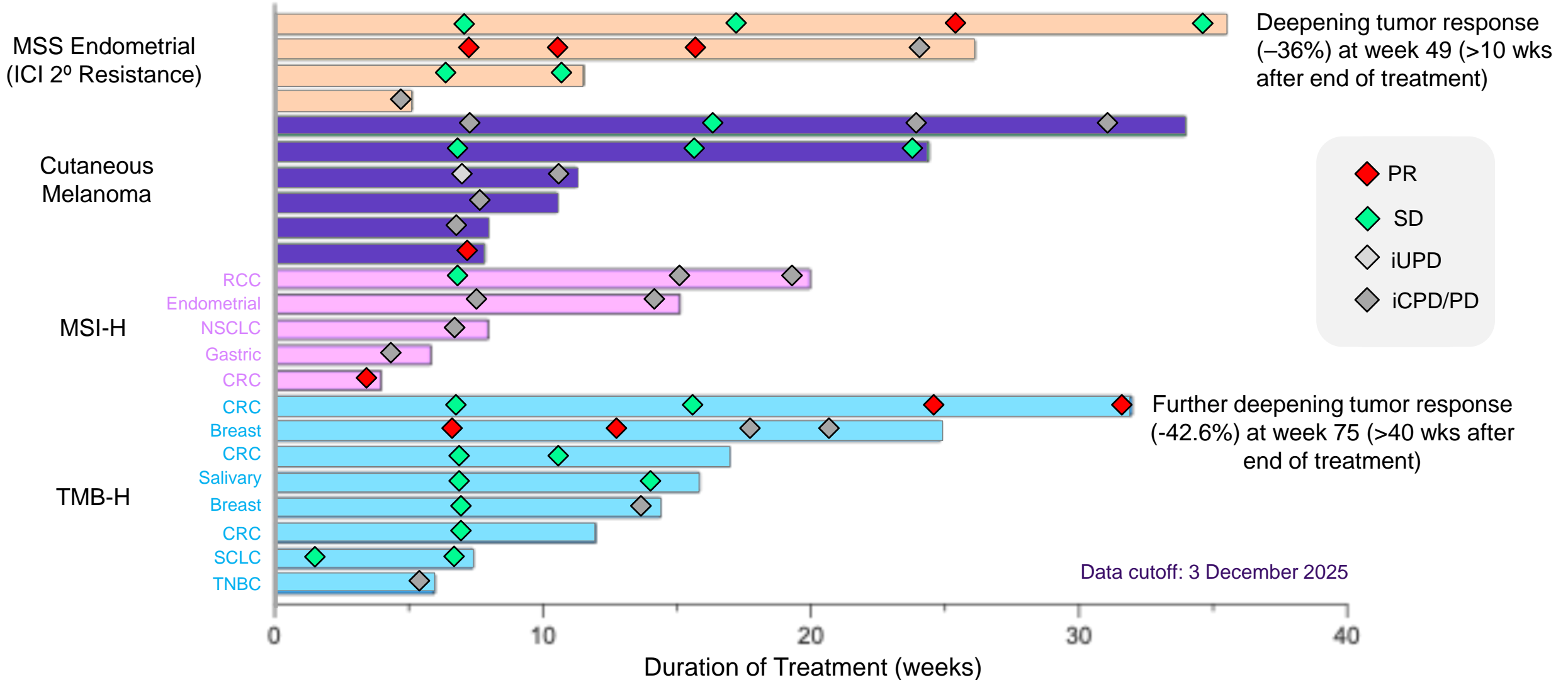
Monotherapy efficacy in ICI-resistant cancers

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

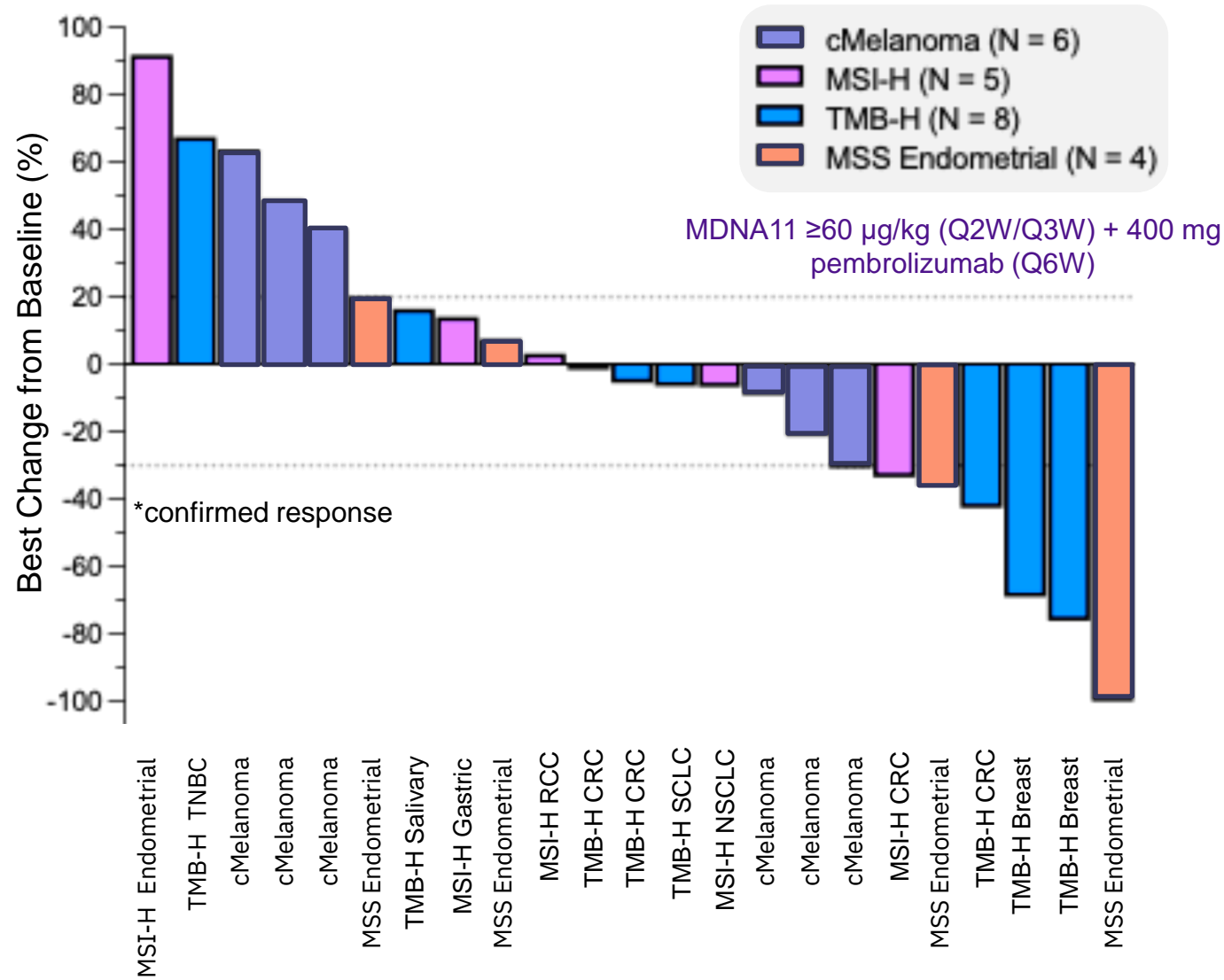
BOR, best overall response

Encouraging Clinical Activity in Combination Phase 2–Eligible Expansion Cohorts

MDNA11 ≥ 60 $\mu\text{g}/\text{kg}$ (Q2W/Q3W) + 400 mg pembrolizumab (Q6W)



Encouraging Clinical Activity with MDNA11 + Pembrolizumab in Phase 2–Eligible Expansion Cohorts



Microsatellite-stable **Endometrial Cancer** (ICI 2^o Resistance):

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

TMB-H (\geq 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

Combination Efficacy in ICI-Resistant/Ineligible Cancer

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8 (roll-over)*
Tumor	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
Age (yr)	60	51	63	67	75	43	70	53
Prior Lines of Therapy	9	2	2	3	1	1	2	4
Prior ICI	Not eligible	Not eligible	Pembrolizumab (+ levatinib)	Pembrolizumab	Not eligible	Nivolumab + Ipilimumab	Not eligible	Not eligible
ICI resistance Feature	-	-	Secondary	Secondary	-	Primary	-	-

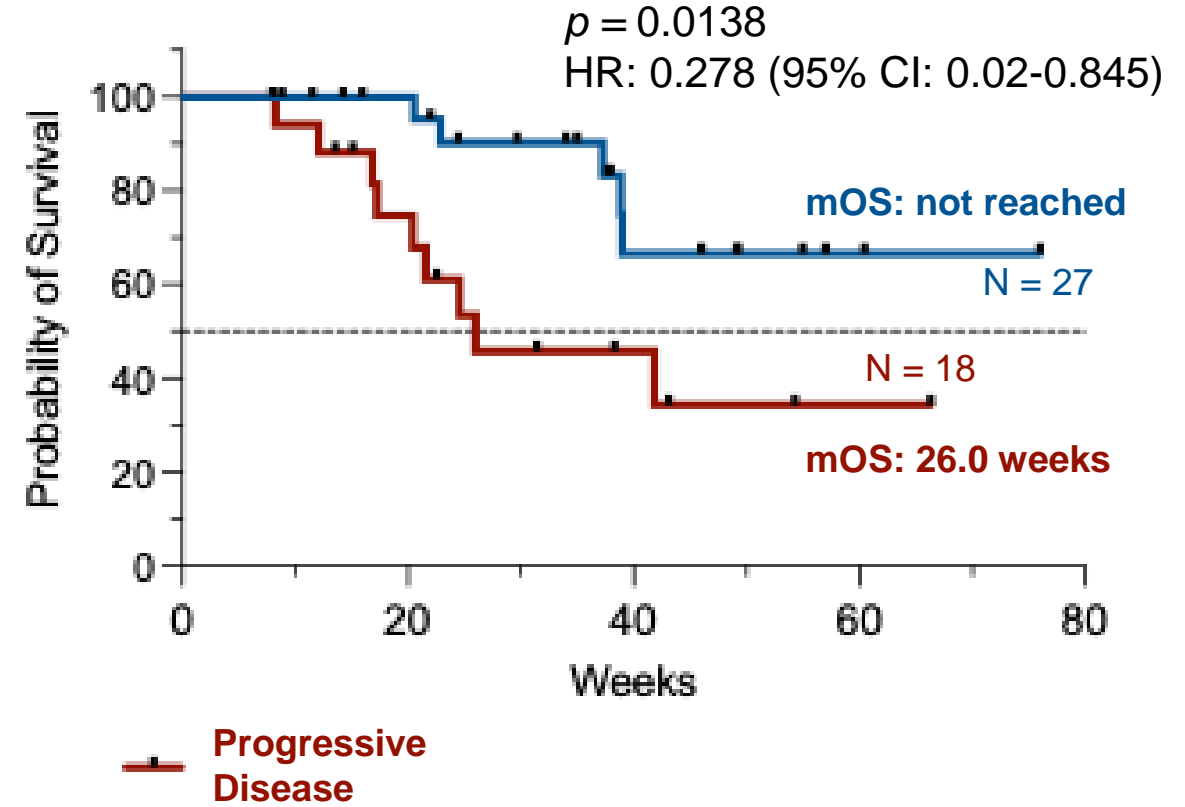
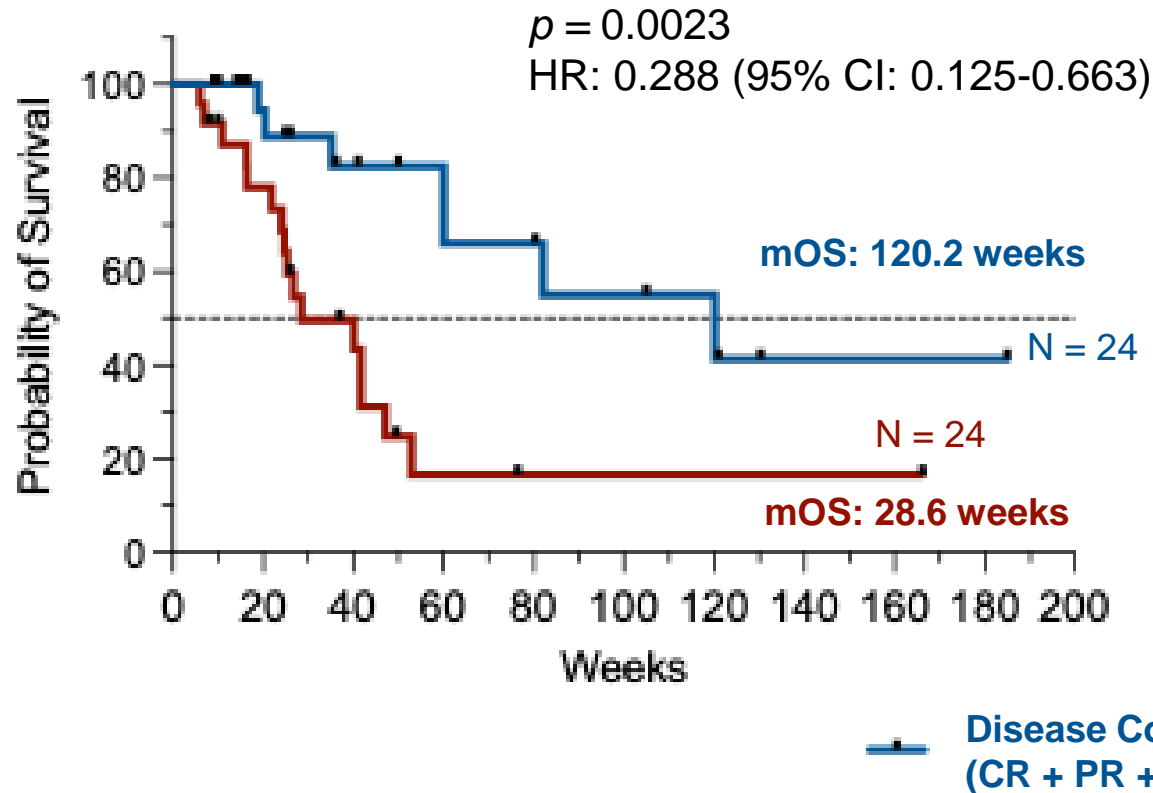
Response to MDNA11 + Pembrolizumab

Target Shrinkage	-76.1%	-42.6%	-100%	-36.1%	-33.4%	-30.7%	-100%	-59.3%
Liver Metastasis	Yes	No	No	No	No	Yes	No	No
BOR	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

Disease Control with MDNA11 is Associated with Significantly Prolonged Overall Survival

Patients enrolled in monotherapy and combination in all tumor types treated with $\geq 60 \mu\text{g/kg}$ MDNA11



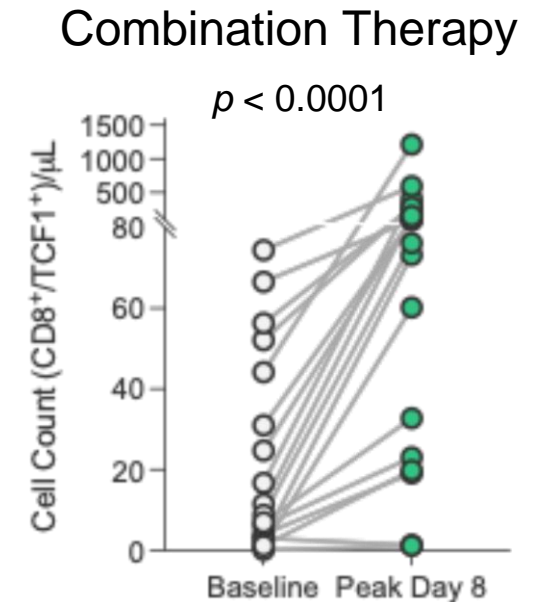
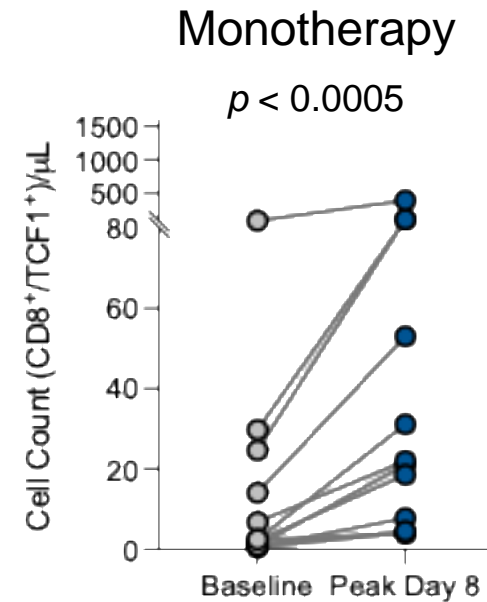
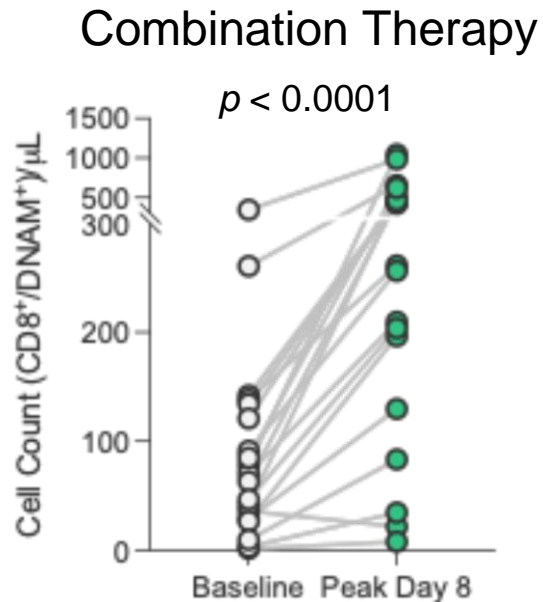
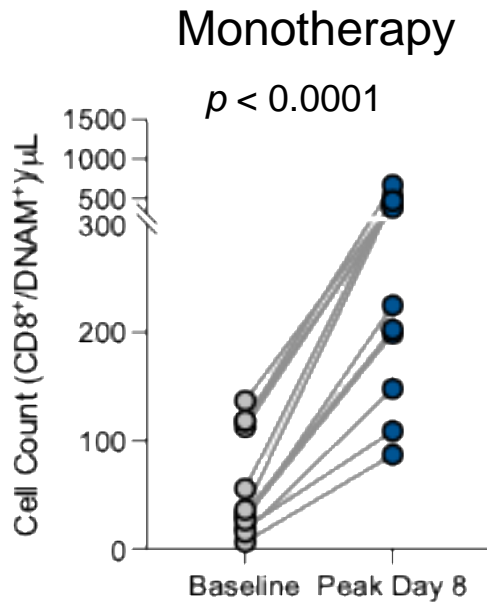
CR, complete response; PR, partial response; SD, Stable Disease; HR, hazard ratio; mOS, median overall survival

Robust Expansion of Effector and Stem-like CD8⁺ T Cells

Peak CD8⁺ T cell response in peripheral blood at 90 µg/kg MDNA11

Effector CD8⁺ T cells

Stem-like CD8⁺ T cells



Statistics using paired t-test

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 ug/kg (Q2W) with the BEDR set at 60 to 120 ug/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

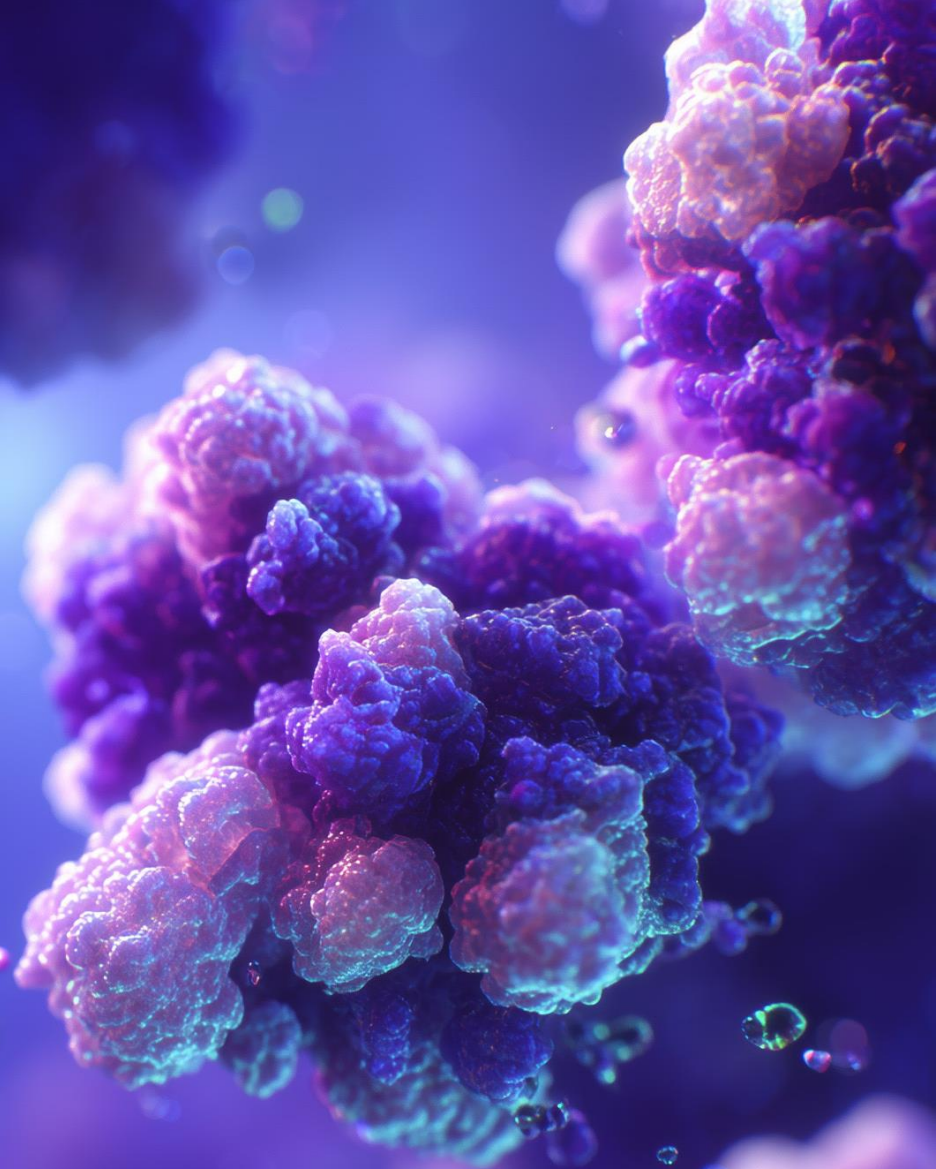
Encouraging efficacy with pembrolizumab: 46 efficacy evaluable patients enrolled across 19 tumor types at BEDR. Among ICI resistant/ineligible cancers in Phase 2 combination expansion cohorts (N = 30), ORR was 20% (95% CI, 9.5-37.3) and DCR was 60%

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

Supplementary Data

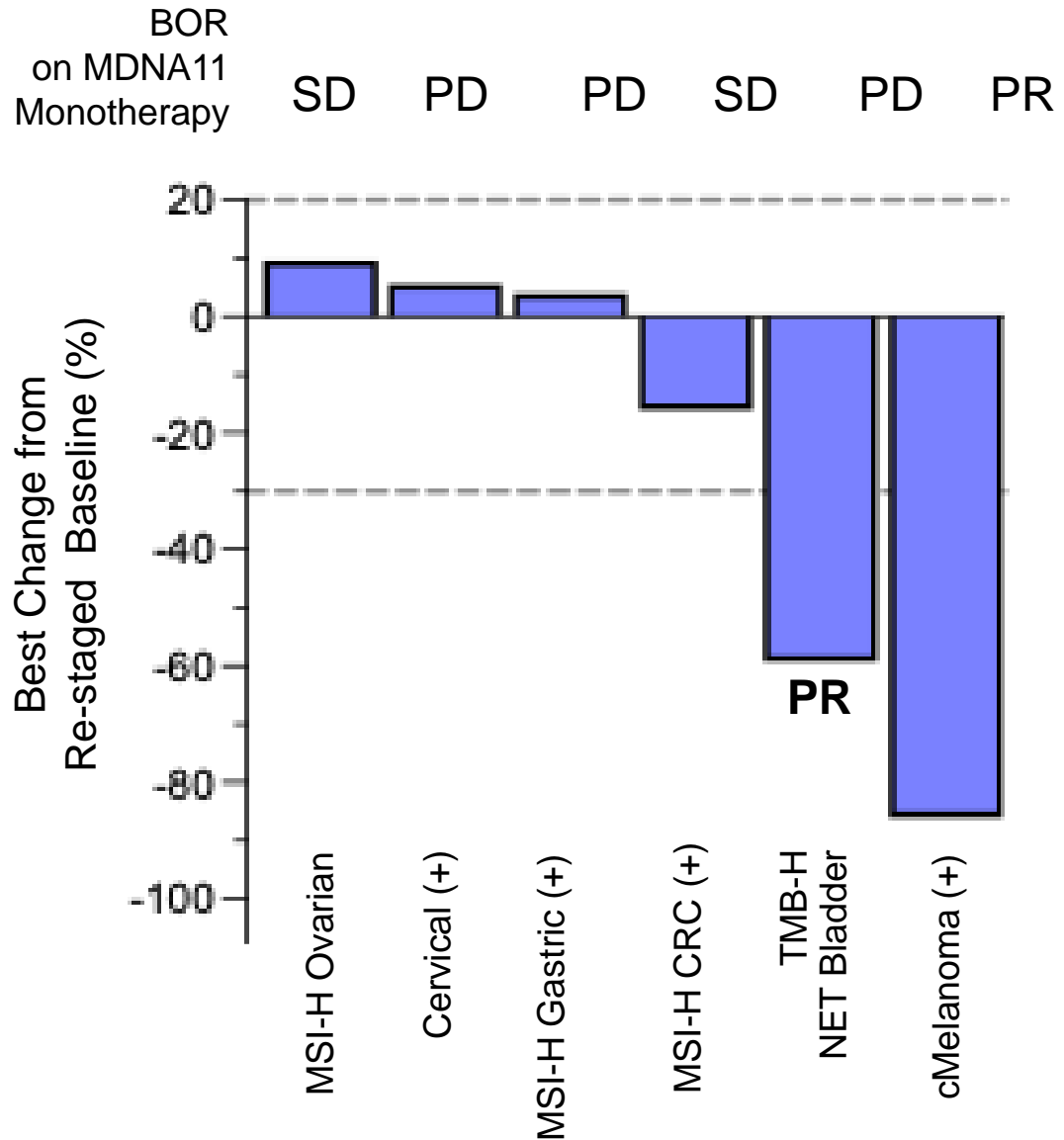


ORR in Phase 2 Eligible Monotherapy and Combination Expansion Cohorts

	MDNA11 Monotherapy		MDNA11 + Pembrolizumab	
	Cutaneous Melanoma (ICI 2 ^o resistance)	MSI-H Tumors (ICI experienced)	Endometrial (ICI 2 ^o resistance)	TMB-H Tumors
ORR	37.5% (3/8) [95% CI: 13.7-69.4]	22.2 % (2/9) [95% CI: 6.3-54.7]	50.0% (2/4) [95% CI: 15-85]	25.0% (2/8) [96% CI: 7.2-59.1]
DCR	75% (6/8)	77.8% (7/9)	75.0% (3/4)	87.5% (7/8)

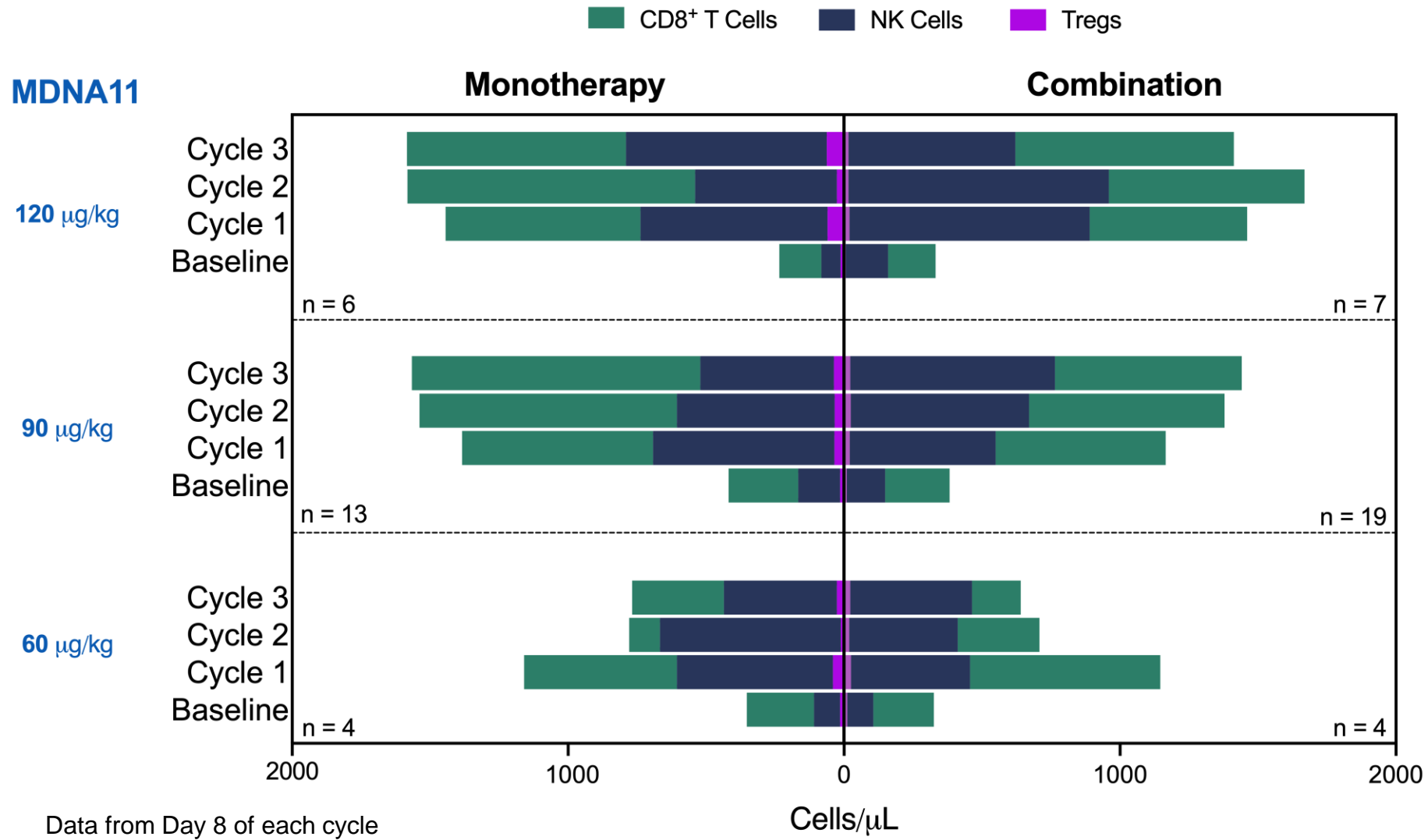
ORR, objective response rate (CR + PR)
DCR, disease control rate (CR + PR + SD)

Tumor Regression in 50% of Monotherapy Roll Over Patients



CRC, colorectal cancer; NET, neuroendocrine tumor; BOR, best overall response

Sustained Expansion and Activation of CD8+ T and NK Cells



Data from Day 8 of each cycle

Cells/µL