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Idecabtagene Vicleucel (ide-cel, bb2121) for Relapsed and Refractory Multiple Myeloma in Elderly Patients: A Subgroup Analysis from the KarMMa Study

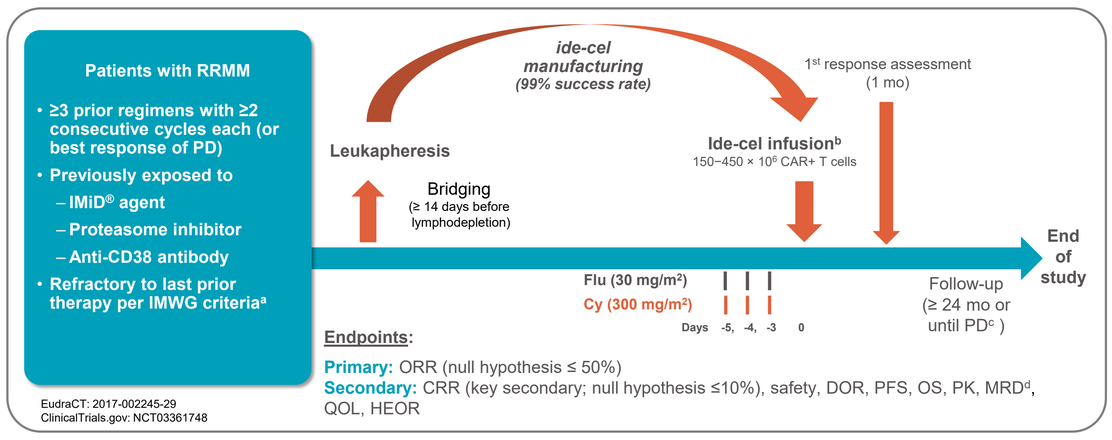
Salomon Manier,[1] Jesús Berdeja,[2] Noopur S. Raje,[3] David S. Siegel,[4] Yi Lin,[5] Larry D. Anderson, Jr,[6] Paula Rodriguez-Otero,[7] Hermann Einsele,[8] Michele Cavo,[9] Anna Truppel-Hartmann,[10] Everton Rowe,[11] Jill Sanford,[11] Julie Wang,[11] Timothy B. Campbell,[11] and Sundar Jagannath[12]

[1]Centre Hospitalier Universitaire de Nantes, Nantes, France; [2]Massachusetts General Hospital, Boston, MA, USA; [3]Hackensack University Medical Center, Hackensack, NJ, USA; [4]Mount Sinai Hospital, New York, NY, USA; [5]Emory School of Medicine, Atlanta, GA, USA; [6]The LeBow Institute for Myeloma Therapeutics and Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [7]University Hospital Heidelberg and National Center for Tumor Diseases, Heidelberg, Germany; [8]"Seràgnoli" Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; [9]bluebird bio, Cambridge, MA, USA; [10]Bristol Myers Squibb, Princeton, NJ, USA; [11]Clinica Universidad de Navarra, CIMA, IDISNA, CIBERONC, Navarra, Spain; and [12]Princess Margaret Cancer Centre, Toronto, ON, Canada

INTRODUCTION

- Multiple myeloma affects the older population more commonly than younger age groups; median age at diagnosis is 69 years in the US[1]
- Advanced age negatively impacts prognosis and limits treatment options for patients with hematologic malignancies, including multiple myeloma[2,3]
- Ide-cel, a BCMA-directed CAR T cell therapy, showed deep and durable responses in the pivotal phase II KarMMa study of patients with triple-class exposed RRMM[4]
- Objective: To examine the efficacy and safety of ide-cel in elderly patients in the KarMMa study

Figure 1. Pivotal phase II KarMMa study[4]



BCMA, B cell maturation antigen; BM, bone marrow; CAR, chimeric antigen receptor; CRR, complete response rate; Cy, cyclophosphamide; DOR, duration of response; Flu, fludarabine; GEP, gene expression profiling; HEOR, health economics and outcomes research; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression free survival; PK, pharmacokinetics; QOL, quality of life; RRMM, relapsed and refractory multiple myeloma.

[a] Defined as documented PD during or within 60 days from last dose of prior antimyeloma regimen. [b] Patients were required to be hospitalized for 14 days postinfusion. Ide cel retreatment was allowed at PD for best response of at least stable disease. [c] Patients were followed for ≥ 24 months or until PD, whichever was longer. Upon study discontinuation, all patients who received ide cel were asked to participate in a separate long term follow up study. [d] By next generation sequencing.

1. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database. 2. Hassan M, et al. Haematologica. 2014;99:1124-1127. 3. Krok-Schoen JL, et al. Cancer Med. 2018;7:3425–3433. 4. Munshi et al. NEJM. 2021;384:705-16.

RESULTS

Table 1. Baseline demographics and clinical characteristics

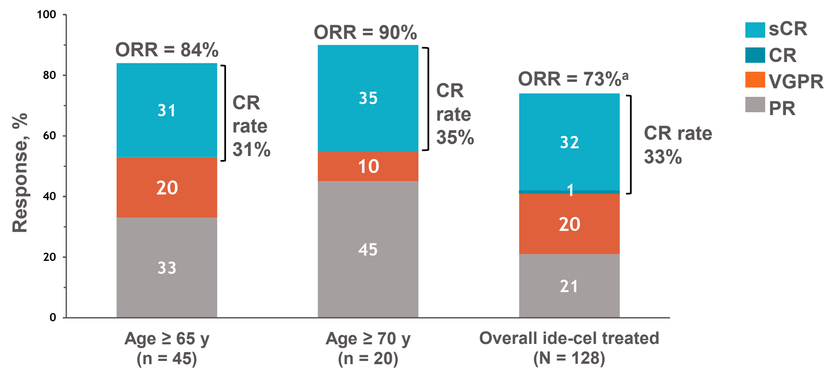
Characteristics	Age ≥ 65 y (n = 45)	Age ≥ 70 y (n = 20)	Overall ide-cel treated (N = 128)
Age, median (range), y	69 (65–78)	73 (70-78)	61 (33–78)
Male, %	67	70	59
ECOG PS, %			
0	44	40	45
1	56	60	53
2	0	0	2
R-ISS disease stage,[a] %			
I	16	15	11
II	69	75	70
III	13	10	16
High-risk cytogenetics,[b] %	31	30	35
High tumor burden (≥ 50% BMPCs), %	49	65	51
Tumor BCMA expression (≥ 50% BCMA+),[c] %	87	90	85
Extramedullary disease, %	40	40	39
Time since initial diagnosis, median (range), y	7 (3–15)	6 (3–15)	6 (1–18)
No. of prior antimyeloma regimens, median (range)	6 (3–16)	5 (3–12)	6 (3–16)
Prior autologous SCT, %			
1	64	75	59
> 1	33	20	34
Any bridging therapies for MM, %	80	85	88
Refractory status, %			
Anti-CD38 Ab-refractory	93	90	94
Triple-refractory	82	75	84

- Baseline characteristics were generally similar in both age groups and in the overall ide-cel treated population
- The proportion of elderly patients treated with 150 (2%), 300 (51%), and 450 (47%) × 10^6 CAR+ T cells was similar to the overall treated population (3%, 55%, and 42%, respectively)
- In both age groups and in the total ide-cel treated population, ≥ 30% of patients had extramedullary disease and high-risk cytogenetics
- 4 patients were aged ≥ 75 years

Data cutoff date: 14 Jan 2020. Ab, antibody; BCMA, B-cell maturation antigen; BMPC, bone marrow plasma cell; ECOG PS, Eastern Cooperative Oncology Group performance status; MM, multiple myeloma; R-ISS, revised International Staging System; SCT, stem cell transplant.

[a]R-ISS stage was assessed at enrollment; unknown for 3 patients, 1 of whom was ≥65 years old. [b]High-risk defined as del(17p), t(4;14), and/or t(14;16). Baseline cytogenetics not evaluable/missing for 17 patients; 45 patients (35%) had 1q amp abnormality. [c]No minimum tumor BCMA expression required for study entry.

Figure 2. Overall response



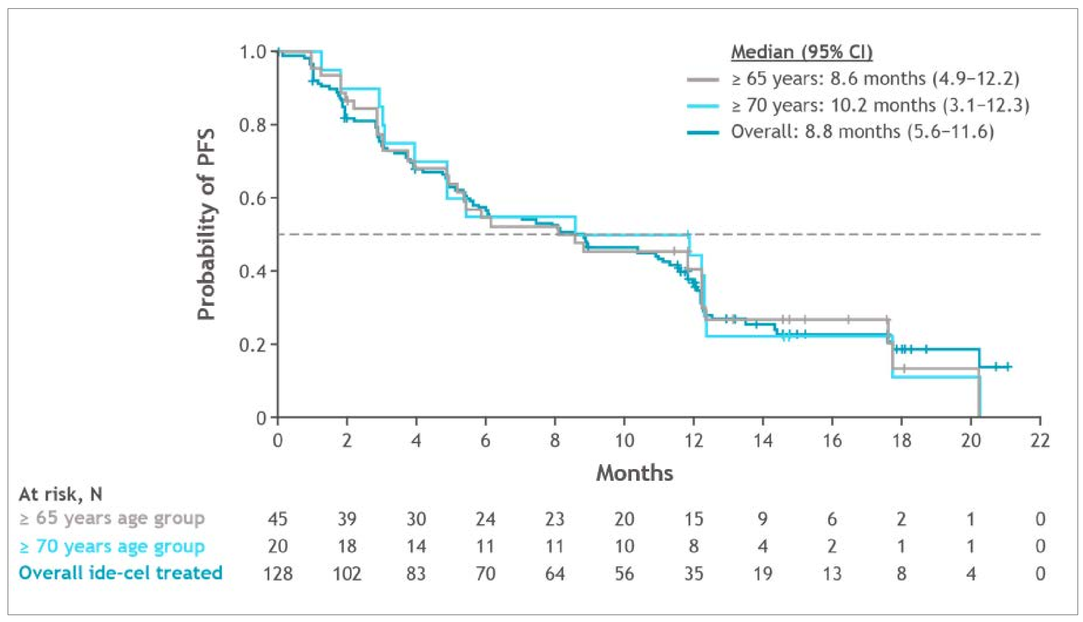
- ORR and CR rates in the elderly groups were comparable with those observed in the overall ide-cel treated population
- Median time to first response was 1.0 month in both elderly groups and in the overall treated population[b]
- Median duration of response was consistent across age groups, ranging from 10.7 to 11.0 months[b]

Data cutoff date: 14 Jan 2020. CR, complete response; ORR, overall response rate (≥ PR); PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

[a]Values may not add up to total due to rounding. [b]Time to first response and duration of response were assessed in responders: n = 38 for ≥ 65 years group, n = 18 for ≥ 70 years group, and n = 94 for overall ide-cel treated population.

RESULTS

Figure 3. Progression-free survival



Data cutoff date: 14 Jan 2020. PFS, progression-free survival.

- Older age did not have a significant impact on PFS
- Survival data are immature with 66% of all ide-cel treated patients censored

Table 2. Incidence and management of CRS and NT

	Age ≥ 65 y (n = 45)	Age ≥ 70 y (n = 20)	Overall ide-cel treated (N = 128)
≥ 1 CRS event, n (%)	40 (89)	20 (100)	107 (84)
Max. grade (Lee criteria),[a] n (%)			
1	23 (51)	10 (50)	61 (48)
2	15 (33)	8 (40)	39 (31)
≥ 3	2 (4)	2 (10)	7 (5)
Time to onset, median (range), d	1 (1–12)	1 (1–12)	1 (1–12)
Duration, median (range), d	5 (1–22)	5 (2–18)	5 (1–63)
Tocilizumab, n (%)	25 (56)	14 (70)	67 (52)
Corticosteroids, n (%)	6 (13)	3 (15)	19 (15)
≥ 1 NT event, n (%)	11 (24)	6 (30)	23 (18)
Max. grade (CTCAE),[b] n (%)			
1	6 (13)	5 (25)	12 (9)
2	1 (2)	0	7 (5)
3	4 (9)	1 (5)	4 (3)
Time to onset, median (range), d	2 (1–6)	2 (1–6)	2 (1–10)
Duration, median (range), d	5 (1–22)	6 (2–16)	3 (1–26)
Tocilizumab, n (%)	2 (4)	1 (5)	3 (2)
Corticosteroids, n (%)	6 (13)	3 (15)	10 (8)

- Safety profiles in elderly patients were comparable with that of the overall ide-cel treated population
- CRS events were frequent overall and in both age groups, but were mostly low grade
- Grade 3 CRS events occurred in 2 elderly patients; no grade 4 or 5 CRS occurred in either elderly group
- NT occurred in 18% of all ide-cel treated patients and in less than one third of elderly patients
- Grade 3 NT was uncommon (≤ 9%) in both age groups; no grade 4 or 5 events were observed
- Use of corticosteroids for CRS and NT was infrequent (≤ 15%) across all groups

CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; Max., maximum; NCI, National Cancer Institute; NT, neurotoxicity (investigator-identified).

[a] CRS graded according to Lee criteria (Lee DW, et al., Blood 2014;124:188-195). [b] Investigator-identified NT events were graded according to the NCI CTCAE v4.03.

CONCLUSIONS

- Multiple myeloma predominantly afflicts the elderly who have fewer effective and tolerable therapeutic options[1,2]
- Efficacy and safety results from the pivotal KarMMa trial demonstrated a favorable benefit-risk profile for ide-cel in patients with triple-class exposed RRMM[3]
- In this subgroup analysis of the KarMMa study, ide-cel continued to show deep and durable responses together with a manageable safety profile in elderly patients
  - Efficacy outcomes (ORR, CR rate, DOR, and PFS) in patients aged ≥ 65 and ≥ 70 years were comparable with those observed in the overall treated population
  - No new safety signals were observed in either age group
- These results suggest that ide-cel is tolerable and effective, even in elderly patients, providing further evidence supporting ide-cel as a promising treatment option in RRMM

1. Hassan M, et al. *Haematologica.* 2014;99:1124-1127. 2. Krok-Schoen JL, et al. *Cancer Med* 2018;7:3425–3433. 3. Munshi et al. NEJM. 2021;384:705-16.

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Email: salomonmanier@yahoo.fr