KarMMa-3 subgroup analysis in older patients with relapsed/refractory multiple myeloma treated with idecabtagene vicleucel

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Disclosures

- Dr K Patel reports consultancy (includes expert testimony) for Oricell, Kite, Genentech, Bristol Myers Squibb, Janssen, Takeda, Caribou, AbbVie, Poseida, Legend Biotech, Sanofi, AstraZeneca, Regeneron, and Novartis

Introduction

- Idecabtagene vicleucel (ide-cel), a B-cell maturation antigen–targeted CAR T cell therapy, has been associated with an increase in PFS and improved response compared with standard regimens in patients with relapsed/refractory multiple myeloma (RRMM) who had received 2 – 4 prior regimens[1]
- Older individuals (aged ≥ 70 years) are the largest increasing population of patients with RRMM, though investigations within this patient subpopulation are limited[2]
- Developing a better understanding of the relationship between patient age and CAR T cell therapy outcomes may help guide treatment and clinical practice[2]

The objective of this analysis of the KarMMa-3 trial data is to describe efficacy and safety outcomes in older and younger patients who received either ide-cel or standard therapy regimens

CAR, chimeric antigen receptor; PFS, progression-free survival.

1. Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388(11):1002–1014. **2.** Turesson I, et al. *Eur J Haematol*. 2018;101(2):237–244.

Study design

- KarMMa-3 (NCT03651128) is an open-label, phase 3 trial in patients with RRMM[1,2]

Key Eligibility Criteria

- ≥ 18 years of age
- Diagnosis of RRMM with documented progressive disease within 60 days of last dose of prior regimen
- ≥ 2 to ≤ 4 prior anti-myeloma regimens including a proteasome inhibitor, an immunomodulatory agent, and CD38 monoclonal antibody
- ECOG performance status 0 or 1

Outcomes Measured

- Overall response rate (ORR)
- Progression-free survival (PFS)
- Overall survival (OS)
- Patient-reported quality of life (QoL)
- Safety

[a]DPd, DVd, EPd, IRd, or Kd. [b]Crossover to ide-cel was allowed after confirmed progressive disease.
DPd, daratumumab, pomalidomide, dexamethasone; DVd, daratumumab, bortezomib, dexamethasone; EPd, elotuzumab, pomalidomide, dexamethasone; ide-cel, idecabtagene vicleucel; IRd, ixazomib, lenalidomide, dexamethasone; Kd, carfilzomib, dexamethasone; LDC, lymphodepleting chemotherapy; R, randomization; RRMM, refractory/relapsed multiple myeloma.
1. Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388(11):1002-1014. **2.** Efficacy and Safety Study of bb2121 Versus Standard Regimens in Subjects With Relapsed and Refractory Multiple Myeloma (RRMM) (KarMMa-3). ClinicalTrials.gov identifier: NCT03651128. Updated December 15, 2022. Accessed January 27, 2026.

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Baseline characteristics

- A total of 386 patients were randomized to ide-cel (n = 254) or standard regimens (n = 132)
- **Among patients receiving ide-cel**
  - High-risk cytogenetics occurred in 32.7% of patients ≥ 70 years of age and 44.4% of patients < 70 years of age
  - Triple-class refractory disease occurred in 55.1% of patients ≥ 70 years of age and 66.8% of patients < 70 years of age
- Median time to progression from last prior anti-myeloma treatment was longer for patients ≥ 70 years of age who received ide-cel vs standard treatment but similar between treatment arms for patients < 70 years of age

Baseline characteristics

Characteristic	Age ≥ 70 years		Age < 70 years	
	Ide-cel (n = 49)	Standard regimens (n = 27)	Ide-cel (n = 205)	Standard regimens (n = 105)
Age, median (range), years	72 (70 – 81)	72 (70 – 83)	60 (30 – 69)	59 (42 – 69)
Sex, male, n (%)	32 (65.3)	17 (63.0)	124 (60.5)	62 (59.0)
Race, n (%)				
White	34 (69.4)	20 (74.1)	138 (67.3)	58 (55.2)
Black or African American	3 (6.1)	2 (7.4)	15 (7.3)	16 (15.2)
Asian	2 (4.1)	1 (3.7)	5 (2.4)	4 (3.8)
Unknown	10 (20.4)	4 (14.8)	44 (21.5)	23 (21.9)
Other	0	0	3 (1.5)	4 (3.9)
Extramedullary disease, n (%)	13 (26.5)	5 (18.5)	48 (23.4)	27 (25.7)
High-risk cytogenetics, n (%)				
Del(17p), t(4;14), and/or t(14;16)	16 (32.7)	15 (55.6)	91 (44.4)	46 (43.8)
Del(17p)	9 (18.4)	12 (44.4)	57 (27.8)	30 (28.6)
t(4;14)	9 (18.4)	3 (11.1)	34 (16.6)	15 (14.3)
t(14;16)	2 (4.1)	1 (3.7)	6 (2.9)	3 (2.9)
ECOG PS, n (%)				
0	19 (38.8)	9 (33.3)	101 (49.3)	57 (54.3)
1	30 (16.2)	17 (63.0)	103 (50.2)	45 (42.9)
≥ 2	0	1 (3.7)	1 (0.5)	3 (2.9)
Prior stem cell transplant, n (%)				
1 transplantation	28 (57.1)	13 (48.1)	139 (67.8)	74 (70.5)
> 1 transplantation	6 (12.2)	4 (14.8)	41 (20.0)	23 (21.9)
R-ISS stage III, n (%)	5 (10.2)	5 (18.5)	26 (12.7)	9 (8.6)
Triple-class refractory disease, n (%)	27 (55.1)	20 (74.1)	137 (66.8)	69 (65.7)
Time to progression from last prior anti-myeloma treatment, months	8.6	6.7	6.5	6.9

ide-cel, idecabtagene vicleucel; R-ISS, Revised International Staging System.

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Overall response rate and overall survival

- ORR was higher among older and younger patients treated with ide-cel when compared with older and younger patients treated with standard regimens

Outcomes	Age ≥ 70 years		Age < 70 years	
	Ide-cel (n = 49)	Standard regimens (n = 27)	Ide-cel (n = 205)	Standard regimens (n = 105)
ORR, % (95% CI)	81.6 (70.8 – 92.5)	48.1 (29.3 – 67.0)	68.8 (62.4 – 75.1)	41.0 (31.5 – 50.4)
***P* value**	0.0037		< 0.0001	

- Median (95% CI) OS was clinically meaningful in older and younger patients who received ide-cel: NR and 39.5 (27.8 – NR) months, respectively
  - Median OS may be confounded by patients who crossed over from standard regimens to ide-cel: 67% of patients ≥ 70 years of age and 53% of patients < 70 years of age

CI, confidence interval; ide-cel, idecabtagene vicleucel; NR, not reached; ORR, overall response rate; OS, overall survival.

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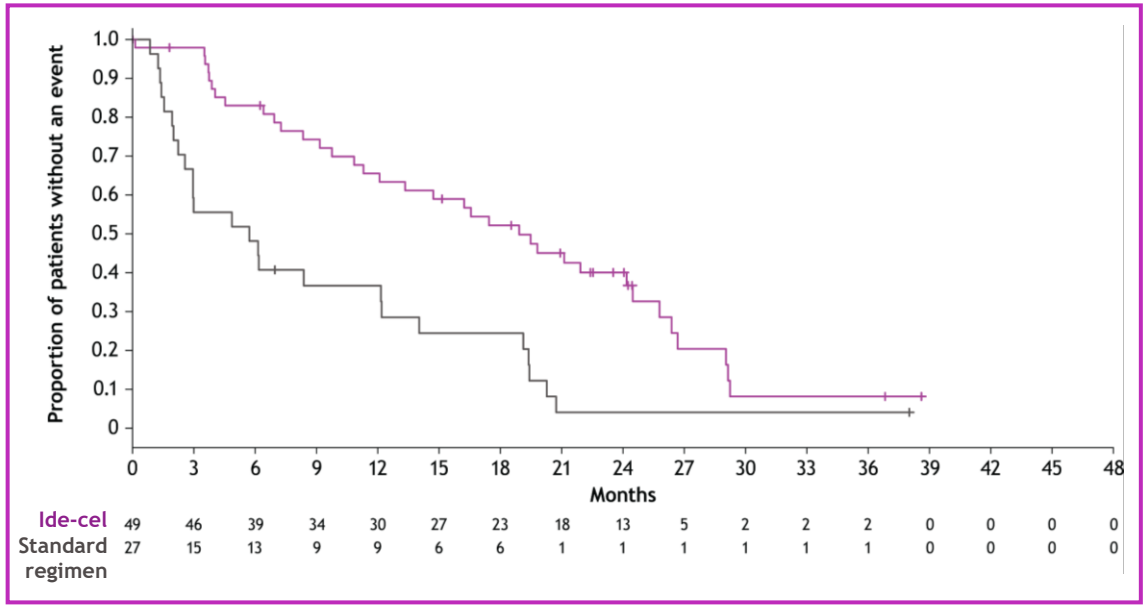
Progression-free survival

- Regardless of age, median PFS was longer among those who received ide-cel compared to those who received standard regimens

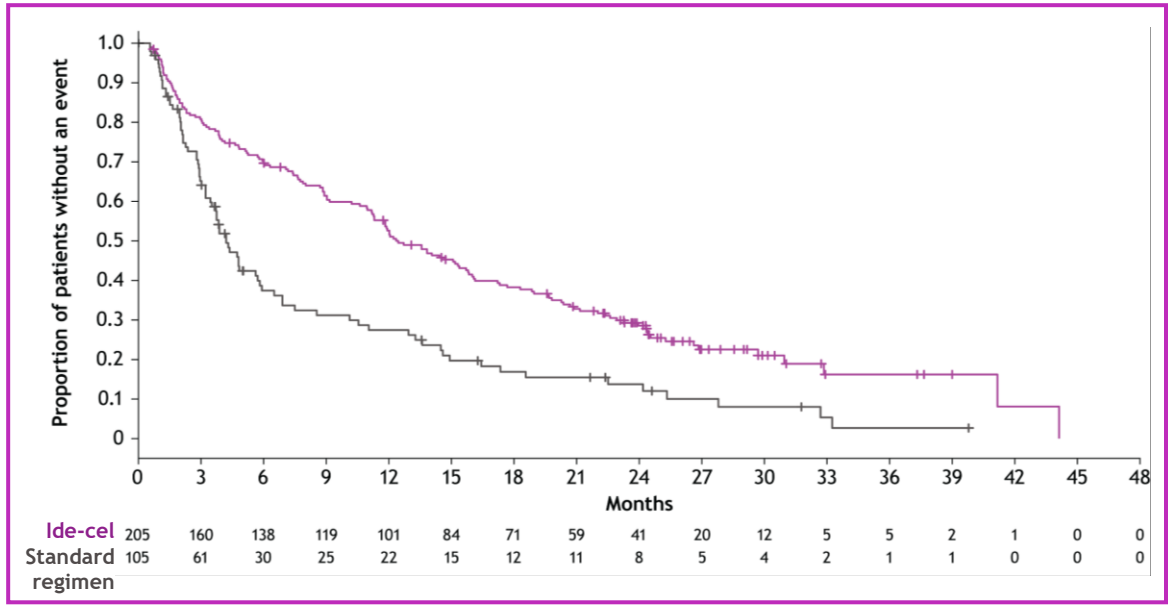
Median PFS (months)

Outcomes	Age ≥ 70 years		Age < 70 years	
	Ide-cel (n = 49)	Standard regimens (n = 27)	Ide-cel (n = 205)	Standard regimens (n = 105)
PFS, median (95% CI)	18.9 (12.1 – 24.5)	5.7 (2.2 – 12.2)	12.5 (11.2 – 15.4)	4.2 (3.5 – 5.7)
P value	0.0012		< 0.0001	

Patients aged ≥ 70 years



Patients aged < 70 years



CI, confidence interval; ide-cel, idecabtagene vicleucel; PFS, progression-free survival.

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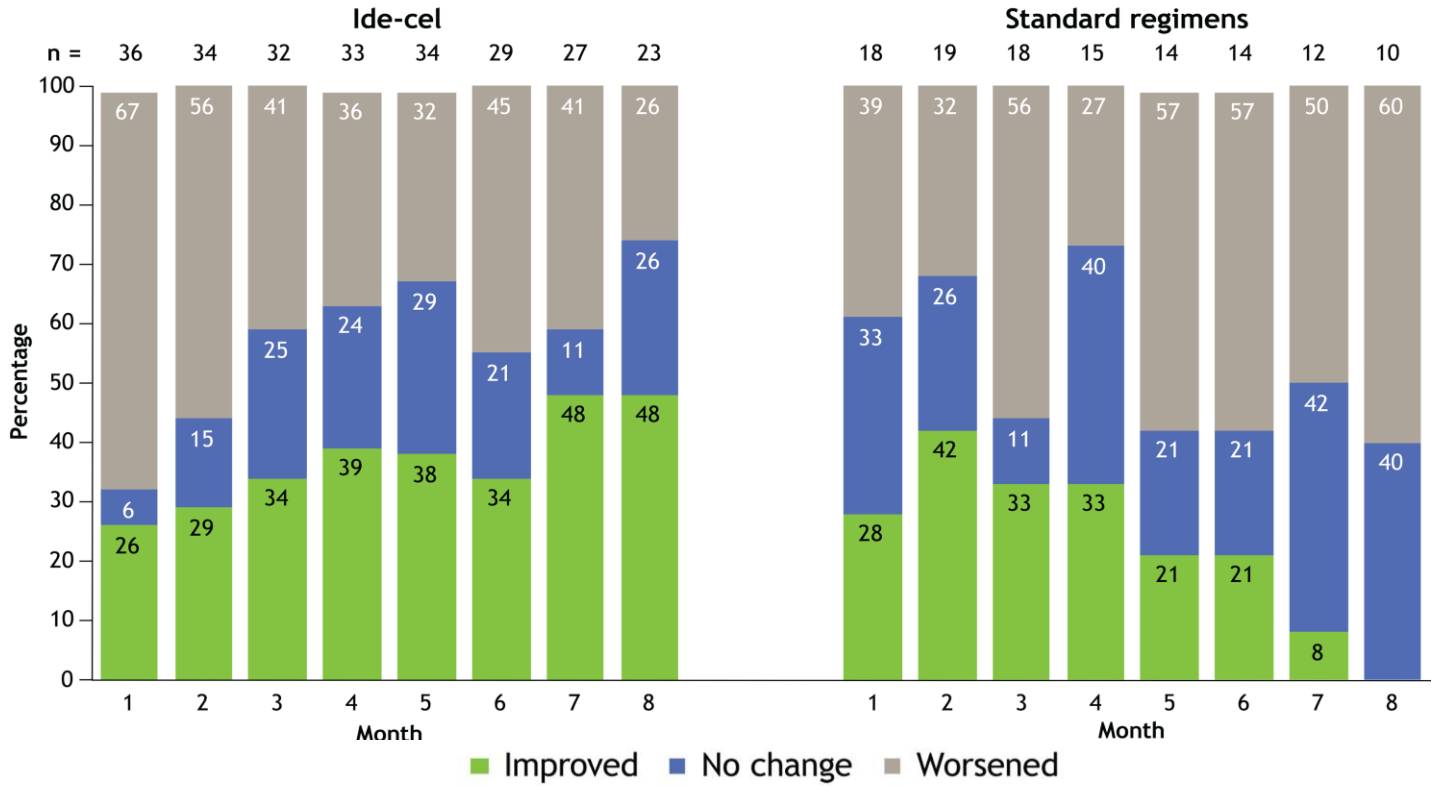
Patient-reported quality of life

- Generally, a consistently higher proportion of patients aged ≥ 70 years treated with ide-cel met the responder definition for improvement in global health status/QoL vs those who were treated with standard regimens

EORTC QLQ-C30 Global Health Status/QoL for patients aged ≥ 70 years



Patient-reported outcomes were assessed using the EORTC QLQ-C30 Global Health Status/QoL questionnaire at monthly visits in patients aged ≥ 70 years, comparing ide-cel with standard regimens. Responders were defined by a change from baseline of ≥ +5 (improvement) or ≤ −5 (deterioration).
EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ide-cel, idecabtagene vicleucel; QoL, quality of life.

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Safety

- No significant differences in safety profile were observed between the older and younger age groups among patients treated with ide-cel

TRAEs of special interest/select AEs grade ≥ 3 (safety population)				
AESI/select AE, n (%)	Age ≥ 70 years		Age < 70 years	
	Ide-cel (n = 47)	Standard regimens (n = 27)	Ide-cel (n = 178)	Standard regimens (n = 99)
At least 1 AESI/select AE[a]	14 (29.8)	13 (48.1)	70 (39.3)	29 (29.3)
CRS	3 (6.4)	-	8 (4.5)	-
Infection	12 (25.5)	6 (22.2)	48 (27.0)	20 (20.2)
iiNT	3 (6.4)	-	4 (2.2)	-

[a]Includes CRS, neurologic toxicity - Focused 2.0 FDA, and infections.
AE, adverse event; AESI, AE of special interest; CRS, cytokine release syndrome; ide-cel, idecabtagene vicleucel; iiNT, investigator identified neurotoxicity; TRAE, treatment-related AE.

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Conclusions

- Patients aged ≥ 70 years from the KarMMa-3 trial experienced benefit from ide-cel treatment compared with patients treated with standard regimens as evidenced by
  - Longer median PFS and notable ORR
  - Greater improvements in patient-reported global health status and QoL
- Although outcomes were consistent between the 2 age groups, patients aged ≥ 70 years had favorable baseline characteristics and less aggressive, heavily pretreated disease at baseline
  - Differences may reflect selection bias toward enrolling older patients considered to be easier to treat in first CAR T-cell trials for multiple myeloma, although more contemporaneous real-world data from late-line settings suggest ide-cel treatment is based on less restrictive selection criteria
- No new safety signals were identified among older and younger patient subpopulations

These observations reinforce the potential for durable benefit with a single ide-cel infusion in a real-world context without additional adverse safety signals, supporting its use across age groups

CAR, chimeric antigen receptor; ide-cel, idecabtagene vicleucel; ORR, overall response rate; MM, multiple myeloma; PFS, progression-free survival; QoL, quality of life.

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