MacroGenics®

Developing
Breakthrough Biologics,
Life-changing Medicines®

TAMARACK Phase 2 Interim Data

May 9, 2024 *(Data Cut-off: April 12, 2024)*

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Investigational Agents

The safety and efficacy of investigational agents and/or investigational uses of approved products have not been established.

TAMARACK mCRPC Phase 2 Study Design Summary

Key Eligibility Criteria:

- mCRPC
- One prior ARAT
- Up to one prior docetaxel-containing regimen[(a)]
- ≤ 3 Prior lines of therapy for mCRPC

Stratification Factors:

- Visceral disease (yes vs. no)
- Prior taxane (yes vs. no)
- Region (US/Canada vs. other)

R 1:1

Patients Enrolled N=91

Experimental Arm A
Vobramitamab duocarmazine
2.0 mg/kg Q4W

Patients Enrolled N=90

Experimental Arm B
Vobramitamab duocarmazine
2.7 mg/kg Q4W

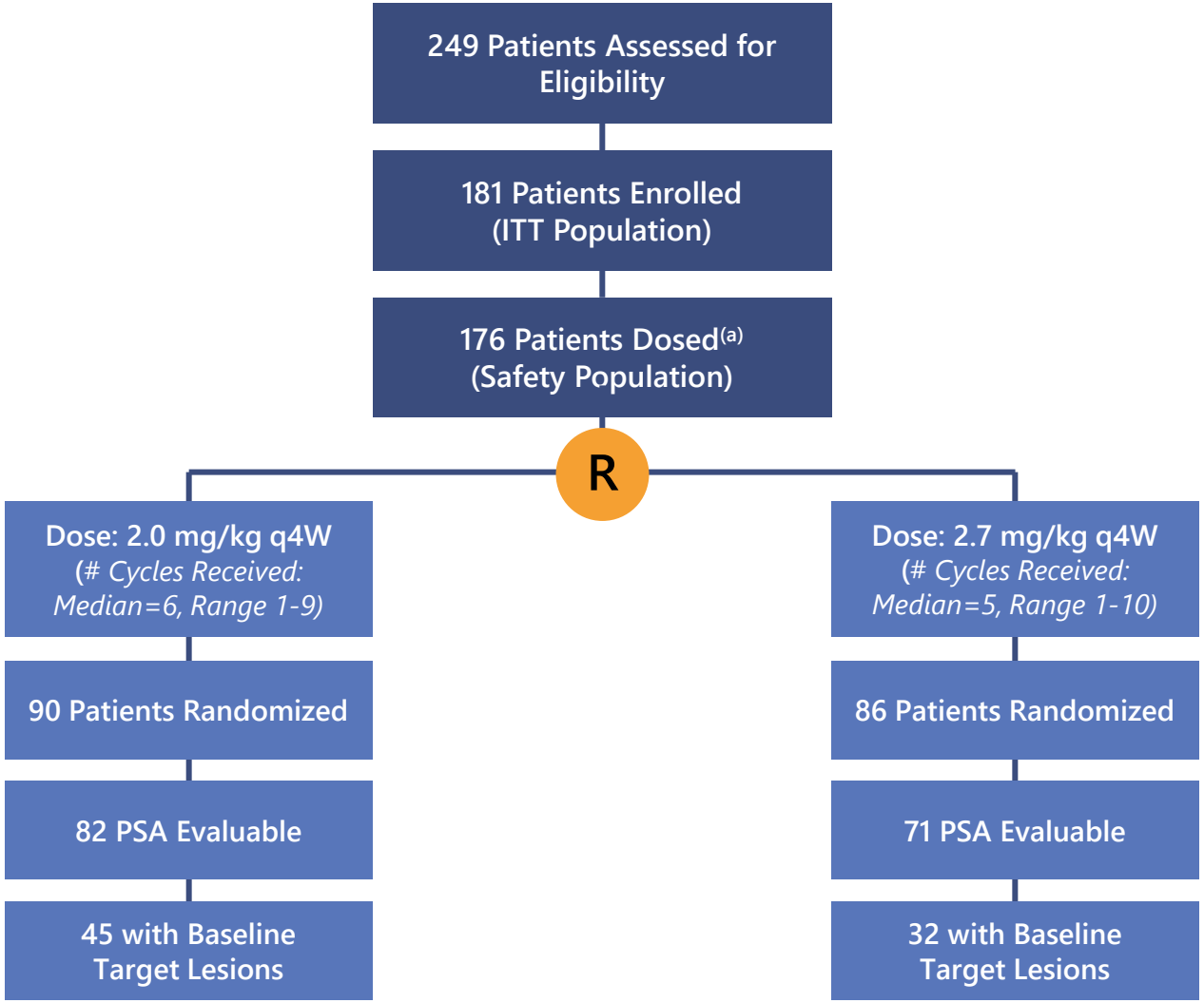
Primary Endpoint:
rPFS

Key Secondary Endpoints:
AEs, PSA outcomes, ORR, DoR, SSEs, PK, ADA, nAb

(a) Participants who received an additional taxane or second ARAT (androgen receptor axis-targeted agent [abiraterone, enzalutamide or apalutamide]) for <60 days as bridging therapy while awaiting lutetium-177 vipivotide tetraxetan are also eligible. Other prior chemotherapy for prostate cancer is not allowed.

mCRPC=metastatic castration-resistant prostate cancer; ORR=objective response rate; PSA=prostate-specific antigen; Q4W=every 4 weeks; R=randomize; rPFS=radiographic progression-free survival.

Patient Flow



(a) Excludes three dosed patients who were on original Androgen Receptor Axis-Targeted therapy control arm. These patients are excluded from any analyses in this presentation.

Baseline Patient Characteristics of ITT Population

Parameter	Vobra Duo 2.0 mg/kg q4W (n=91)	Vobra Duo 2.7 mg/kg q4W (n=90)	All (n=181)
Age, years			
Mean ± SD	70.3 ± 9.03	69.1 ± 8.94	69.7 ± 8.98
Median (range)	71 (46-89)	70 (35-86)	70 (35-89)
ECOG Performance Status, n (%)			
0	42 (46.2)	52 (57.8)	94 (51.9)
1	48 (52.7)	35 (38.9)	83 (45.9)
2	1 (1.1)	2 (2.2)	3 (1.7)
Baseline PSA (ng/mL)	(n=89)	(n=85)	(n=174)
Mean ± SD	180.5 ± 542.60	182.6 ± 433.06	181.6 ± 490.74
Median (range)	26.4 (0.8, 3447.0)	24.7 (0.2, 2778.0)	24.7 (0.2, 3447.0)
Measurable Disease at Baseline, n (%)	45 (49.5)	34 (37.8)	79 (43.6)
Prior Taxane, n (%)	52 (57.1)	52 (57.8)	104 (57.5)
Prior ARAT, n (%)			
Abiraterone	46 (50.5)	46 (51.1)	92 (50.8)
Enzalutamide	36 (39.6)	33 (36.7)	69 (38.1)
Apalutamide	12 (13.2)	10 (11.1)	22 (12.2)
Location, n (%)			
Western Europe	66 (72.5)	68 (75.6)	134 (74.0)
US	11 (12.1)	10 (11.1)	21 (11.6)
Eastern Europe	8 (8.8)	8 (8.9)	16 (8.8)
Australia/Korea	6 (6.6)	4 (4.4)	10 (5.5)

ECOG=Eastern Cooperative Oncology Group; PSA=prostate-specific antigen; ARAT=Androgen Receptor Axis-Targeted therapy.

Interim Summary of Prostate-Specific Antigen (PSA) Response

PSA response evaluable population

Parameter	Vobra Duo 2.0 mg/kg q4W (N=82)	Vobra Duo 2.7 mg/kg q4W (N=71)
Any ≥50% PSA Reduction, n (%) *(95% CI)*	41 (50.0%) *(38.7 – 61.3)*	36 (50.7%) *(38.6 – 62.8)*
PSA Response (Confirmed ≥50% PSA Reduction), n (%) *(95% CI)*	36 (43.9%) *(33.0 – 55.3)*	26 (36.6%) *(25.5 – 48.9)*

Interim Summary of Tumor Response

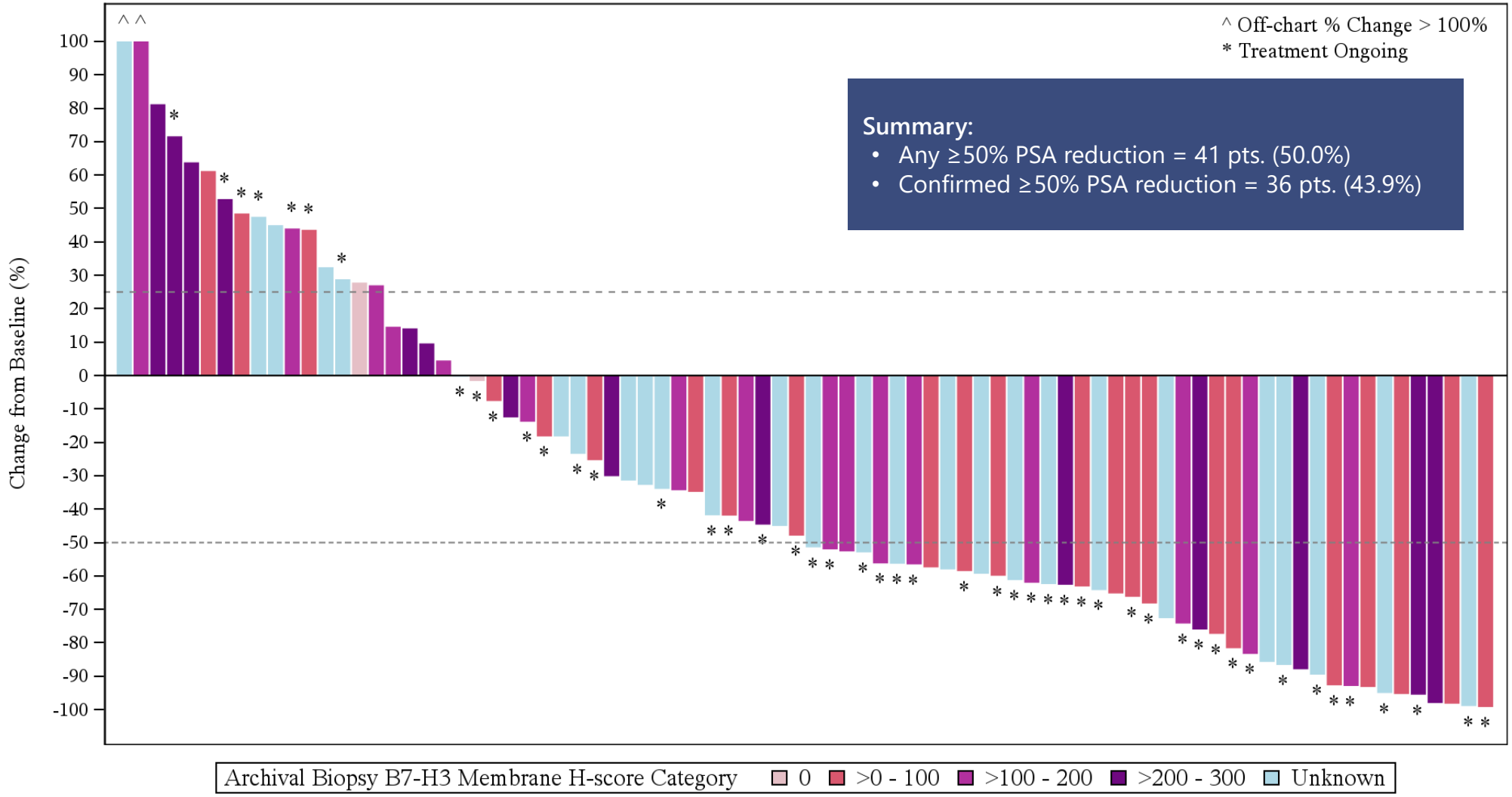
RECIST evaluable patients with measurable disease at baseline

Parameter	Vobra Duo 2.0 mg/kg q4W (N=45)	Vobra Duo 2.7 mg/kg q4W (N=32)
Confirmed Objective Response Rate (ORR) (CR+PR), n (%) *(95% CI)*	8 (17.8%) *(8.0 – 32.1%)*	8 (25.0%) *(11.5 – 43.4%)*
Confirmed + Unconfirmed ORR, n (%)	11 (24.4%)	14 (43.8%)
Disease Control Rate (CR+PR+SD)[(a)], n (%) *(95% CI)*	41 (91.1%) *(78.8 – 97.5%)*	28 (87.5%) *(71.0 – 96.5%)*
Best Overall Response (BOR)[(b)], n (%)		
Complete Response (CR)	0	1 (3.1%)
Partial Response (PR)	8 (17.8%)	7 (21.9%)
Stable Disease (SD)	33 (73.3%)	20 (62.5%)
Progressive Disease (PD)	3 (6.7%)	2 (6.3%)
Not Available (NA)	1 (2.2%)	2 (6.3%)
Confirmed + Unconfirmed BOR, n (%)		
CR	0	1 (3.1%)
PR	11 (24.4%)	13 (40.6%)
SD	30 (66.7%)	14 (43.8%)
PD	3 (6.7%)	2 (6.3%)
NA	1 (2.2%)	2 (6.3%)

(a) Disease Control Rate (DCR) = sum of confirmed responses for patients with CR, PR and SD. Protocol-defined DCR in final analysis will include patients with CR, PR, and SD for ≥ 3 months.
(b) Confirmed CR/PR assessed per RECIST v1.1.

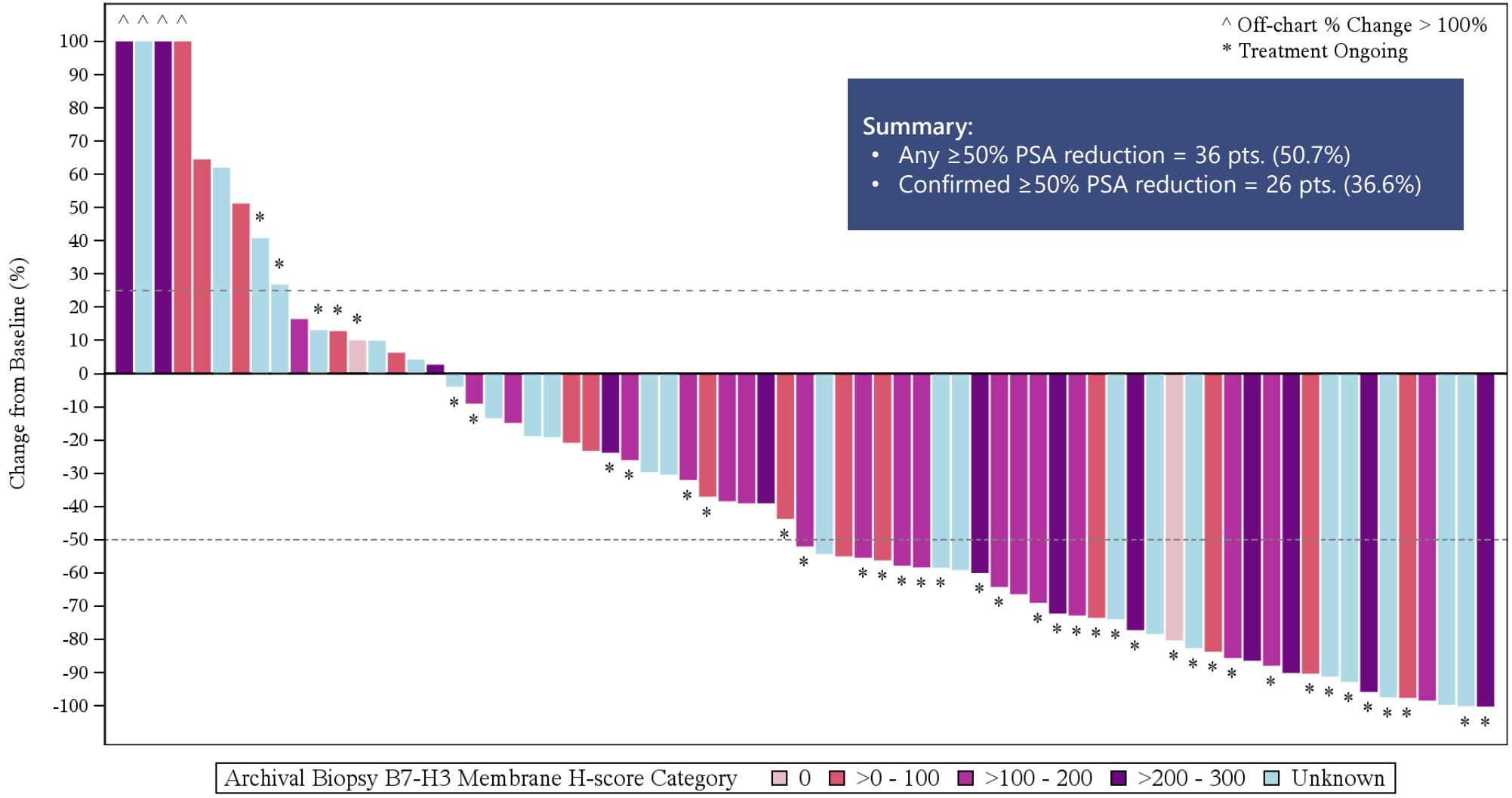
Best % Change from Baseline in PSA (2.0 mg/kg q4W)

PSA response evaluable population (n=82)



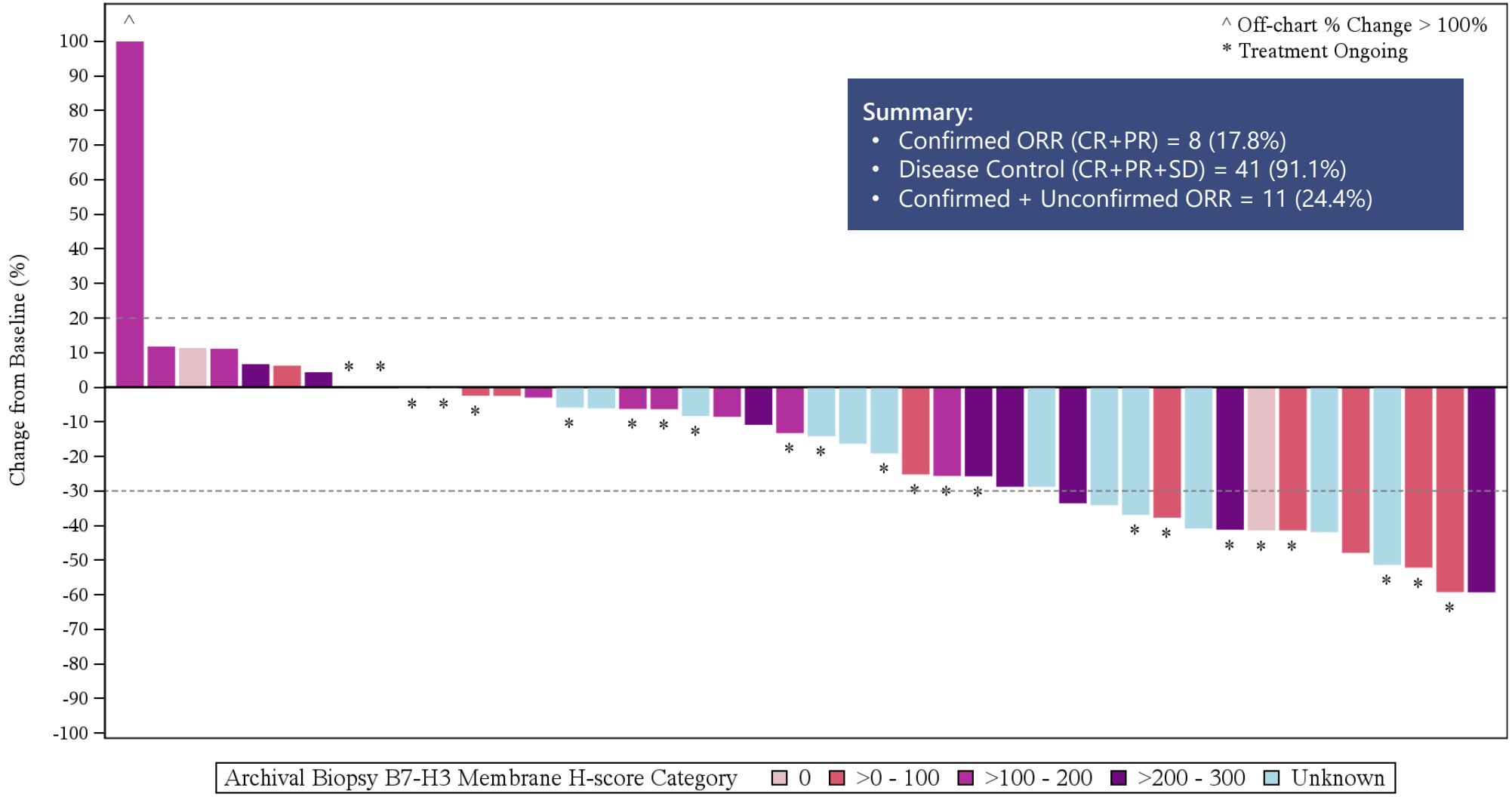
Best % Change from Baseline in PSA (2.7 mg/kg q4W)

PSA response evaluable population (n=71)



Best % Change from Baseline in Investigator-Assessed Tumor Size (2.0 mg/kg q4W)

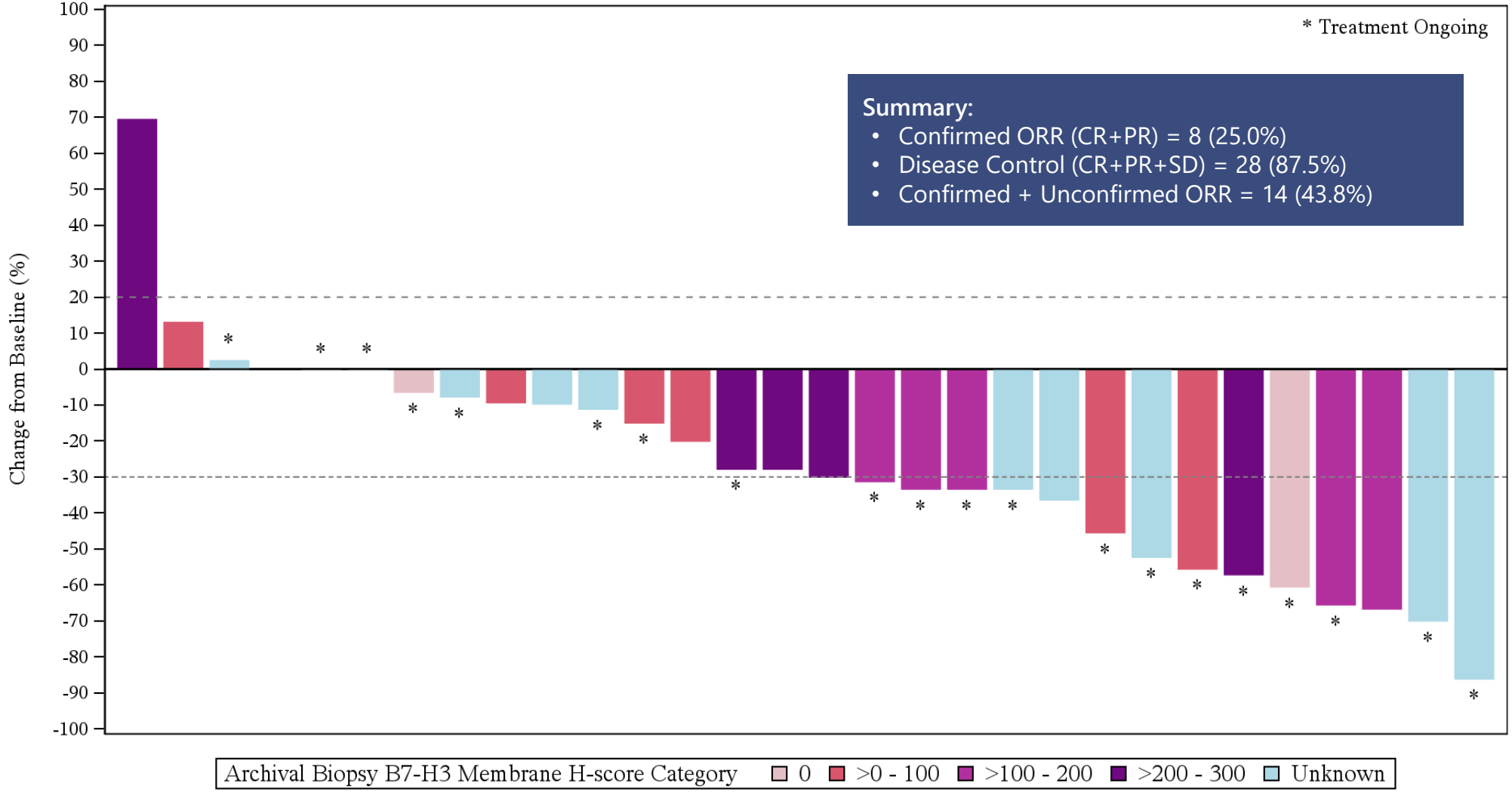
RECIST evaluable patients with baseline and post-baseline target lesion measurements (n=44)[(a)]



(a) One of the 45 patients with measurable disease at baseline did not have any post-baseline tumor assessment.

Best % Change from Baseline in Investigator-Assessed Tumor Size (2.7 mg/kg q4W)

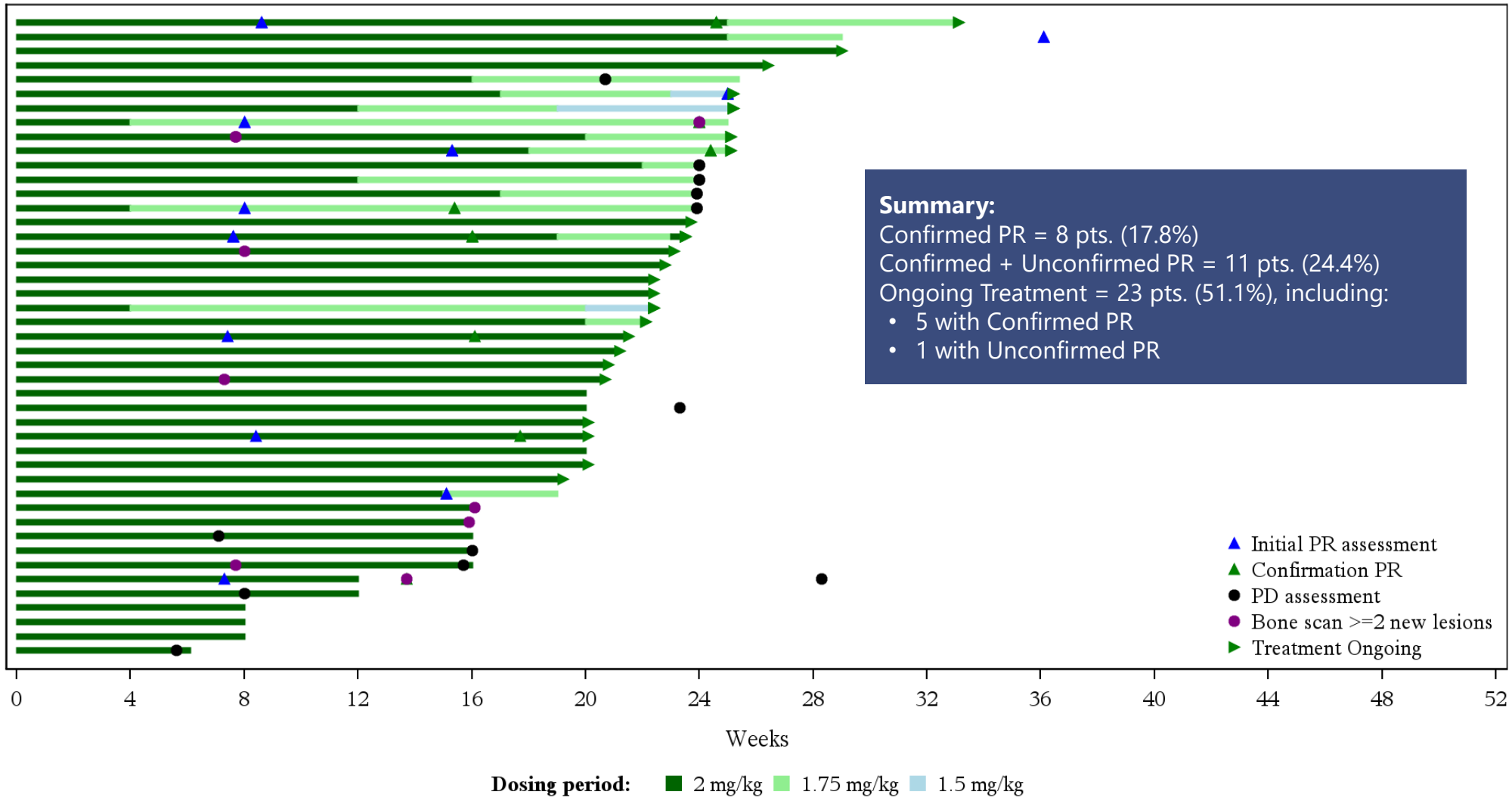
RECIST evaluable patients with baseline and post-baseline target lesion measurements (n=30)[(a)]



(a) Two of the 32 patients with measurable disease at baseline did not have any post-baseline tumor assessment.

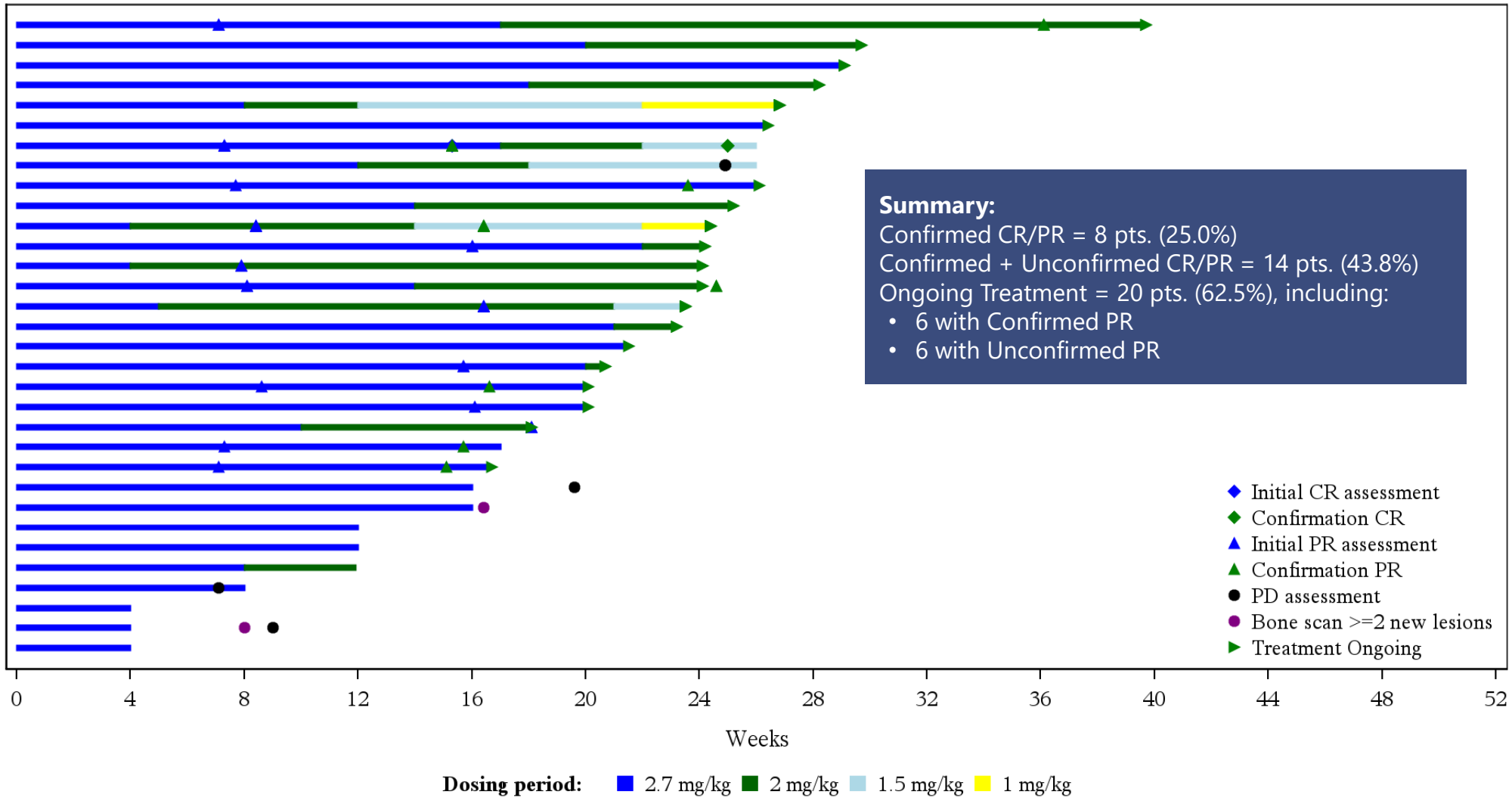
Interim Investigator-Assessed Tumor Response (2.0 mg/kg q4W)

RECIST evaluable patients with measurable disease at baseline (n=45)



Interim Investigator-Assessed Tumor Response (2.7 mg/kg q4W)

RECIST evaluable patients with measurable disease at baseline (n=32)



Interim Overall Summary of Adverse Events

Safety population (n=176)

	Vobra Duo 2.0 mg/kg q4W (N=90)	Vobra Duo 2.7 mg/kg q4W (N=86)	All (N=176)
Any TEAE	89 (98.9%)	86 (100%)	175 (99.4%)
Study Treatment Related AE	87 (96.7%)	83 (96.5%)	170 (96.6%)
TEAE with Severity Grade ≥3	49 (54.4%)	44 (51.2%)	93 (52.8%)
Study Treatment Related AE with Severity Grade ≥3	29 (32.2%)	30 (34.9%)	59 (33.5%)
Any SAE	25 (27.8%)	30 (34.9%)	55 (31.3%)
Study Treatment Related SAE	12 (13.3%)	14 (16.3%)	26 (14.8%)
TEAE Resulting in Study Drug Discontinuation	10 (11.1%)	13 (15.1%)	23 (13.1%)
TEAE Leading to Study Drug Dose Reduction	39 (43.3%)	44 (51.2%)	83 (47.2%)
TEAE Leading to Study Drug Interruption	38 (42.2%)	48 (55.8%)	86 (48.9%)
TEAE with Fatal Outcome[(a)]	1 (1.1%)	4 (4.7%)	5 (2.8%)

(a) Note: one Grade 5 event occurred in 2.0 mg/kg dosing cohort: acute myocardial infarction (considered unrelated to study drug by investigator); three Grade 5 events occurred in 2.7 mg/kg dosing cohort: one cardiac arrest (considered unrelated to study drug by investigator) and two events of pneumonitis. In addition, a patient in the 2.7 mg/kg dosing cohort had a Grade 3 pleural effusion that is recorded as having a fatal outcome. The latter three deaths are being investigated, as follow-up is incomplete on this ongoing trial.

Interim Treatment-Emergent Adverse Events (TEAE) ≥10% (Any Grade)

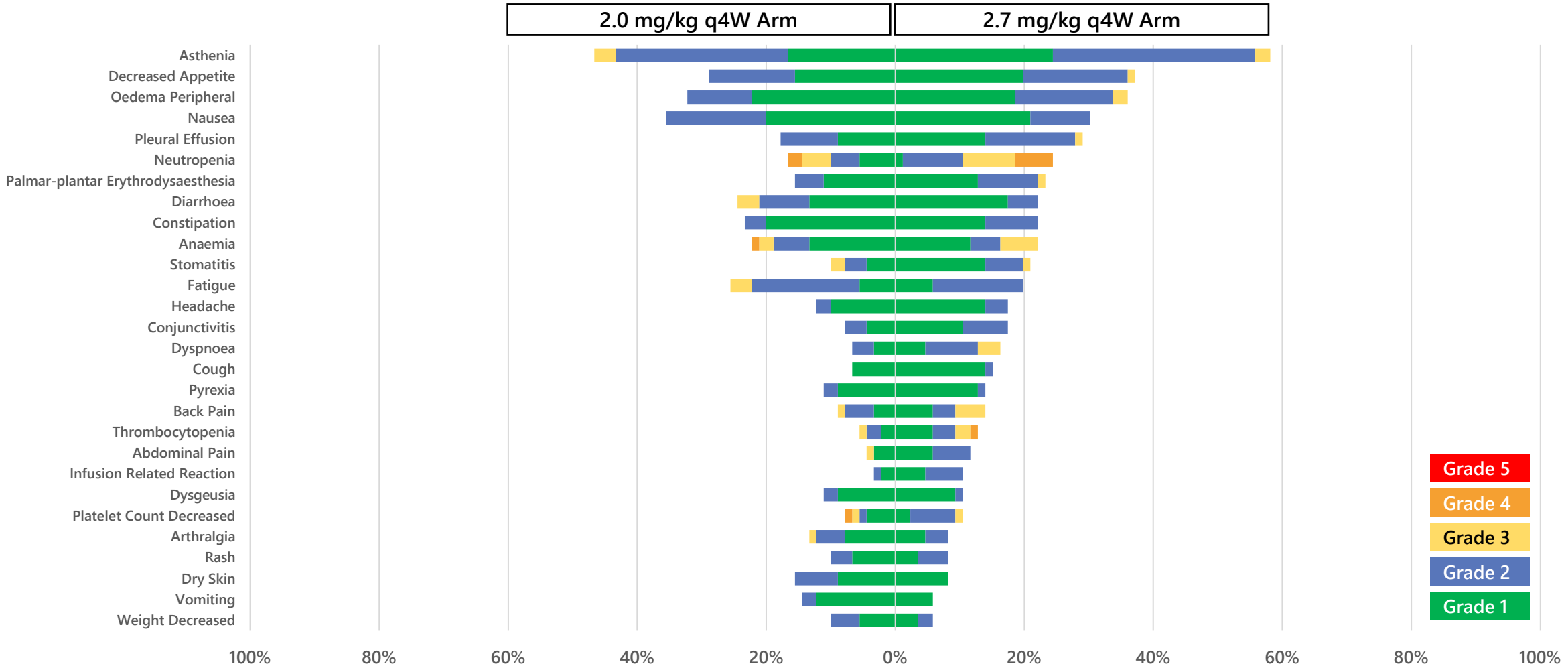
Safety population (n=176); Ranked by # All Grade events for 2.7 mg/kg cohort

AE Preferred Term (MedDRA v26.1)	Vobra Duo 2.0 mg/kg q4W (n=90)		Vobra Duo 2.7 mg/kg q4W (n=86)	
	All Grade	Grade ≥3	All Grade	Grade ≥3
Asthenia	42 (46.7%)	3 (3.3%)	50 (58.1%)	2 (2.3%)
Decreased Appetite	26 (28.9%)	0	32 (37.2%)	1 (1.2%)
Oedema Peripheral	29 (32.2%)	0	31 (36.0%)	2 (2.3%)
Nausea	32 (35.6%)	0	26 (30.2%)	0
Pleural Effusion	16 (17.8%)	0	25 (29.1%)	1 (1.2%)
Neutropenia	15 (16.7%)	6 (6.7%)	21 (24.4%)	12 (14.0%)
Palmar-plantar Erythrodysaesthesia Syndrome	14 (15.6%)	0	20 (23.3%)	1 (1.2%)
Anaemia	20 (22.2%)	3 (3.3%)	19 (22.1%)	5 (5.8%)
Constipation	21 (23.3%)	0	19 (22.1%)	0
Diarrhoea	22 (24.4%)	3 (3.3%)	19 (22.1%)	0
Stomatitis	9 (10.0%)	2 (2.2%)	18 (20.9%)	1 (1.2%)
Fatigue	23 (25.6%)	3 (3.3%)	17 (19.8%)	0
Conjunctivitis	7 (7.8%)	0	15 (17.4%)	0
Headache	11 (12.2%)	0	15 (17.4%)	0
Dyspnoea	6 (6.7%)	0	14 (16.3%)	3 (3.5%)
Cough	6 (6.7%)	0	13 (15.1%)	0
Back Pain	8 (8.9%)	1 (1.1%)	12 (14.0%)	4 (4.7%)
Pyrexia	10 (11.1%)	0	12 (14.0%)	0
Thrombocytopenia	5 (5.6%)	1 (1.1%)	11 (12.8%)	3 (3.5%)
Abdominal Pain	4 (4.4%)	1 (1.1%)	10 (11.6%)	0
Platelet Count Decreased	7 (7.8%)	2 (2.2%)	9 (10.5%)	1 (1.2%)
Dysgeusia	10 (11.1%)	0	9 (10.5%)	0
Infusion Related Reaction	3 (3.3%)	0	9 (10.5%)	0
Dry Skin	14 (15.6%)	0	7 (8.1%)	0
Rash	9 (10.0%)	0	7 (8.1%)	0
Arthralgia	12 (13.3%)	1 (1.1%)	7 (8.1%)	0
Weight Decreased	9 (10.0%)	0	5 (5.8%)	0
Vomiting	13 (14.4%)	0	5 (5.8%)	0

(a) Incidence of pleural effusion for 2.0 mg/kg dosing cohort was Grade 1=8 (8.9%) and Grade 2=8 (8.9%). For 2.7 mg/kg dosing cohort, incidence was Grade 1=12 (14.0%), Grade 2=12 (14.0%) and Grade 3=1 (1.2%).
(b) Incidence of palmar-plantar erythrodysaesthesia syndrome for 2.0 mg/kg dosing cohort was Grade 1=10 (11.1%) and Grade 2=4 (4.4%). For 2.7 mg/kg dosing cohort, incidence was Grade 1=11 (12.8%), Grade 2=8 (9.3%) and Grade 3=1 (1.2%).

Interim Treatment-Emergent Adverse Events[(a)] (TEAE) ≥10% (Any Grade)

Safety population (n=176)



(a) Adverse event preferred terms as per MedDRA v26.1.

Thank You!

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