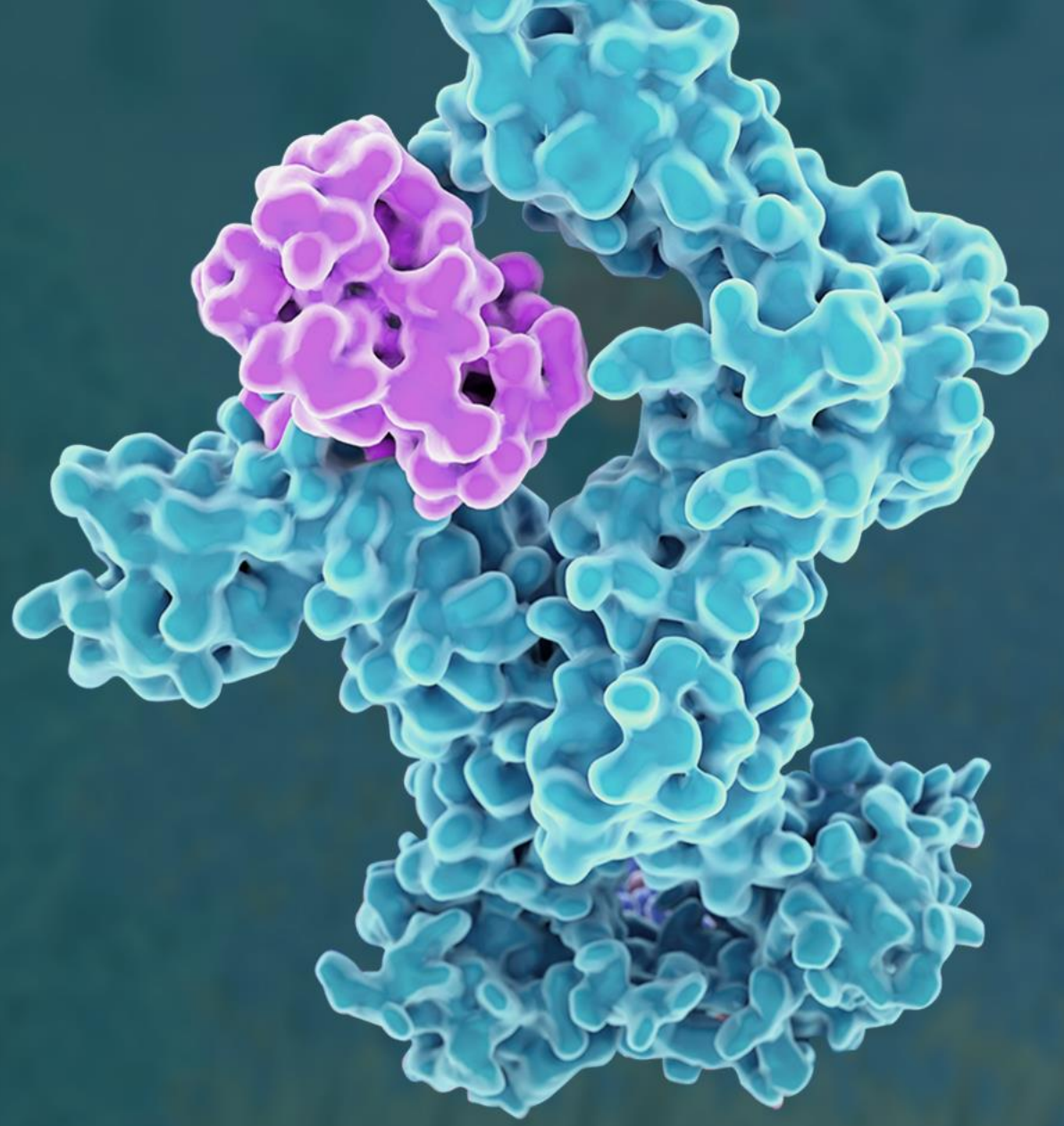
April 28, 2025

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

AACR 2025

Chicago, Illinois, USA



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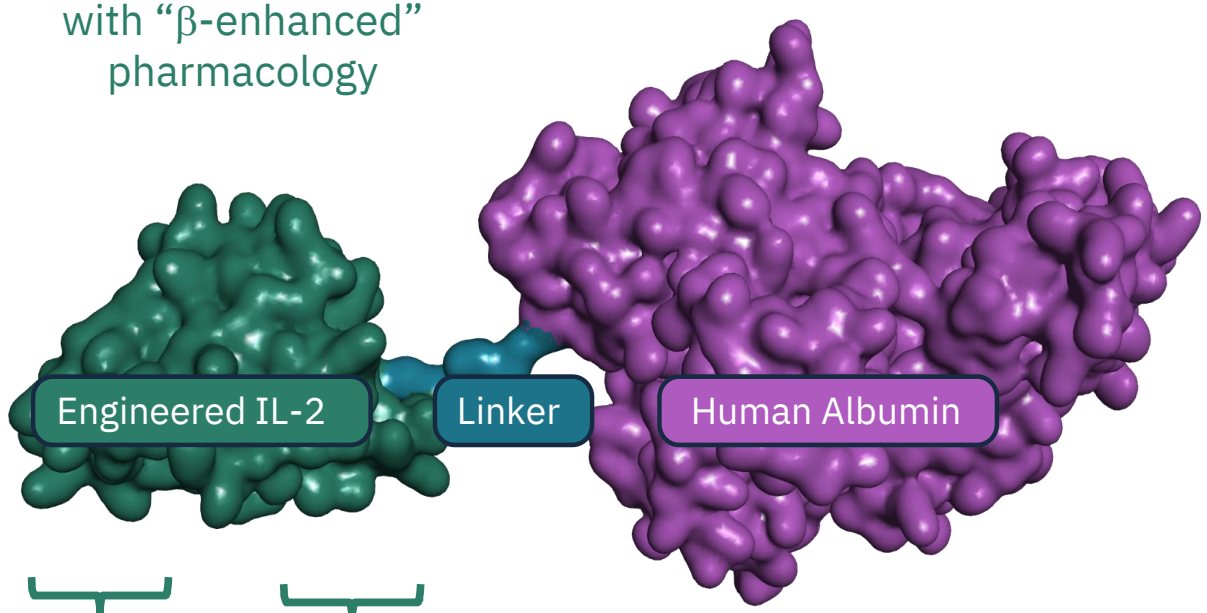
MDNA11: A Unique ‘β-enhanced Not-α’ Albumin-fused IL-2 Superkine

MDNA11 - the Only “Beta-enhanced not-Alpha” Albumin-fused IL-2

- **Beta-enhanced (30x):** preferential CD8⁺ T cell expansion
- **Not-alpha:** reduced Treg stimulation & improved safety
- **Albumin fusion:** half-life extension (Q2W dosing) and enhanced retention in the 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**

Superior selectivity with “β-enhanced” pharmacology

Improved PK profile



*Structure is an artistic render using PDB (1M4C (hIl2) - 1AO6 (HSA)
TDLN, tumor draining lymph node

ABILITY-1 Phase 1/2 Study: FIH Trial of MDNA11 in Patients with Advanced Solid Tumors

Dose Escalation/Evaluation (Phase 1)

Part 1 MDNA11 monotherapy in advanced solid tumors	Part 2 MDNA11 + pembrolizumab in advanced solid tumors
3-30 µg/kg cohorts no DLT, Q2W	
60 µg/kg cohort* no DLT, Q2W	**60 µg/kg cohort*** no DLT, Q2W
90 µg/kg cohort no DLT, Q2W **RDE**	**90 µg/kg cohort** no DLT, Q2W
120 µg/kg cohort no DLT Q2W/Q3W	**120 µg/kg cohort** no DLT, Q2W/Q3W

*lowest dose with confirmed objective response

Dose Expansion (Phase 2)

Part 3 MDNA11 monotherapy in advanced refractory solid tumors	Part 4 MDNA11 + pembrolizumab in advanced solid tumors
MSI-H / dMMR Cohort	**MSI-H / dMMR Cohort**
TMB-H Cohort	**TMB-H Cohort**
Cutaneous Melanoma Cohort anti-PD(L)1 experienced	**Cutaneous Melanoma Cohort** anti-PD(L)1 experienced
Virally Associated Tumor Cohort#	**Gynecological Cancer Cohort**

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

#replaced non-melanoma skin cancer cohort

'Phase 2 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%)

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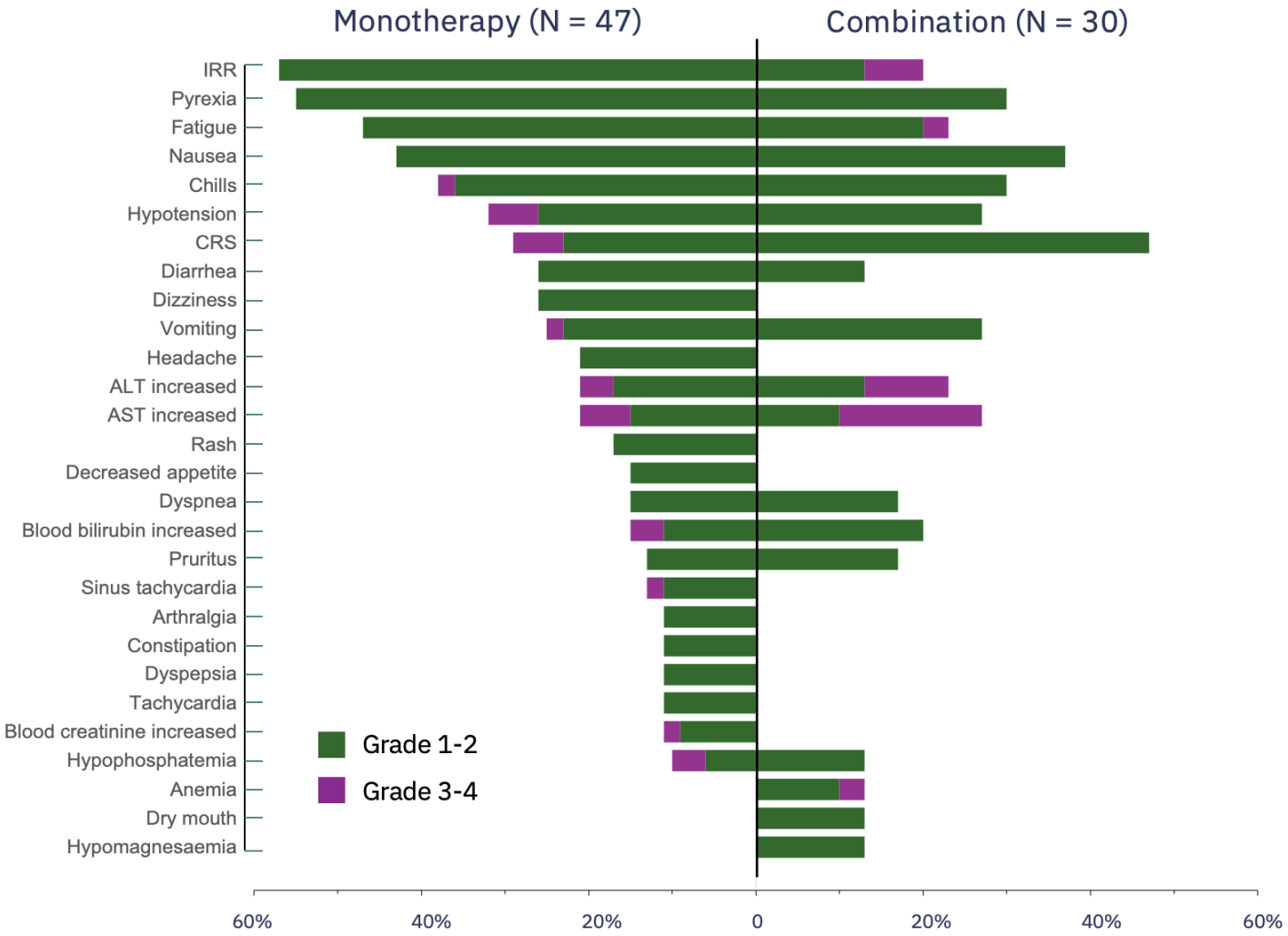
*information not available for 1 patient

TRAEs in ≥ 10% of Patients in 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

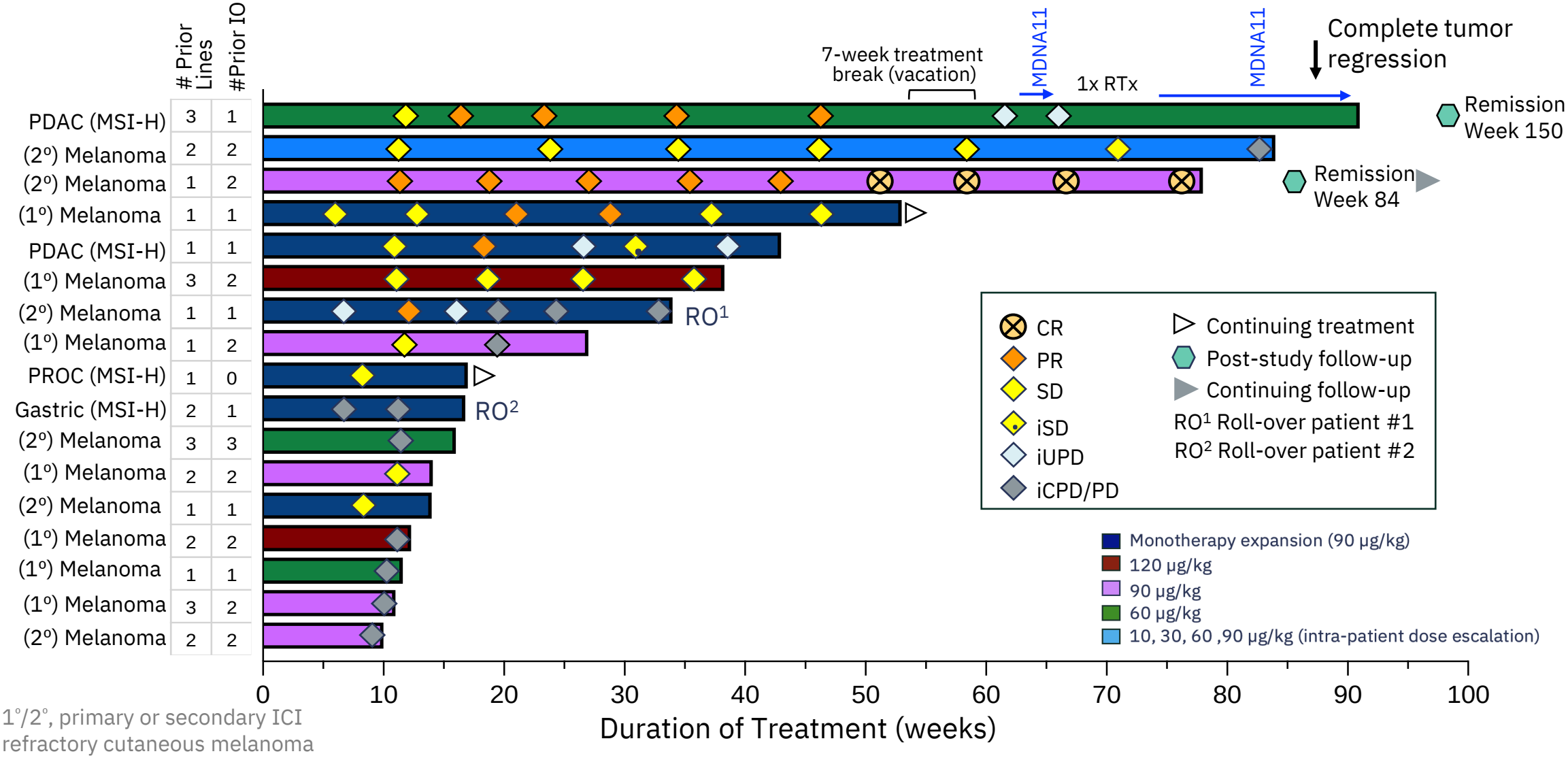
Combination Therapy

- 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

MDNA11 Monotherapy: Durable Single Agent Activity

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

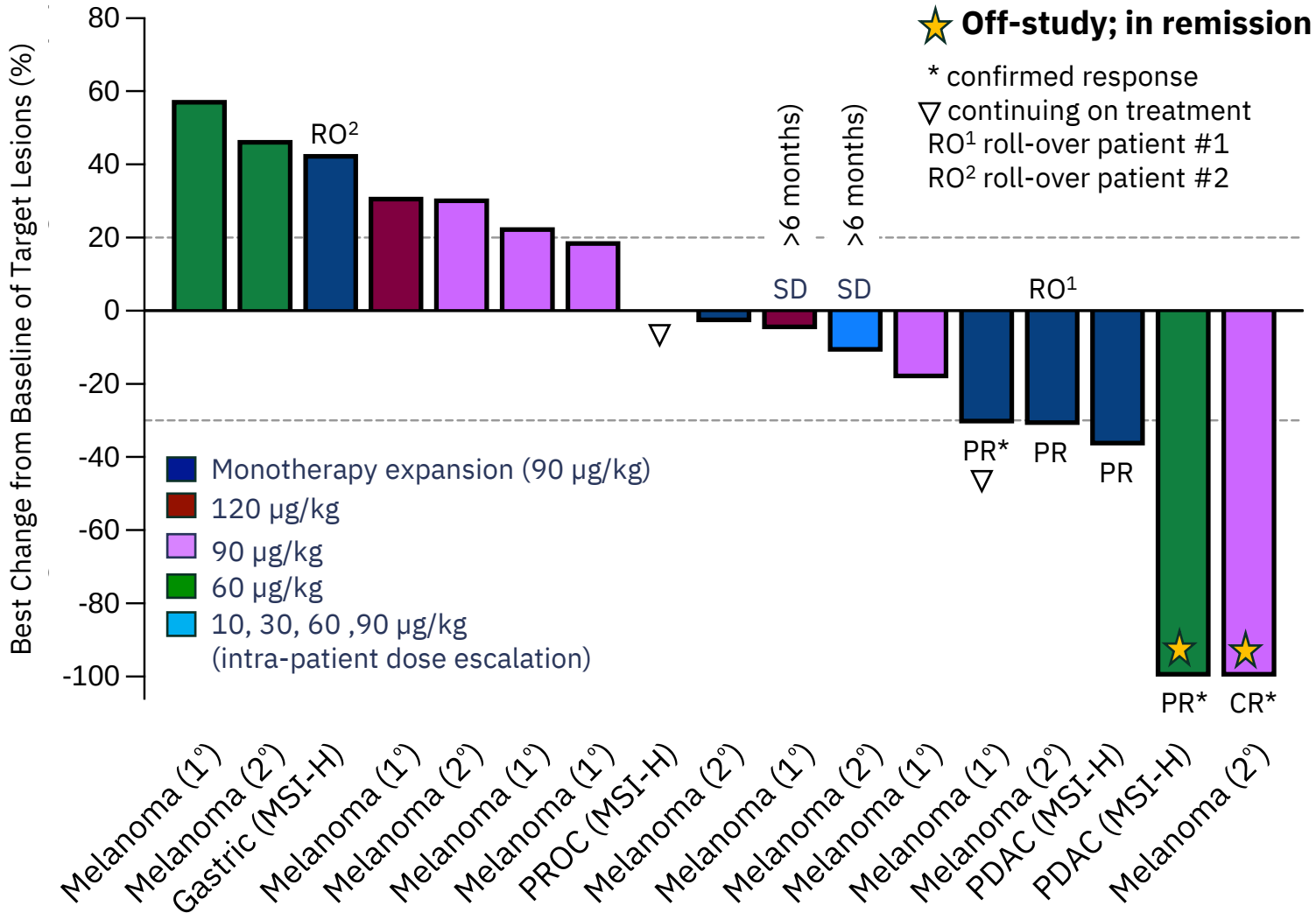


1º/2º, primary or secondary ICI refractory cutaneous melanoma

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

Compelling Single Agent Activity in ICI Resistant Patients

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



Monotherapy ORR

29.4%	40%
(1 CR, 4 PRs)	(1 CR, 3 PRs)
P2 eligible + 1° ICI-resistant melanoma (n = 17)	P2 eligible patients (n = 10)
95% CI: 13.3-53.1%	95% CI: 16.8-68.7%

Tumor-Specific ORR

50%	33%
(2 PRs)	(1 CR, 1 PR)
MSI-H tumors (n = 4)	2° 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)

2 patients (1 CR + 1 PR) **continuing in remission** post end of MDNA11 treatment

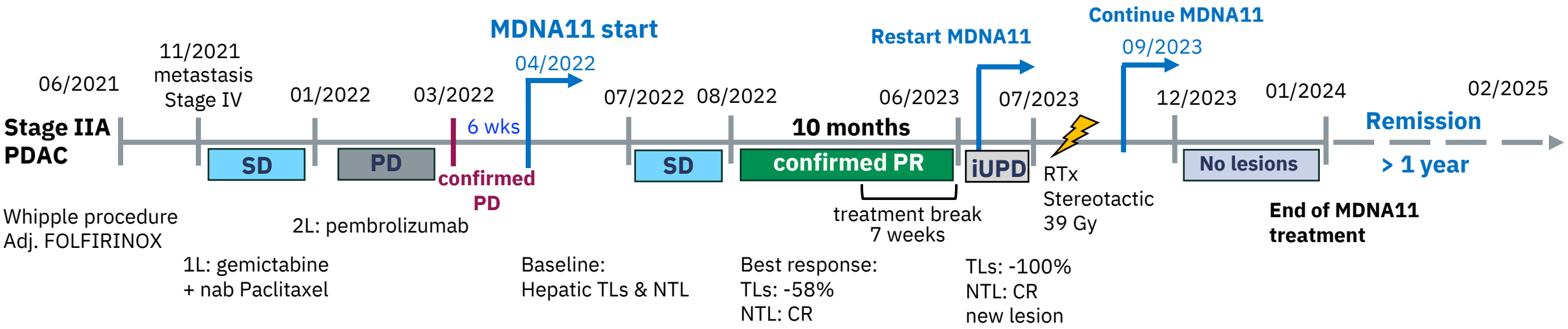
1°/2°, primary or secondary ICI (check-point inhibitor) refractory cutaneous melanoma
PDAC, pancreatic ductal adenocarcinoma; PROC, platinum resistant ovarian cancer

Data cut-off: April 15, 2025

MDNA11 Monotherapy: Case Highlights

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

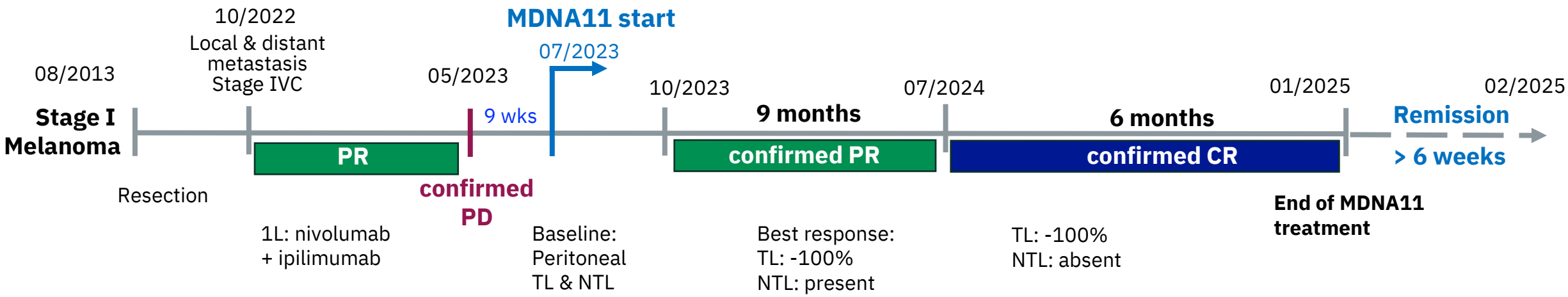
Patient 1: ICI-progressed MSI-H PDAC treated with single agent MDNA11 (60 µg/kg, Q2W)



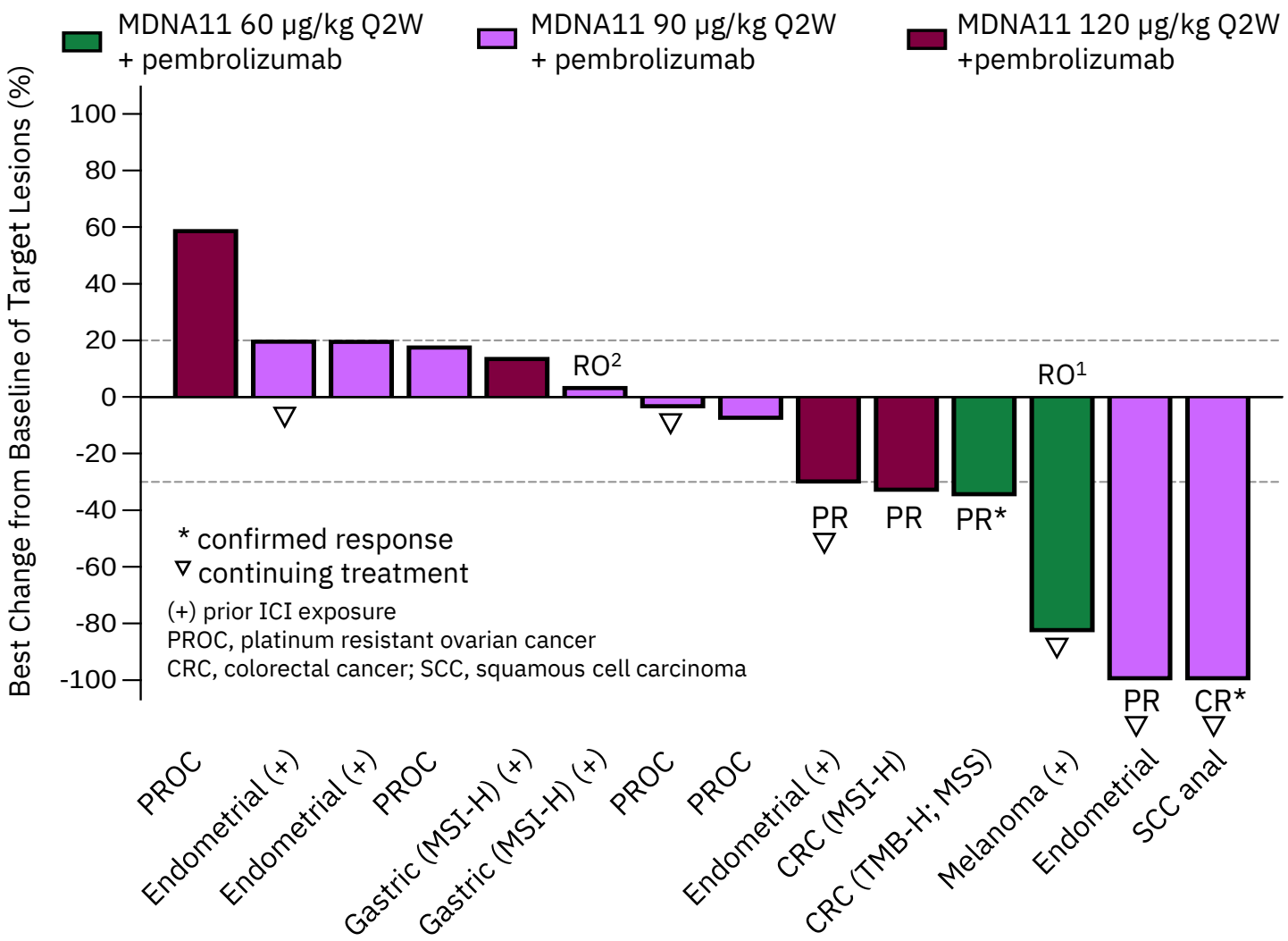
MDNA11 Monotherapy: Case Highlights

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

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



Combination Dose Escalation: Clinical Activity Across Multiple Tumor Types



Combination ORR

35.7%
(1 CR, 4 PRs)
P2 eligible + 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

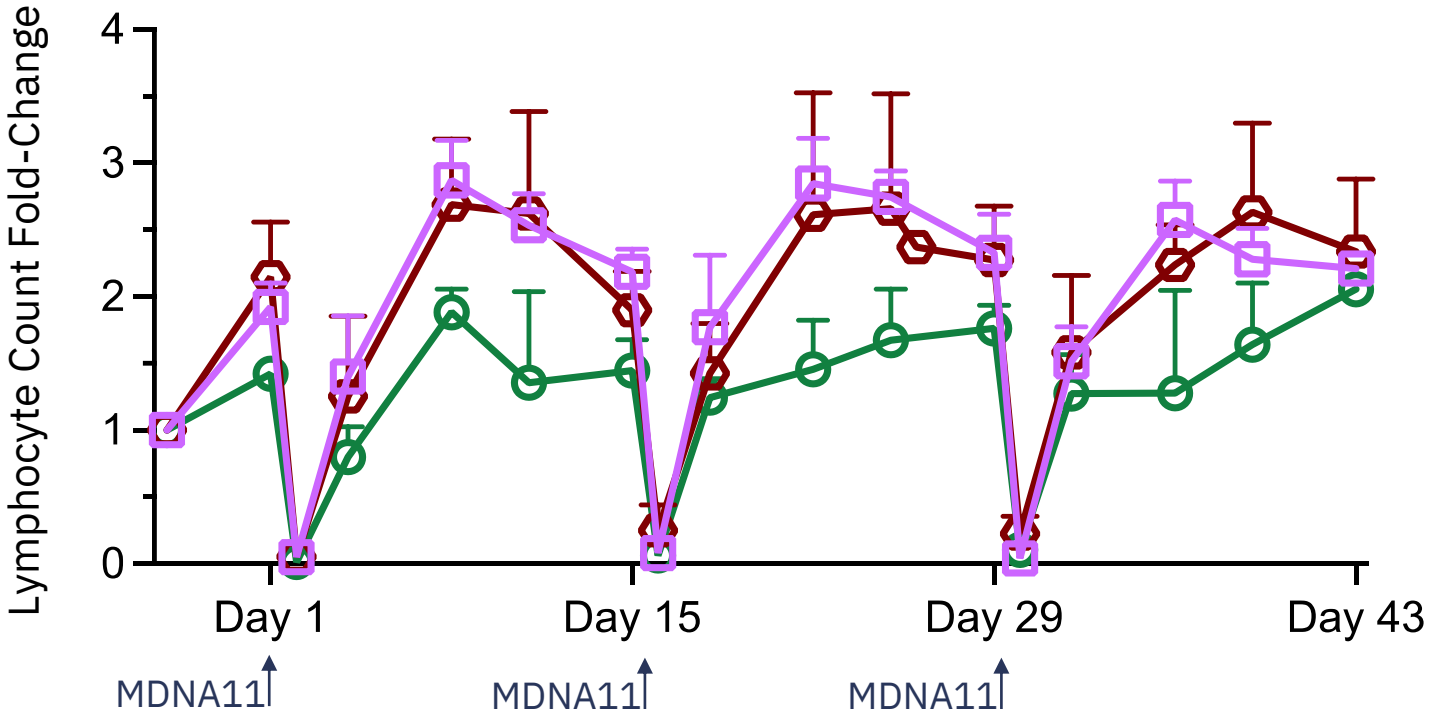
50%
(2 PRs)
Endometrial tumors (n = 4)

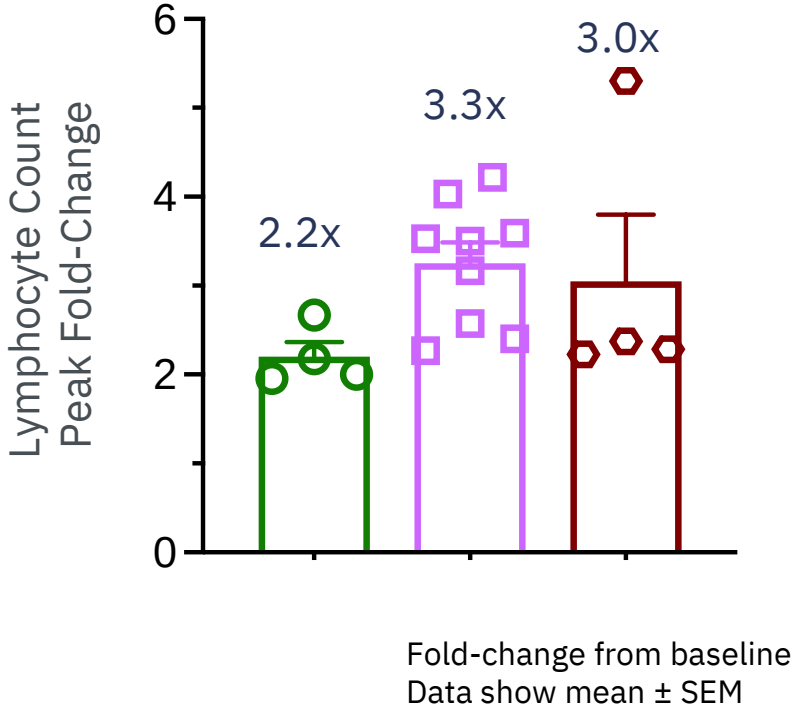
Disease Control Rate: 57.1%
1 CR, 4 PRs, 3 SDs (8/14)

This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.
Pembrolizumab: 400 mg (Q6W)

Data cut off: April 15, 2025

Robust Lymphocyte Expansion with MDNA11 + Pembrolizumab Combination Therapy





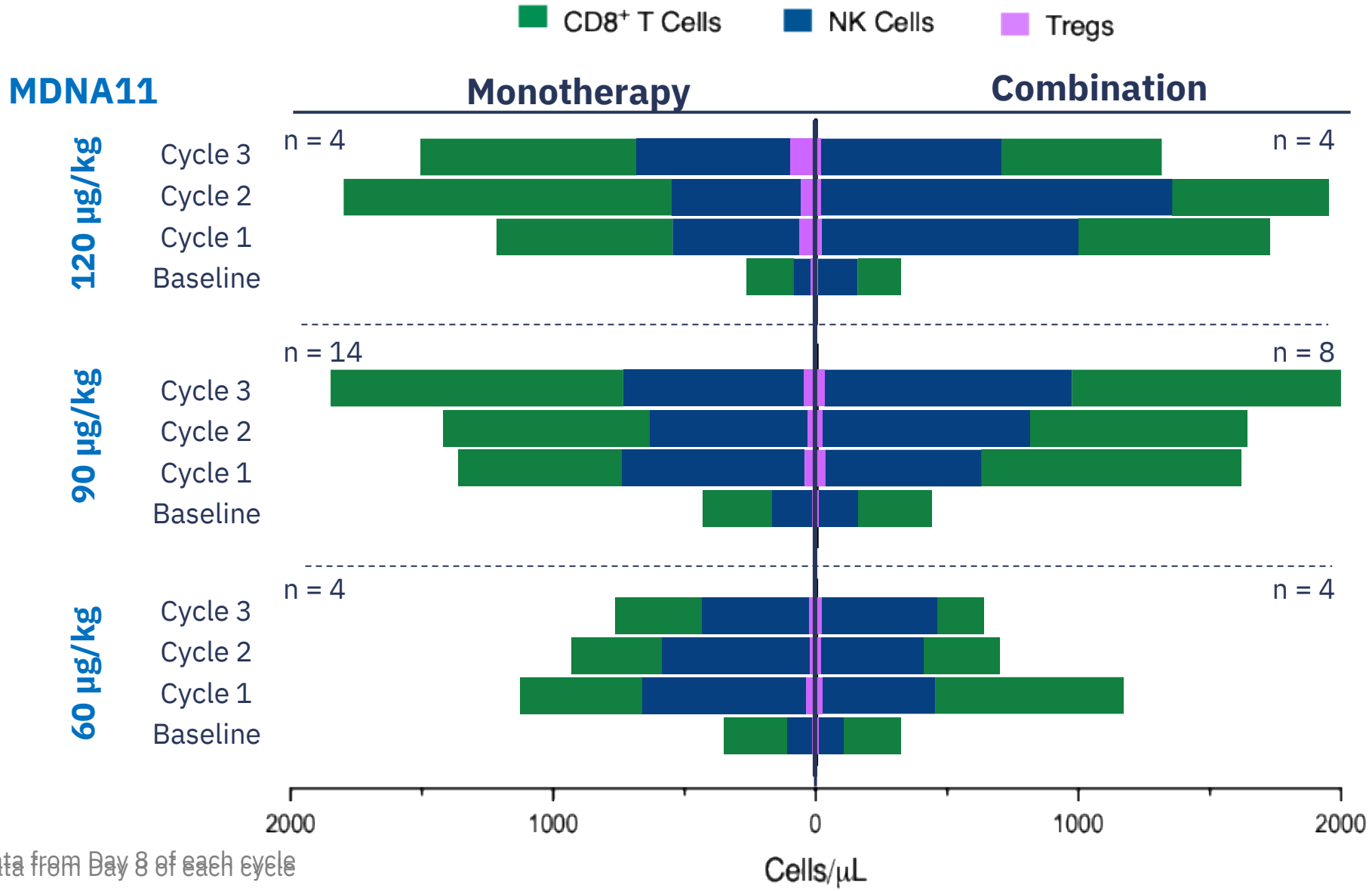
Fold-change from baseline
Data show mean ± SEM

MDNA11 (60 µg/kg, Q2W) + pembrolizumab (400 mg, Q6W) (N = 4)

MDNA11 (90 µg/kg, Q2W) + pembrolizumab (400 mg, Q6W) (N = 9)

MDNA11 (120 µg/kg, Q2W) + pembrolizumab (400 mg, Q6W) (N = 4)

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



Data from Day 8 of each cycle

Data from Day 8 of each cycle

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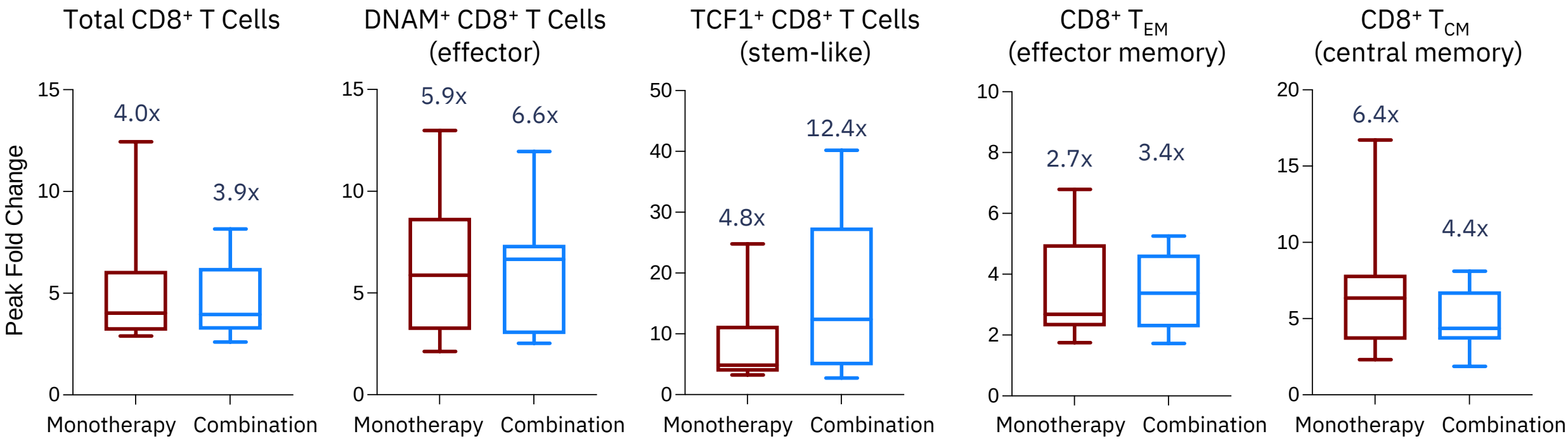
MDNA11 Induces Expansion of Effector, Stem-like and Memory CD8+ T Cells

90 µg/kg MDNA11 (Q2W) ± 400 mg pembrolizumab (Q6W)



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

Data show median (range); monotherapy, N = 14; combination, N = 9

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

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 and 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 weeks and >1 year)

***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 observed 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

Appendix

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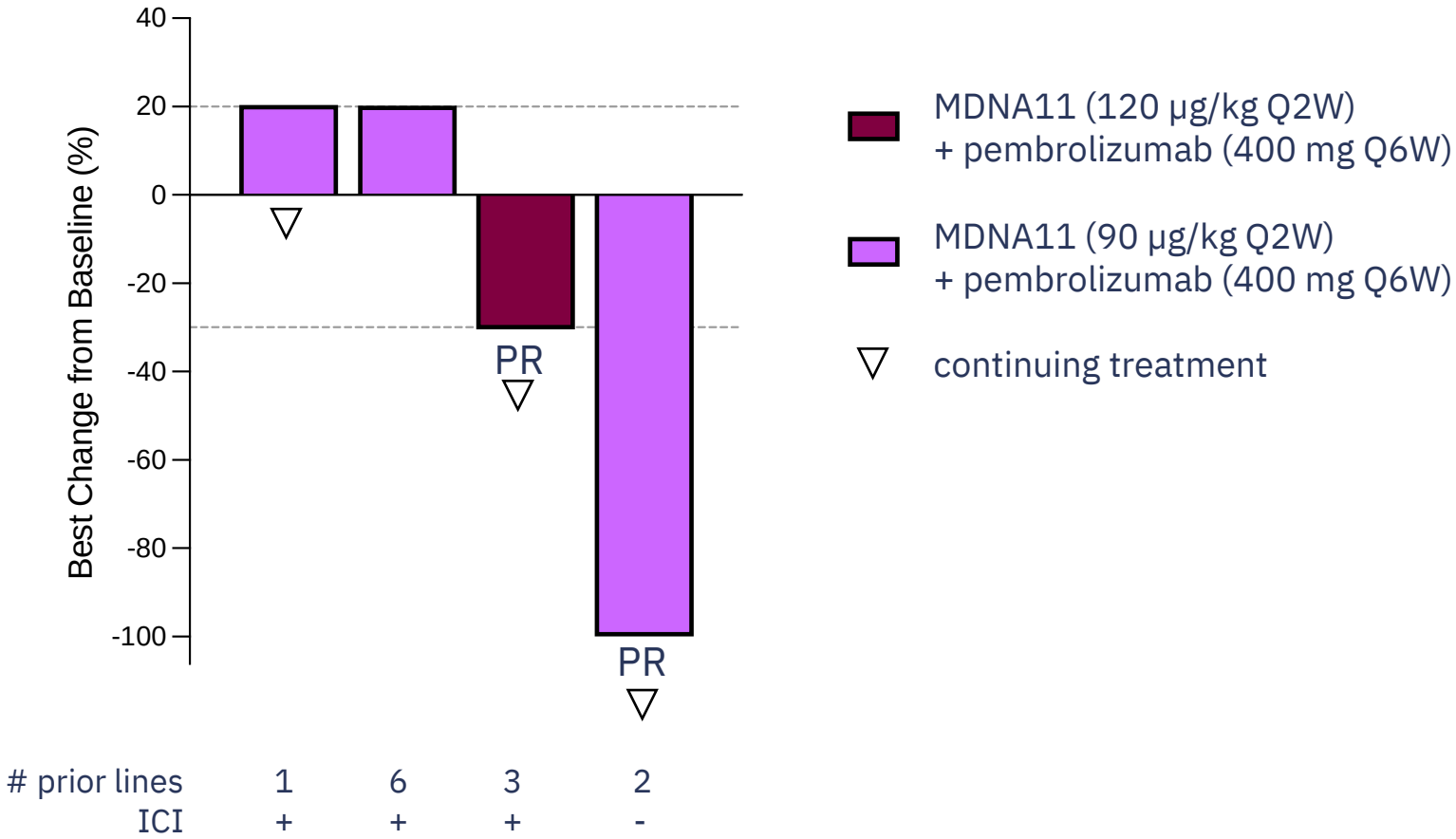
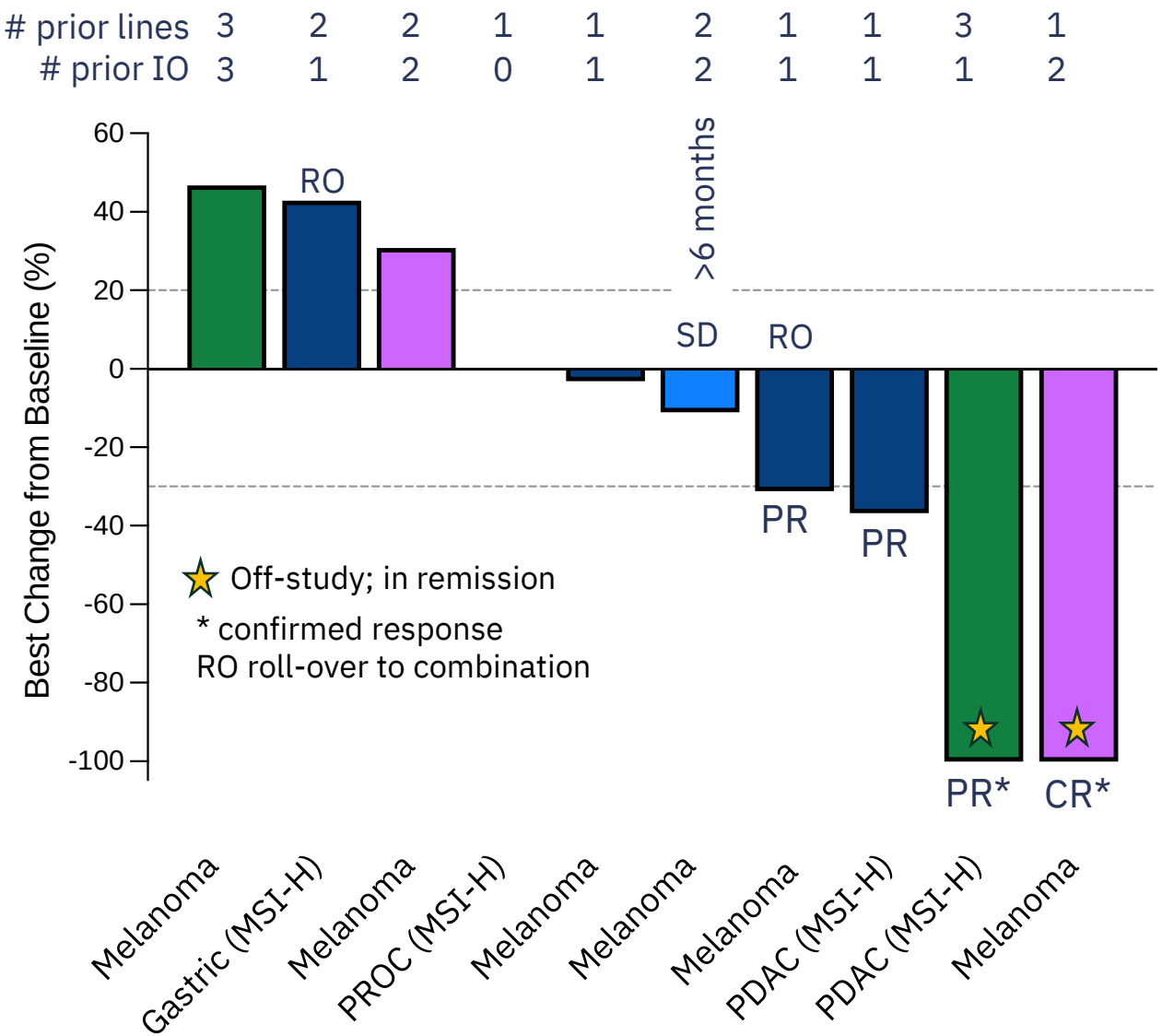
Objective Response in 2 of 4 (ORR 50%) Endometrial Tumors in MDNA11 + Pembrolizumab Combination Cohort



ICI, immune checkpoint inhibitor

MDNA11 Monotherapy: ORR of 40% (4 of 10) in Planned Phase 2 Expansion Cohorts



MSI-H/dMMR cancers
ICI secondary resistant melanoma

Patients treated with ≥ 60 µg/kg MDNA11

- Monotherapy Expansion (90 µg/kg Q2W)
- 90 µg/kg Q2W
- 60 µg/kg Q2W
- 10, 30, 60, 90 µg/kg Q2W (intra-patient dose escalated)

Monotherapy Dose Escalation/Evalulation Cohorts

2 patients continuing in remission following stop of MDNA11 treatment (both had complete regression of all tumor lesions):

- confirmed CR in melanoma (>6 weeks off treatment)
- confirmed PR in PDAC (>1 year off treatment)

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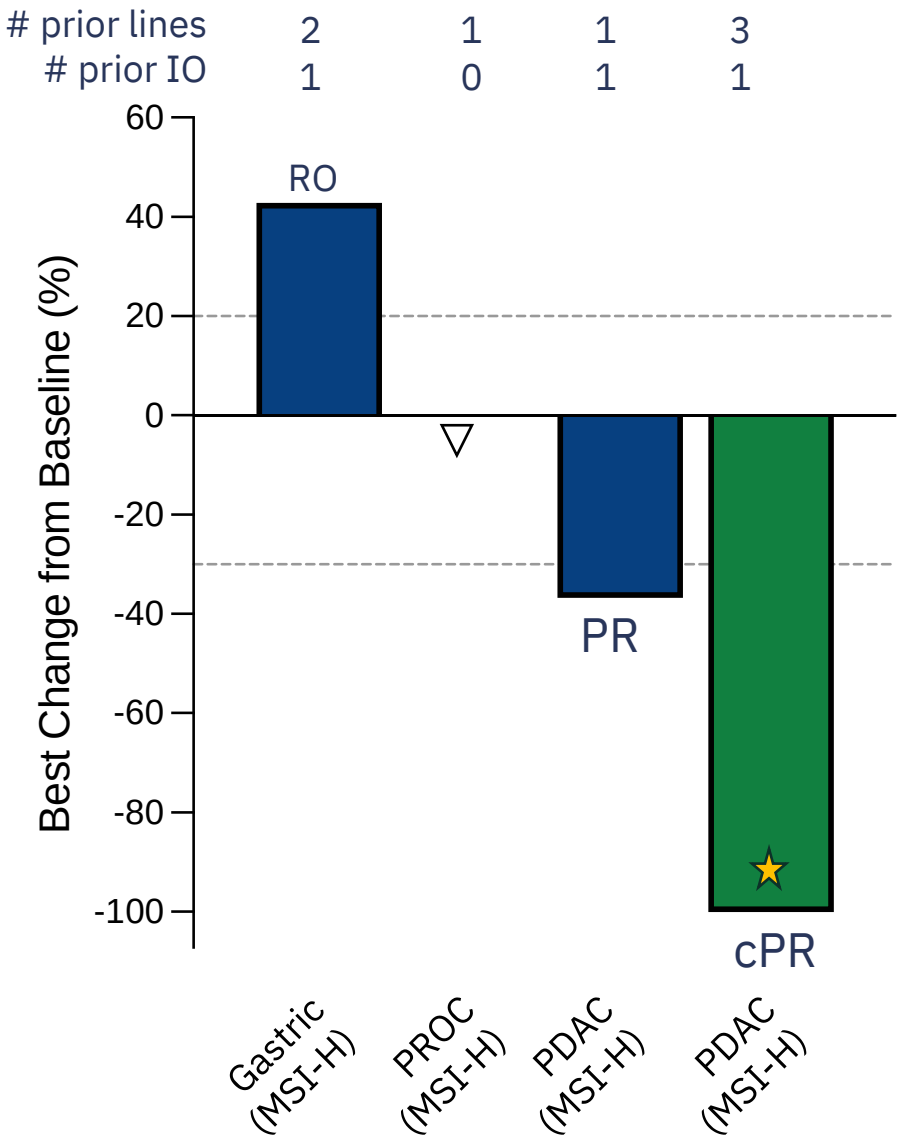
ICI, immune checkpoint inhibitor

Single Agent MDNA11 Achieved 50% ORR (2 of 4) in MSI-H Cancers



Objective response in 2 patients with MSI-H PDAC

Disease Control Rate: 75%
(1 CR + 1 PR + 1 SD)

Monotherapy Expansion (90 µg/kg Q2W)

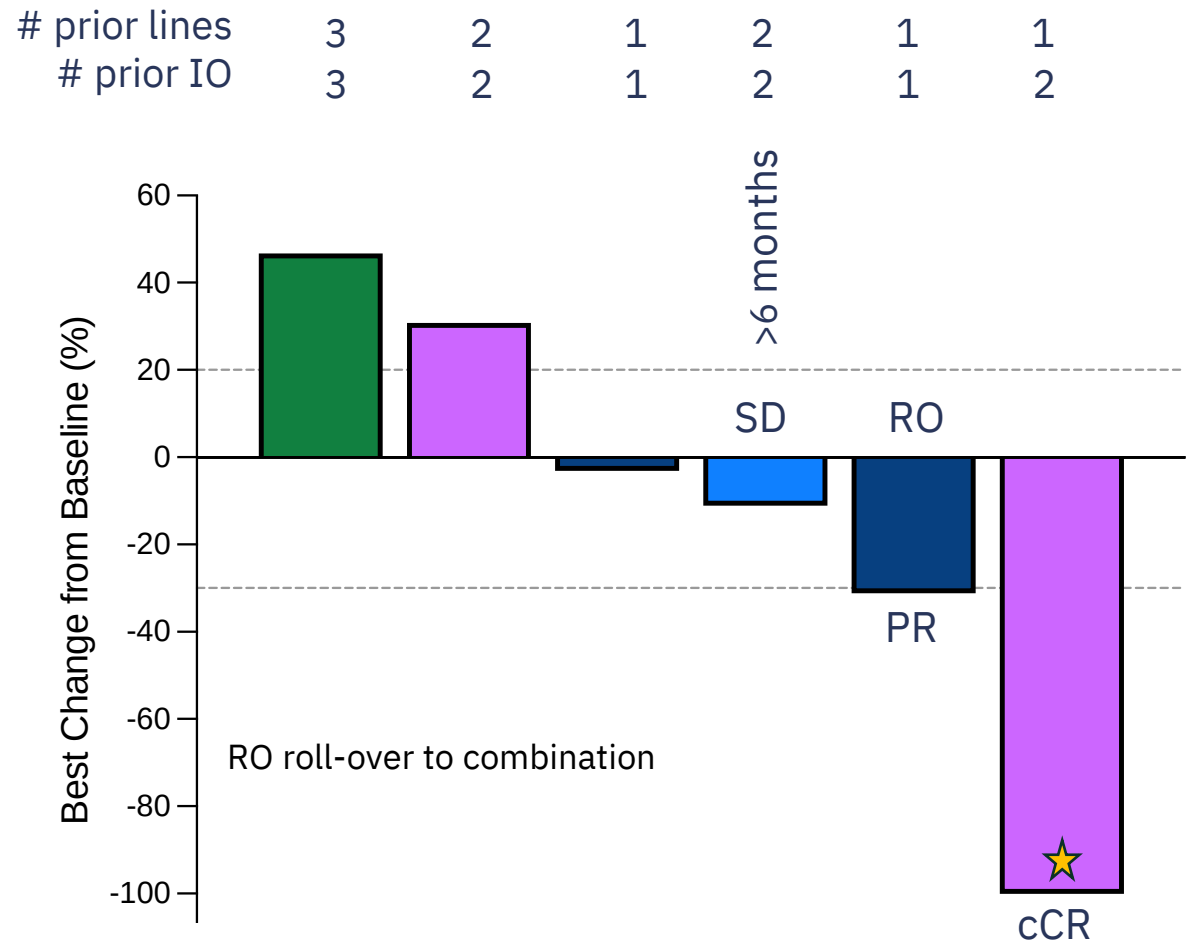
90 µg/kg Q2W

▽ continuing treatment

RO roll-over to combination

★ complete regression of all tumor lesion; continuing in remission (> 1 year) following end of MDNA11 treatment

Single Agent MDNA11 Achieved 33% ORR (2 of 6) in ICI Secondary Resistant Melanoma



Disease Control Rate: 66%
(1 CR + 1 PR + 2 SD)

Clinical Benefit Rate: 50%
(1 CR + 1 PR + 1 SD > 6 months)

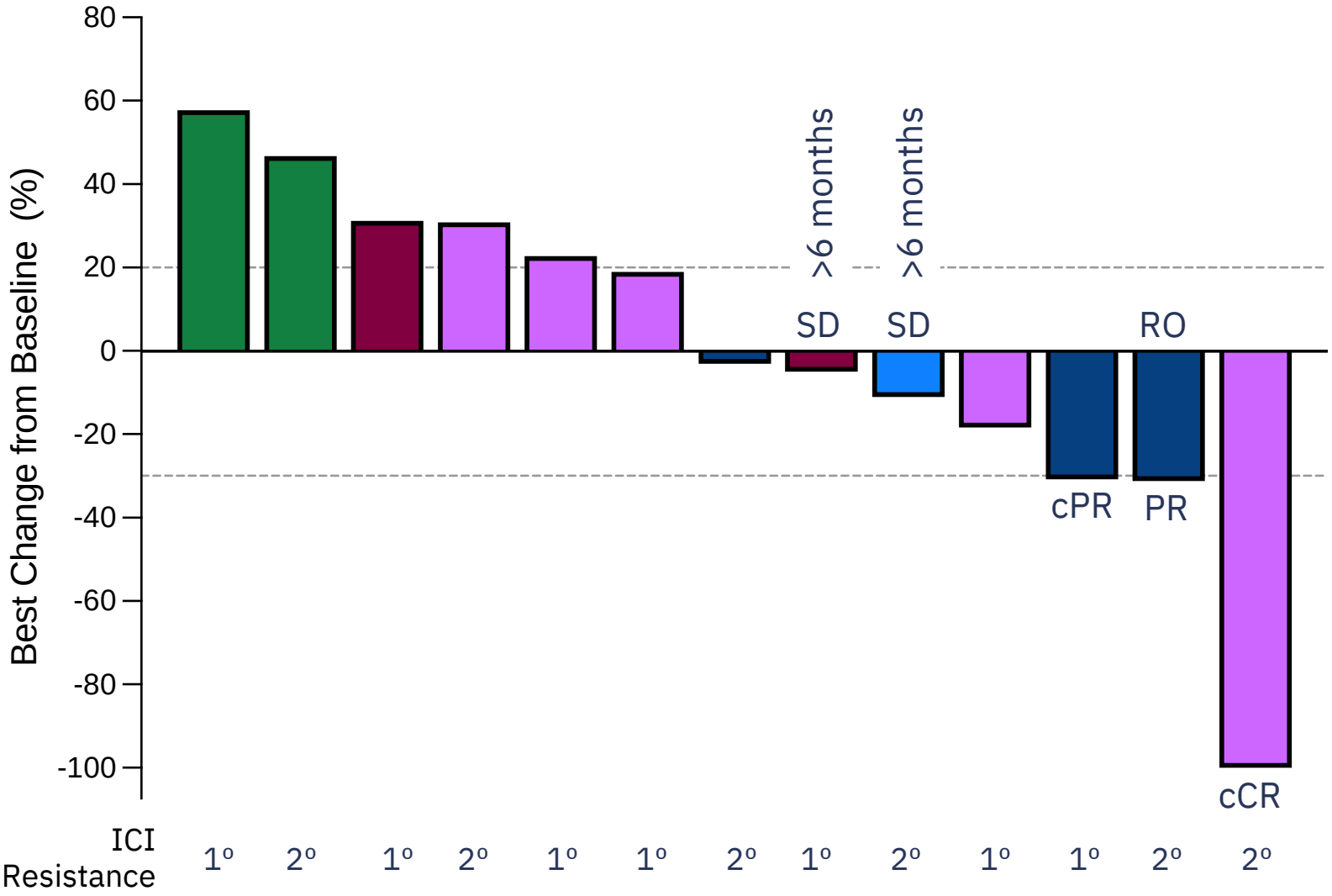
- Monotherapy Expansion (90 µg/kg Q2W)
- 90 µg/kg Q2W
- 60 µg/kg Q2W
- 10, 30, 60, 90 µg/kg Q2W (intra-patient dose escalated)

Monotherapy Dose Escalation/Evalulation Cohorts

★ continuing in remission (> 6 weeks) following end of MDNA11 treatment

ICI, immune checkpoint inhibitor

Single Agent MDNA11 Clinical Activity in ICI Primary/Secondary Resistant Melanoma



ORR of 23.1% (3 of 13)

Monotherapy Expansion (90 µg/kg Q2W)

90 µg/kg Q2W

60 µg/kg Q2W

10, 30, 60, 90 µg/kg Q2W (intra-patient dose escalated)

Disease Control Rate: 53.8%
(1 CR + 2 PR + 4 SD)

Clinical Benefit Rate: 38.4%
(1 CR + 2 PR + 2 SD >6 months)

ICI, immune checkpoint inhibitor