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OA-10: BMS-986453, a Dual-Targeting BCMA × GPRC5D Autologous Chimeric Antigen Receptor (CAR) T Cell Therapy in Patients With Relapsed/Refractory Multiple Myeloma: Initial Results From a Phase 1 Trial

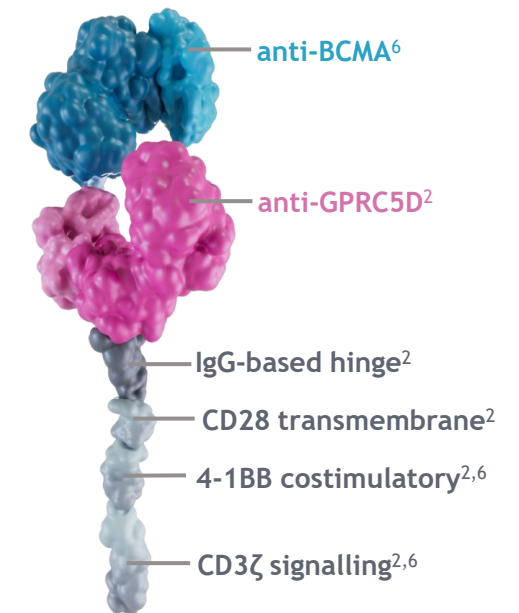
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Background

- Despite recent MM treatment advances, **most patients relapse**, presenting a need for novel, effective therapeutic strategies upfront to improve long-term survival^{1,2}
- **BCMA** and **GPRC5D** are highly expressed and **clinically validated as independent, T-cell-redirecting therapy targets** for MM.³ However, single-antigen-targeting approaches have limitations, partly due to baseline tumor heterogeneity and target modification³⁻⁵
- Simultaneously targeting BCMA and GPRC5D with a **dual-targeting CAR T cell approach** may prevent resistance and allow for **deeper and more durable responses** in patients with RRMM⁵
- **BMS-986453** is an autologous, dual-targeting BCMA × GPRC5D CAR T cell therapy under investigation in a **phase 1 trial** in patients with RRMM

Domain structure of dual-targeting CAR (BCMA × GPRC5D), BMS-986453



Objective

To present the initial phase 1 safety and preliminary efficacy results of a first-in-human study evaluating BMS-986453 in patients with RRMM

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; GPRC5D, G-protein coupled receptor C group 5 member D; IgG, immunoglobulin G; MM, multiple myeloma; RRMM, relapsed/refractory multiple myeloma.

1. Nijhof IS, et al. *Drugs*. 2018;78(1):19-37. 2. Smith EL, et al. *Sci Transl Med*. 2019;11(485):eaau7746. 3. van de Donk NWCJ, et al. *HemaSphere*. 2025;9(11):e70260. 4. Lu Y, et al. *Mol Cancer*. 2025;24(1):126.

5. van de Donk NWCJ, et al. *Blood*. 2026;147(19):2176-2193. 6. Harrington K, et al. Presented at the 59th American Society of Hematology (ASH) Annual Meeting & Exposition; December 9-12, 2017; Atlanta, GA. Abstract 1813.

Hansen D, et al. IMS 2026, Presentation OA-10

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Study Design

Phase 1, first-in-human, multicenter, open-label, dose-finding study evaluating BMS-986453 in patients with RRMM (NCT06153251)

Key eligibility criteria

- **Adults:** ≥ 18 y
- **Confirmed progressive disease** on or within 12 mo of completing anti-myeloma regimen^a
- **Prior LOT:** ≥ 3 , including a PI, an IMiD, and CD38 mAb
- **ECOG PS:** 0 or 1
- **Measurable disease**
- **Prior BCMA/GPRC5D-targeted therapy allowed**

Screening

Leukapheresis

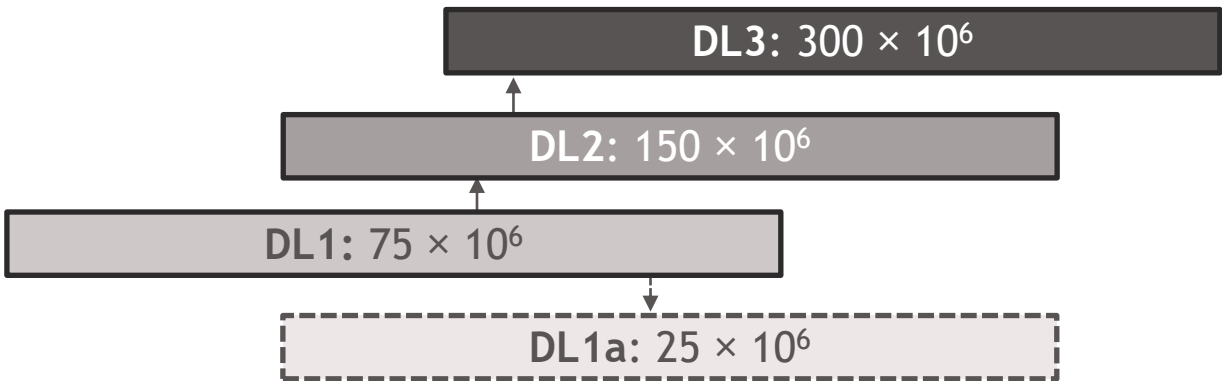
Bridging therapy (optional)^b

LDC

One-time infusion of BMS-986453

Post-treatment safety follow-up, up to 48 mo

BMS-986453: dose-escalation and expansion



Objectives

Primary

- Safety and tolerability
- MTD or BMS-986453 RP2D

Secondary

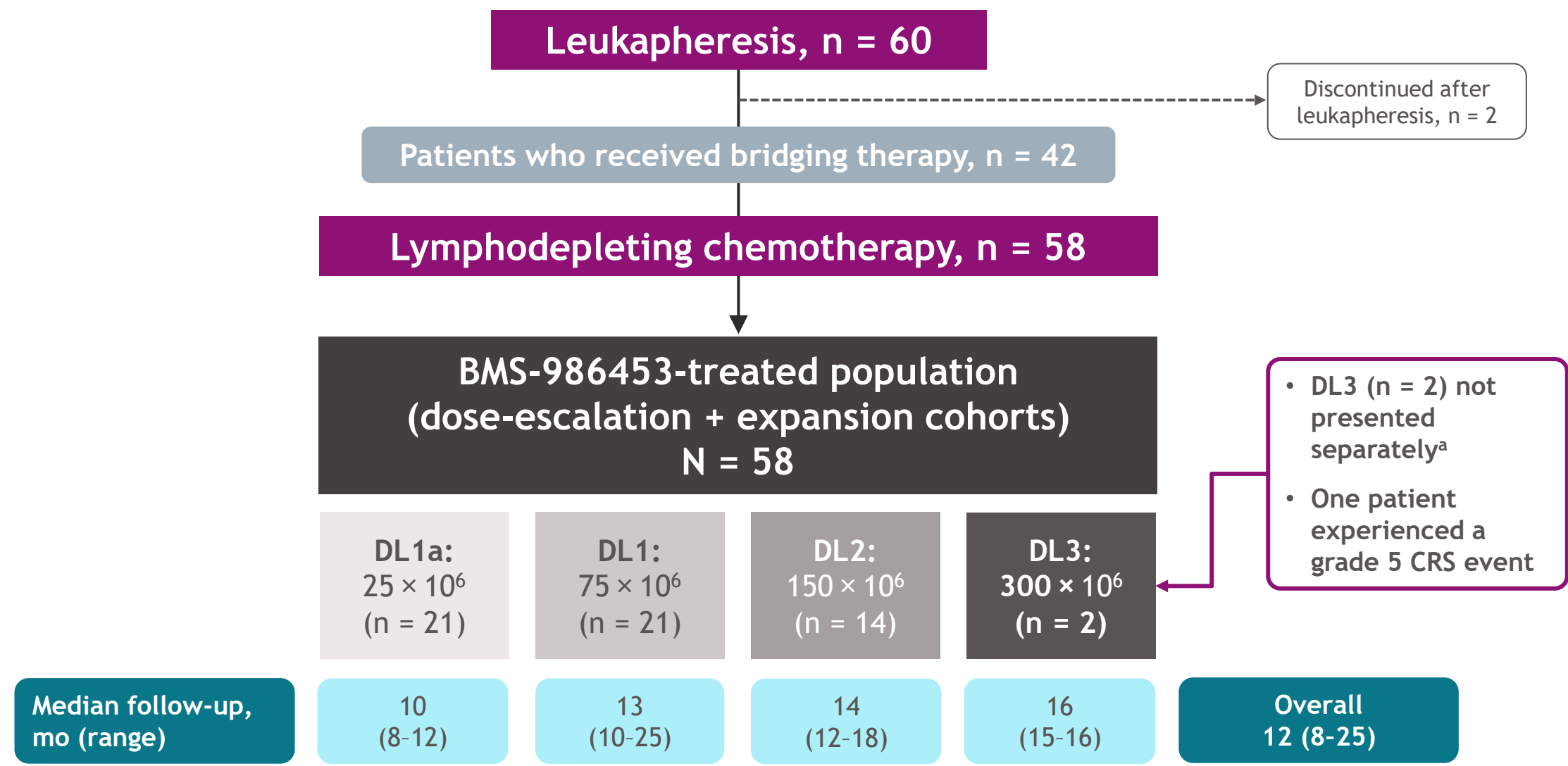
- Pharmacokinetic profile
- Preliminary efficacy (ORR, PFS, OS, TTR, and DOR)

^aMeasured from the last dose.

^bCompleted at investigator discretion.

BCMA, B-cell maturation antigen; DL, dose level; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GPRC5D, G-protein coupled receptor C group 5 member D; IMiD, immunomodulatory drug; LDC, lymphodepleting chemotherapy; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; MTD, maximum tolerated dose; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma; TTR, time to response.

Study Flow Diagram



Data cutoff: April 27, 2026.
^aDL3 is included in the all treated (N = 58) results.
CRS, cytokine release syndrome; DL, dose level.

Baseline Demographics and Disease Characteristics

Characteristic	DL1a: 25 × 10 ⁶ CAR T cells, n = 21	DL1: 75 × 10 ⁶ CAR T cells, n = 21	DL2: 150 × 10 ⁶ CAR T cells, n = 14	All treated patients, N = 58
Age, median (range), y	66 (54-79)	69 (54-77)	65.5 (50-77)	67 (50-79)
Sex, male, n (%)	14 (67)	12 (57)	11 (79)	38 (65.5)
Race, n (%)				
White	16 (76)	18 (86)	13 (93)	48 (83)
Black/African American	2 (10)	0	0	2 (3)
Other ^a	1 (5)	1 (5)	1 (7)	3 (5)
Not reported	2 (10)	2 (10)	0	5 (9)
Prior LOT, median (range)	4.0 (3-12)	4.0 (3-14)	5.5 (3-9)	4.0 (3-14)
Refractory status, n (%)				
Triple-refractory	13 (62)	11 (52)	5 (36)	29 (50)
Penta-refractory	6 (29)	2 (10)	1 (7)	9 (16)
Prior BCMA-exposed, n (%)	15 (71)	11 (52)	8 (57)	35 (60)
CAR T cell therapy	14 (67)	10 (48)	8 (57)	33 (57)
TCE / ADC	3 (14) / 2 (10)	4 (19) / 1 (5)	0 / 0	7 (12) / 3 (5)
Prior exposure to GPRC5D and BCMA, n (%) ^b	5 (24)	3 (14)	1 (7)	10 (17)
High risk cytogenetics at diagnosis, n (%) ^c	7 (33)	8 (38)	3 (21)	19 (33)
Extramedullary disease, n (%) ^d	8 (38)	2 (10)	4 (29)	15 (26)

Key baseline demographics and disease characteristics were similar across the assessed dose groups

Data cutoff: April 27, 2026.

^aOther races included Asian and American Indian/Alaska native.

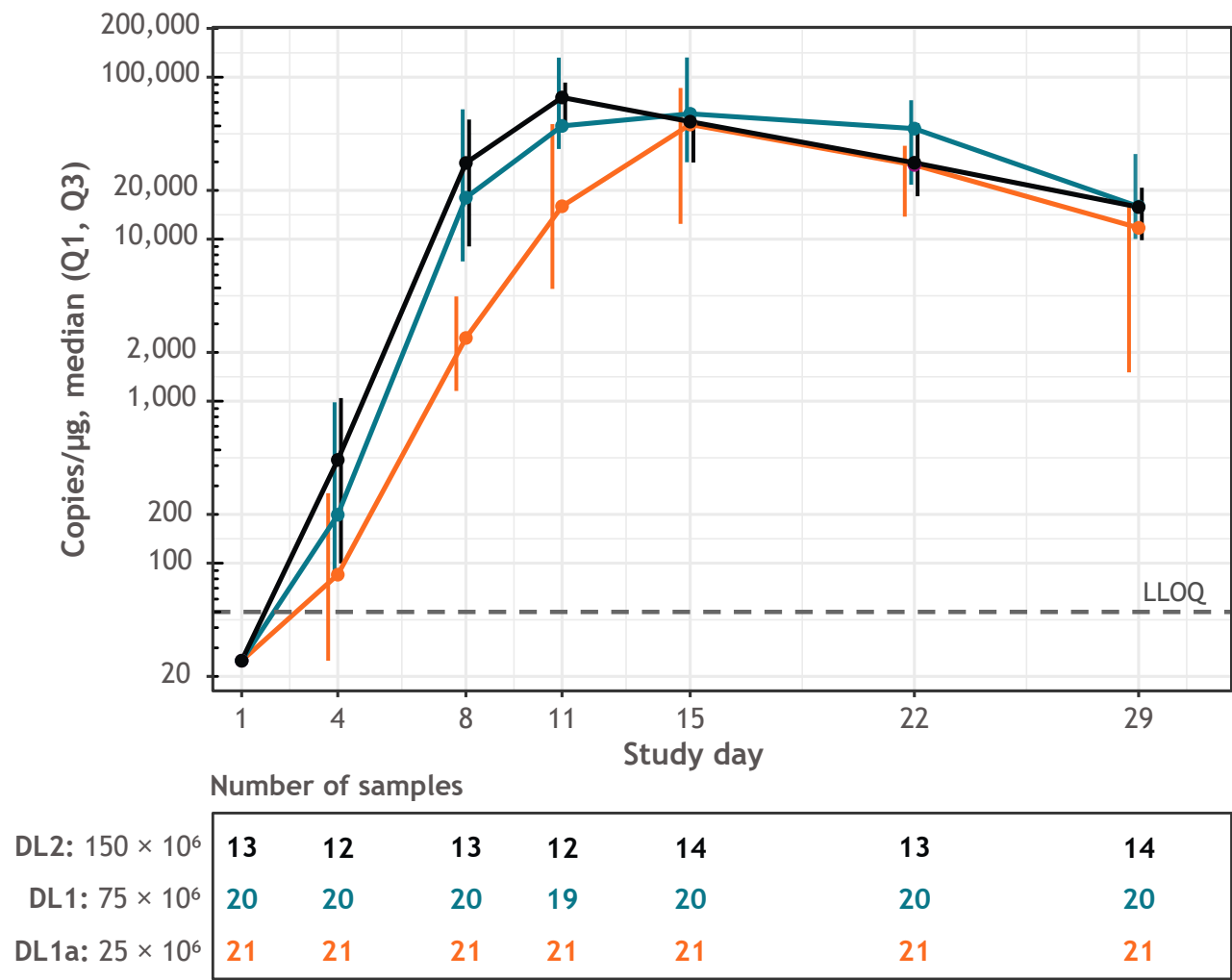
^bAll patients with prior GPRC5D exposure also had prior BCMA exposure.

^cHistory of one or more of the following: translocation (4;14), translocation (14;16), 17p-, 1q21 amplification.

^dExtramedullary disease includes parasosseous and extraosseous lesions.

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; DL, dose level; GPRC5D, G-protein coupled receptor C group 5 member D; LOT, line of therapy; TCE, T-cell engager.

Pharmacokinetic Profile



Cohort	C _{max} (copies/μg)	T _{max} (day)	AUC(0-28) (days*copies/μg)
DL1a: 25 × 10 ⁶	32,400 [21] (726)	14.0 [21] (3.00-28.0)	333,000 [21] 602
DL1: 75 × 10 ⁶	92,500 [20] (96.3)	14.0 [20] (3.00-28.0)	1,070,000 [20] 117
DL2: 150 × 10 ⁶	71,700 [14] (62.4)	14.0 [14] (7.00-21.0)	872,000 [13] 58.7

AUC = geometric mean [N] (geometric CV%); C_{max} = geometric mean [N] (geometric CV%); T_{max} = median [N] (minimum-maximum).

Analysis showed similar results for DL1 (75 × 10⁶) and DL2 (150 × 10⁶) cohorts for:

- T_{max}
- C_{max}
- AUC(0-28)

Compared with DL1a (25 × 10⁶), both the DL1 and DL2 cohorts had:

- Higher peak values
- Greater total exposure

Safety: TEAEs

	DL1a: 25 × 10 ⁶ CAR T cells, n = 21		DL1: 75 × 10 ⁶ CAR T cells, n = 21		DL2: 150 × 10 ⁶ CAR T cells, n = 14		All treated patients, N = 58	
	Any	Grade 3/4	Any	Grade 3/4	Any	Grade 3/4	Any	Grade 3/4
Any TEAE, n (%)	21 (100)	20 (95)	21 (100)	21 (100)	14 (100)	14 (100)	58 (100)	57 (98)
Hematologic TEAEs (≥ 30% in all patients)								
Neutropenia	19 (91)	18 (86)	20 (95)	20 (95)	12 (86)	11 (79)	53 (91)	51 (88)
Thrombocytopenia	15 (71)	10 (48)	17 (81)	11 (52)	8 (57)	6 (43)	41 (71)	28 (48)
Anemia	13 (62)	7 (33)	15 (71)	9 (43)	4 (29)	3 (21)	33 (57)	20 (35)
Leukopenia	8 (38)	7 (33)	9 (43)	9 (43)	4 (29)	3 (21)	23 (40)	21 (36)
Lymphopenia	4 (19)	4 (19)	7 (33)	7 (33)	7 (50)	6 (43)	18 (31)	17 (29)
Non-hematologic TEAEs (≥ 30% in all patients)								
CRS	12 (57)	0	18 (86)	1 (5)	13 (93)	0	45 (78) ^a	2 (3) ^a
ALT increased	6 (29)	3 (14)	5 (24)	0	7 (50)	3 (21)	19 (33)	6 (10)
Dysgeusia ^b	2 (10)	—	8 (38)	—	7 (50)	—	18 (31)	—
Infections and infestations	9 (43)	5 (24)	12 (57)	4 (19)	8 (57)	3 (21)	30 (52)	12 (21)

DLTs occurred in 19% of patients, including hematologic DLTs in 12%.
Hematologic TEAEs were the most common, consistent with known CAR T cell class effects

Data cutoff: April 27, 2026. AEs were coded using MedDRA (v28.1) and graded using CTCAE (v5.0).
A patient with multiple TEAEs was counted only once in each TEAE category. TEAEs were defined as (1) any AEs reported from the initial BMS-986453 infusion through 6 mo (180 days) after infusion and (2) any AEs related to therapy or study procedures and all SAEs (regardless of causality) and all SPMs from 6 mo after BMS-986453 infusion until EOS. Any AEs occurring after the initiation of subsequent anticancer treatment were not considered TEAEs.
^aA single grade 5 TEAE occurred on study: a grade 5 event of CRS in a BCMA-naïve patient treated at the DL3 (300 × 10⁶) cell dose. This was attributed to BMS-986453.
^bDysgeusia is limited to grades 1-2 per CTCAE.
AE, adverse event; ALT, alanine aminotransferase; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DL, dose level; DLT, dose-limiting toxicity; EOS, end of study; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SPM, second primary malignancy; TEAE, treatment-emergent adverse event.

Safety: Treatment-related AEs of Special Interest

	DL1a: 25 × 10 ⁶ CAR T cells, n = 21		DL1: 75 × 10 ⁶ CAR T cells, n = 21		DL2: 150 × 10 ⁶ CAR T cells, n = 14		All treated patients, N = 58	
	Any	Grade 3/4	Any	Grade 3/4	Any	Grade 3/4	Any	Grade 3/4
TRAЕ of special interest, n (%)								
CRS	12 (57)	0	18 (86)	1 (5)	13 (93)	0	45 (78) ^a	2 (3) ^a
ICANS	1 (5)	1 (5)	1 (5)	1 (5)	0	0	2 (3)	2 (3)
IEC-HS	1 (5)	0	1 (5)	0	0	0	2 (3)	0
Ataxia and balance disorders ^b	0	0	2 (10)	0	0	0	2 (3)	0
Weight loss	1 (5)	0	2 (10)	1 (5)	2 (14)	0	6 (10)	1 (2)
On-target, off-tumor ^c	4 (19)	0	15 (71)	1 (5)	9 (64)	1 (7)	29 (50)	2 (3)
Skin	0	0	4 (19)	0	6 (43)	0	11 (19)	0
Oral	2 (10)	0	10 (48)	1 (5)	7 (50)	1 (7)	20 (35)	2 (3)
Nail	3 (14)	0	11 (52)	0	6 (43)	0	21 (36)	0

Although TRAЕs of special interest were common among all assessed doses, few resulted in grade 3 or 4 events

Data cutoff: April 27, 2026. AEs were coded using MedDRA (v28.1) and graded using CTCAE (v5.0). ASTCT grading was used for CRS and ICANS.¹ Multiple events occurring within 1 day from each other were considered as one episode. TRAЕs were defined as (1) any AEs reported from the initial BMS-986453 infusion through 6 mo (180 days) after infusion and (2) any AEs related to therapy or study procedures and all SAEs (regardless of causality) and all SPMs from 6 mo after BMS-986453 infusion until EOS. Any AEs occurring after the initiation of subsequent anticancer treatment were not considered TRAЕs.

^aIncludes one case of grade 5 CRS in a BCMA-naïve patient treated at the DL3 (300 × 10⁶) cell dose.

^bPreviously reported as OSN for arlocabtagene autoleucel (arlo-cel). For ataxia and balance disorders, the treatment-related preferred terms include ataxia, neurotoxicity, nystagmus, dysarthria, diplopia, dysmetria, and gait disturbance (excluding dizziness).

^cThe preferred terms include ageusia, alopecia, dermatitis acneiform, dry skin, dysgeusia, dysphagia, nail discoloration, nail disorder, nail dystrophy, nail ridging, onychoclasia, onychomadesis, pruritus, pruritus allergic, purpura, rash, rash maculo-papular, skin exfoliation, skin ulcer, taste disorder, tongue dry, tongue ulceration.

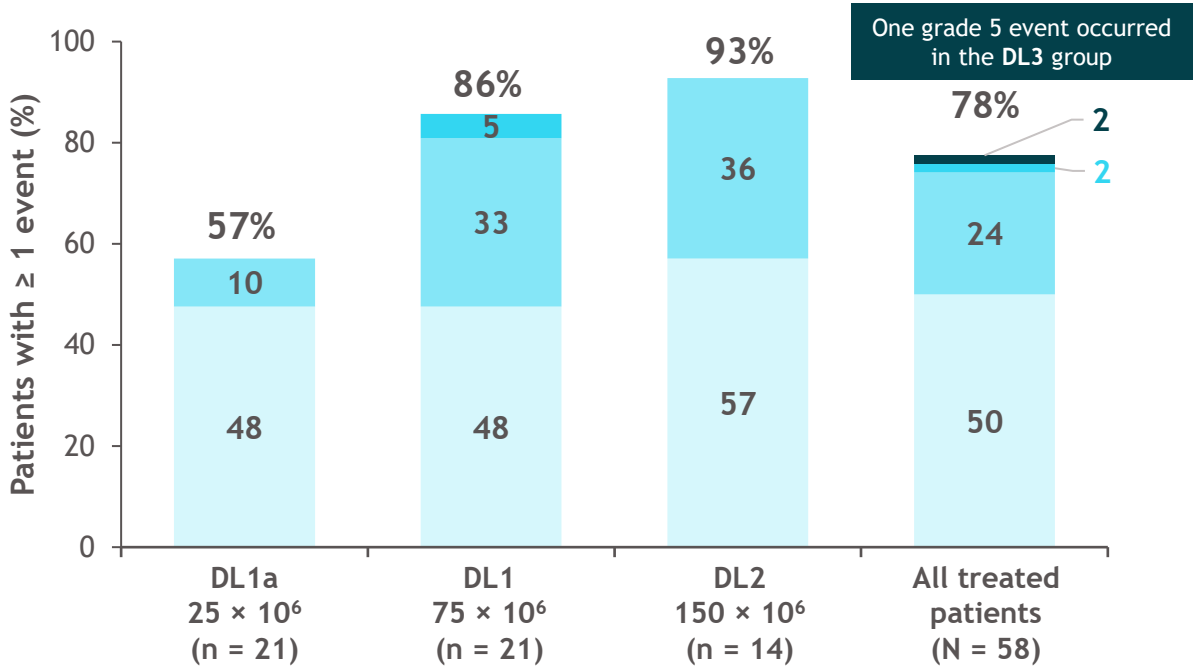
AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DL, dose level; EOS, end of study; GPRC5D, G-protein coupled receptor C group 5 member D; ICANS, immune effector cell-associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; MedDRA, Medical Dictionary for Regulatory Activities; OSN, other select neurotoxicity; SAE, serious adverse event; SPM, second primary malignancy; TRAЕ, treatment-related adverse event.

1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625-638.

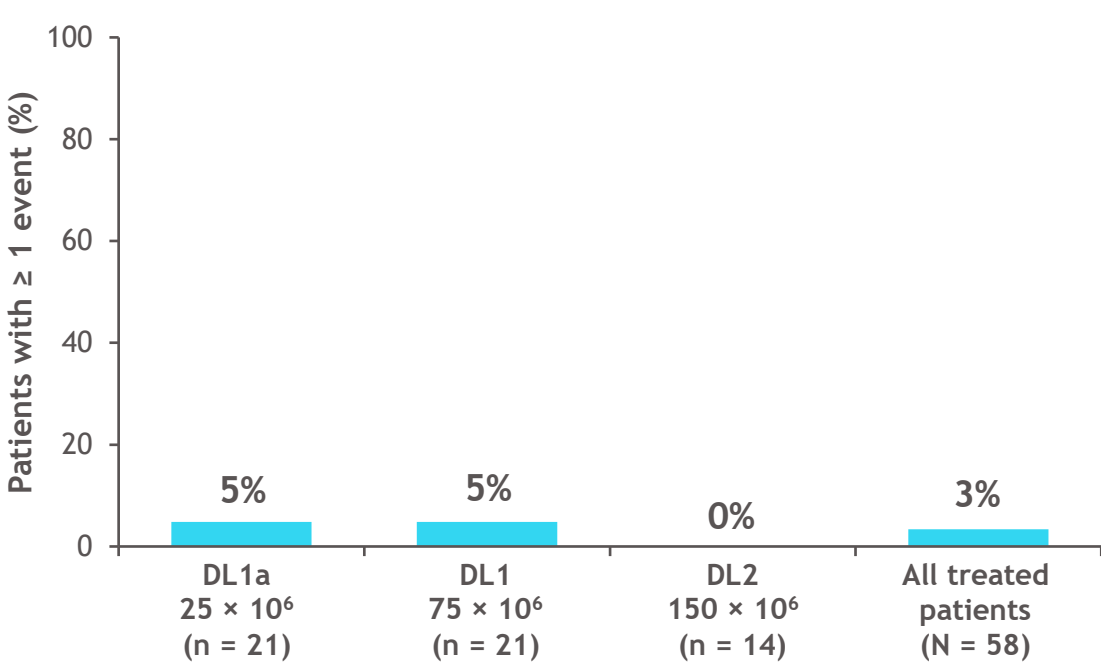
Safety: Treatment-related CRS and ICANS

Grade 1 Grade 2 Grade 3 Grade 4 Grade 5

CRS



ICANS

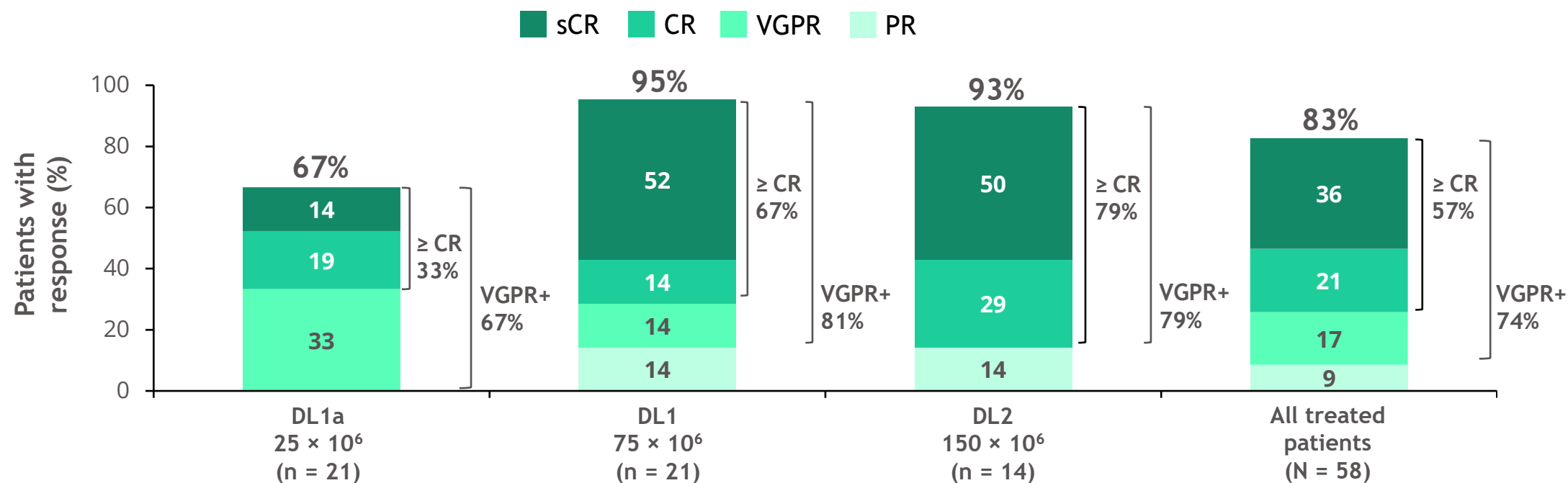


Median time to onset, days (range) ^a	4.5 (2-13) (n = 12)	3 (1-10) (n = 18)	2 (1-10) (n = 13)	3 (1-13) (n = 45)
Median time to resolution, days ^b	1 (n = 12)	3 (n = 19)	3 (n = 13)	2.5 (n = 46)

Median time to onset, days (range) ^c	13 (n = 1)	3 (n = 1)	NR (n = 0)	8 (3-13) (n = 2)
Median time to resolution, days ^d	9 (n = 1)	26 (n = 1)	NR (n = 0)	17.5 (n = 2)

Data cutoff: April 27, 2026. ASTCT grading was used for CRS and ICANS.¹
^aTime to first onset of CRS: first start date of CRS infusion date + 1. ^bTime to resolution was calculated per episode and only resolved episodes were considered. ^cMultiple events occurring within 7 days from each other were considered as one episode. Individual ICANS events were considered. ^dOnly resolved episodes included.
CRS, cytokine release syndrome; DL, dose level; ICANS, immune effector cell-associated neurotoxicity syndrome; NR, not reached.
1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625-638.

Efficacy: ORR by Dose Level, All Treated



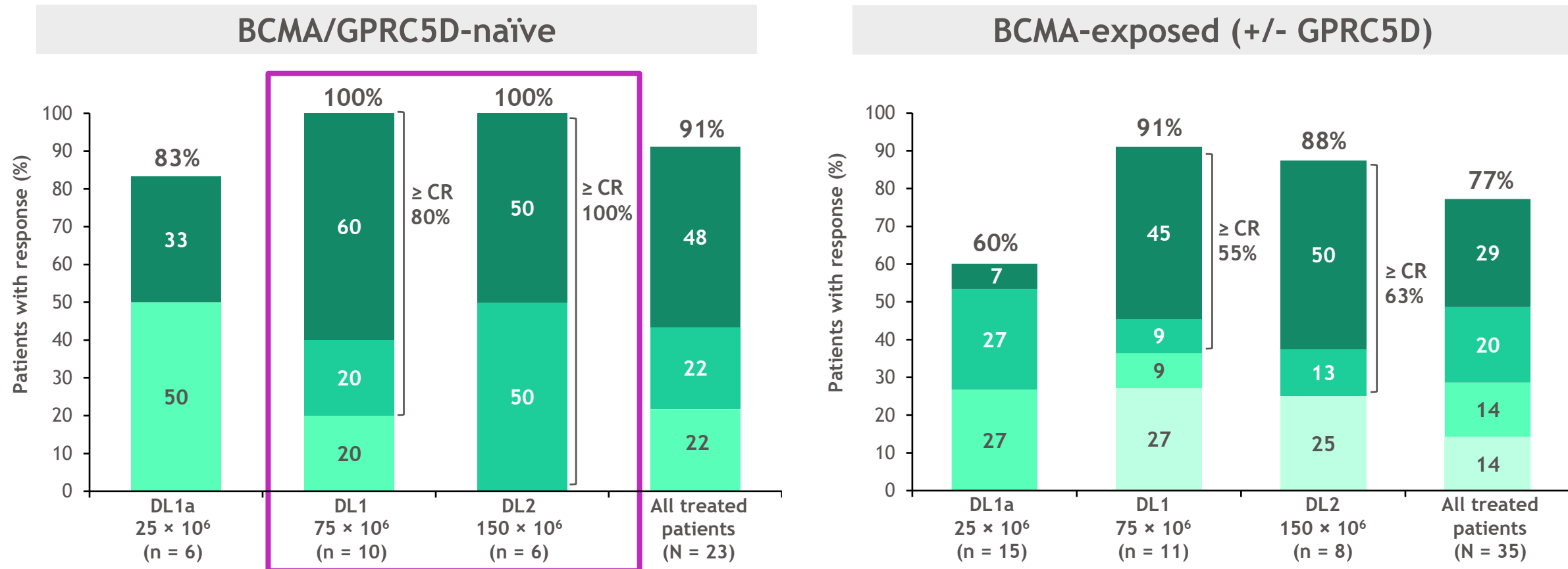
	DL1a (n = 21)	DL1 (n = 21)	DL2 (n = 14)	All treated patients (N = 58)
Median TTR (range), mo ^a	1 (0.9-6.1)	1 (1.0-3.3)	1 (0.9-6.0)	1 (0.9-6.1)
Time to CR or better	4.93 (1.0-6.1)	5.96 (1.0-14.6)	4.90 (1.0-14.8)	4.99 (1.0-14.8)

High response rates were observed with BMS-986453 across the assessed DLs; 74% of all patients treated with BMS-986453 achieved VGPR or better. CRR was at least 67% for patients treated with DL1 or DL2. Median DOR was not reached across DLs

Data cutoff: April 27, 2026. ORR is defined as the rate of patients whose response is PR or better (ie, sCR, CR, VGPR, or PR).
^aAnalyses are based on responders only. A 3-day window was added to each mo for mo 1 to 8; and a 14-day window was added to mo 9 and onwards.
CR, complete response; CRR, complete response rate; DL, dose level; DOR, duration of response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; TTR, time to response; VGPR+, very good partial response or better.

Efficacy: ORR by Prior BCMA Exposure

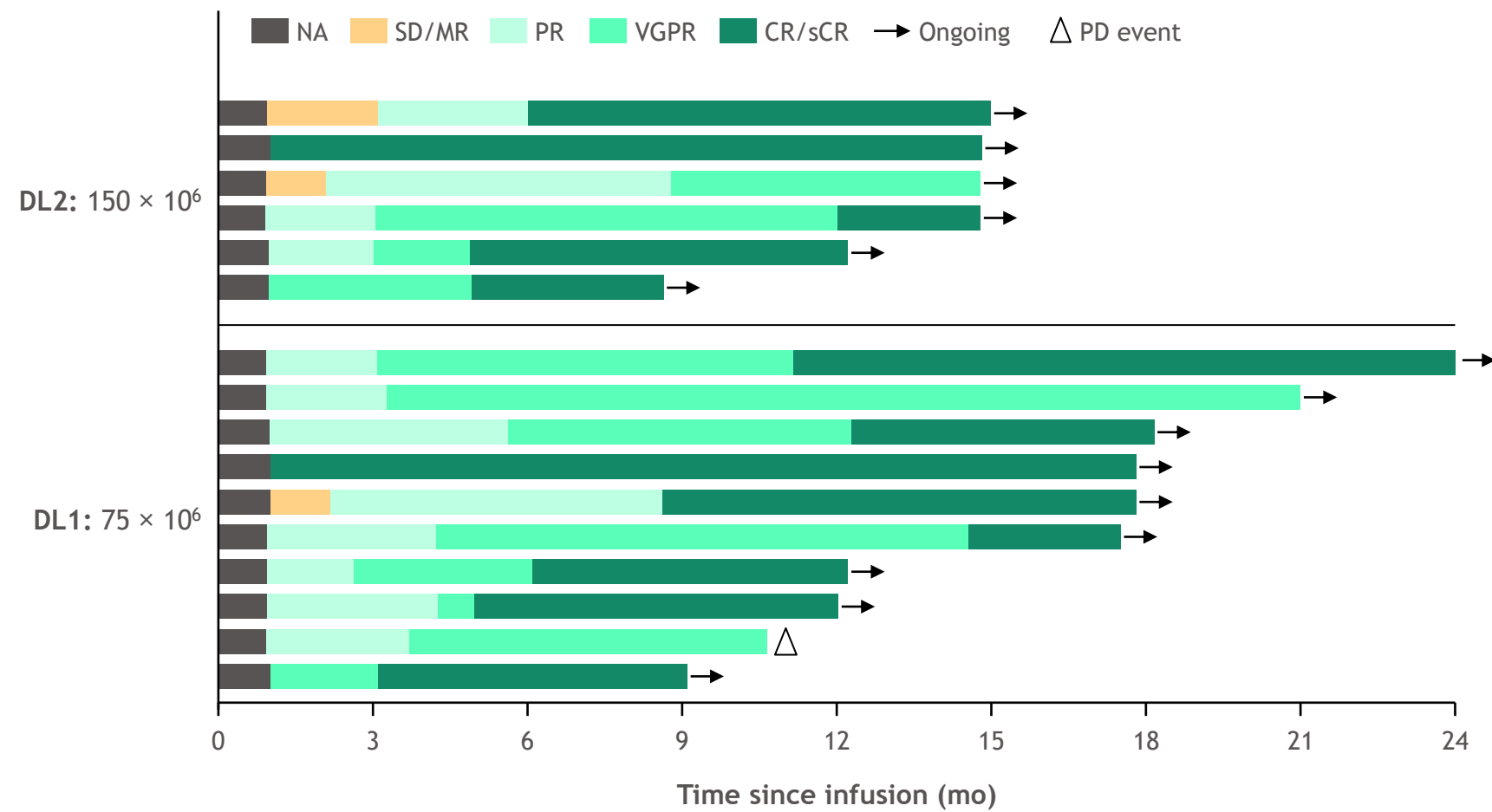
sCR CR VGPR PR



Among the BCMA/GPRC5D-naïve population, 100% of the patients receiving DL1 (75 × 10⁶) and DL2 (150 × 10⁶) achieved VGPR or better (n = 16) and the CRR was 88% (n = 14/16)

Data cutoff: April 27, 2026. ORR is defined as the rate of patients whose response is PR or better (ie, sCR, CR, VGPR, or PR).
BCMA, B-cell maturation antigen; CR, complete response; CRR, complete response rate; DL, dose level; GPRC5D, G-protein coupled receptor C group 5 member D; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR+, very good partial response or better.

Efficacy: Responses in BCMA/GPRC5D-Naïve Patients at DL1 and DL2

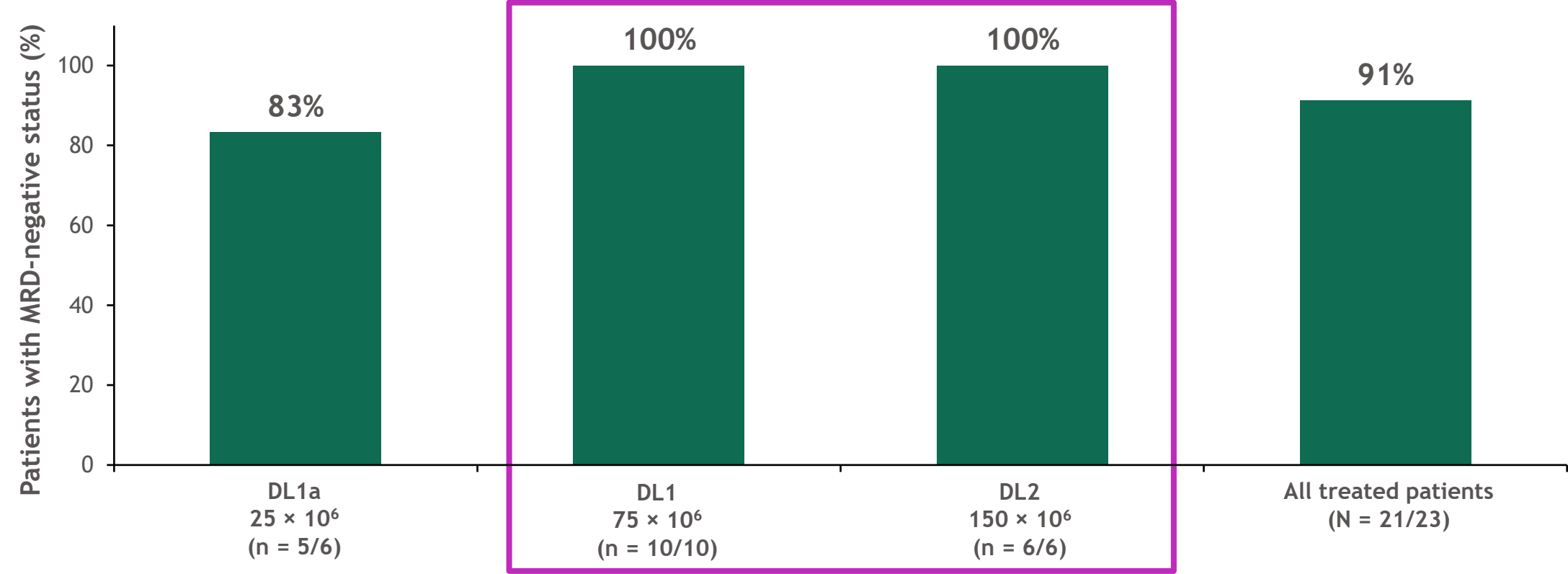


Responses deepened with extended follow-up

- Most responses (15/16, 94%) were ongoing at data cutoff

Data cutoff: April 27, 2026.
BCMA, B-cell maturation antigen; CR, complete response; DL, dose level; GPRC5D, G-protein coupled receptor C group 5 member D; MR, minimal response; NA, not available; PD, progressive disease; PR, partial response; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

Efficacy: MRD Negativity Overall in BCMA/GPRC5D-Naïve Patients



All patients who were BCMA/GPRC5D-naïve and treated at DL1 and DL2 (n = 16) were MRD-evaluable and 100% were MRD-negative at the 10⁻⁵ threshold as assessed by flow cytometry

Data cutoff: April 27, 2026.
The MRD negativity rate is the proportion of patients with MRD-negative status at a sensitivity of 10⁻⁵, at any time point after treatment as assessed by flow cytometry.
BCMA, B-cell maturation antigen; DL, dose level; GPRC5D, G-protein coupled receptor C group 5 member D; MRD, minimal residual disease.
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Authors Conclusions

- Across the 25, 75, 150, and 300 × 10⁶ CAR T cell dose cohorts, BMS-986453 demonstrated **good tolerability** with a low frequency of grade ≥ 3 CRS, ICANS, and other AESI
- Across 75 and 150 × 10⁶ dose cohorts, the pharmacokinetic profiles were similar, with higher C_{max} values and greater AUC compared with the 25 × 10⁶ dose cohort
- BMS-986453 demonstrated **high efficacy** in patients with RRMM and a median of 4 prior LOT in this phase 1 trial. At a median follow-up of 12 mo:
 - **ORR was 83%** for all patients and **100%** for patients who were BCMA/GPRC5D-naïve and treated with 75 × 10⁶ or 150 × 10⁶ CAR T cells (n = 16)
 - Among the patients treated with 75 × 10⁶ or 150 × 10⁶ CAR T cells who were BCMA/GPRC5D-naïve, **100% achieved ≥ VGPR**, and **responses continued to deepen** with extended follow-up; the **CRR was 88%** (n = 14/16)
 - Among the MRD-evaluable patients treated with 75 × 10⁶ or 150 × 10⁶ CAR T cells who were BCMA/GPRC5D-naïve (n = 16), **100% were MRD-negative** at the 10⁻⁵ threshold

BMS-986453 demonstrated a favorable safety profile and promising efficacy in patients with heavily pretreated RRMM; the study is ongoing