Clinical Characteristics And Response Outcomes in Older Multiple Myeloma Patients Who Received *Idecabtagene Vicleucel* : A Single Center Study

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Background

- Multiple myeloma (MM) is a disease of older adults with a median age of 69 years at the time of diagnosis. Older patients remain at higher risk for poor outcomes due to physical and physiological decline with aging. The physical and physiological decline led to several older patients excluded from the KarMMa trials which led to regulatory approval of Idecabtagene Vicleucel (ide-cel).[1] The efficacy and safety outcomes for these patients are not well characterized in the standard of care setting s/p ide-cel therapy.

Methods

- All patients at our institution infused with standard of care ide-cel between 8/30/2021-5/31/2022 were included to allow for ≥ 30 days of follow-up.
- The clinical characteristics such as age, polypharmacy, comorbidities, history of fall, peripheral neuropathy (active or history), and organ dysfunction (active or history; cardiac, pulmonary, neuro, and/or renal) at ide-cel infusion were analyzed.
- Response outcomes and progression were evaluated using International Myeloma Working Group (IMWG) criteria[2] with the best overall response rate (ORR) recorded and compared to KarMMa study results for older patients (≥65y, n=45)[1].
- Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded as per ASTCT consensus guidelines.[3]
- Anemia, Thrombocytopenia, and neutropenia were graded by CTCAE v5.[4]
- Statistical analysis was descriptive in nature.

Results

Table 1. Baseline Patient Characteristics

	< 65 years	≥ 65 years	≥ 70 years
Number of Patients	17	16	8
Median Age (Range)	55 (38-63)	70 (65-83)	73 (71-83)
Gender			
Male	12 (71%)	11 (69%)	5 (62%)
Female	5 (29%)	5 (31%)	3 (38%)
Median ECOG PS @ consult (0-5)	1 (1)	1 (0-2)	1 (1)
Median ECOG PS @ LD chemo (0-5)	1 (0-3)	1 (0-3)	1 (1)
R-ISS Stage			
I	2 (13%)	3 (21%)	1 (12%)
II	7 (47%)	8 (57%)	5 (63%)
III	6 (40%)	3 (21%)	2 (25%)
High-Risk FISH*	5 (29%)	5 (31%)	3 (38%)
IgG	10 (59%)	10 (62%)	4 (50%)
IgA	4 (23%)	3 (19%)	2 (25%)
IgD	0 (0%)	1 (6%)	1 (13%)
FLC	3 (18%)	2 (13%)	1 (13%)
Median Prior Lines of Therapy	7 (4-16)	6.5 (4-18)	6.5 (4-16)
Median years between diagnosis and CAR-T infusion	4 (2-10)	8 (3-16)	10 (4-16)
Ineligible patients for KarMMa Study	13 (76%)	12 (75%)	6 (75%)

ECOG PS = Eastern Cooperative Oncology Group Performance Status; LD chemo = Lymphodepletion chemo; R-ISS = Revised International Staging System; FISH = fluorescence in-situ hybridization; FLC = Free light chainable disease
*High-risk FISH defined by del(17p), t(4;14), or t(14;16)

Table 2. Best Overall Response Stratified by Age Groups

	< 65 years	≥ 65 years	≥ 70 years
Number evaluable	14	14	8
ORR	12 (86%)	11 (79%)	8 (100%)
Best Response			
sCR	6 (43%)	5 (36%)	4 (50%)
CR	1 (7%)	1 (7%)	1 (12%)
VGPR	3 (21%)	4 (29%)	3 (37%)
PR	2 (14%)	1 (7%)	0
SD	0	3 (21%)	0

ORR = overall response rate; sCR = stringent complete response; CR = complete response; VGPR = very good partial response; PR = partial response; SD = stable disease; PD = progressive disease

Table 3. Progressive Disease Stratified by Age Groups

	< 65 years	≥ 65 years	≥ 70 years
Number evaluable	14	14	8
All	8 (57%)	4 (28%)	1 (12%)
Never responded	2 (14%)	0	0
After response	6 (43%)	4 (28%)	1 (12%)

Table 4. Geriatric Assessments Stratified by Age Groups

	< 65 years	≥ 65 years	≥ 70 years
Number evaluable	17	16	8
Polypharmacy (5+)	11 (65%)	15 (94%)	8 (100%)
Excessive polypharmacy (10+)	3 (18%)	6 (37%)	4 (50%)
Comorbidities (≥4)	9 (53%)	13 (81%)	7 (87%)
History of falls	1 (6%)	6 (37%)	3 (37%)
Neuropathy	6 (35%)	10 (62%)	5 (62%)
Organ dysfunction (Neuro, Cardiac, Renal, & Pulmonary)	5 (29%)	8 (50%)	5 (62%)

*Neuro: H/O or presence of CNS pathology (epilepsy, seizure, paresis, aphasia, stroke, CNS bleed, brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, or psychosis); Cardiac: H/O Class III or IV CHF or severe nonischemic cardiomyopathy, unstable or poorly controlled angina, myocardial infarction, or ventricular arrhythmia within 6 months, LVEF <45%; Renal: CrCl < 45 mL/min; Pulmonary: SpO2 <92%.

Figure 1. Prior Therapies vs. Time Since Diagnosis

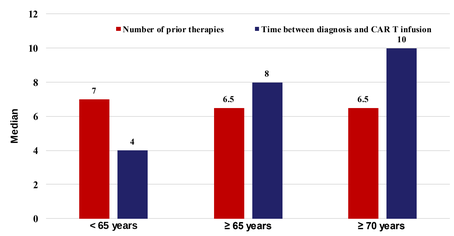

Figure 2. Durability of Response

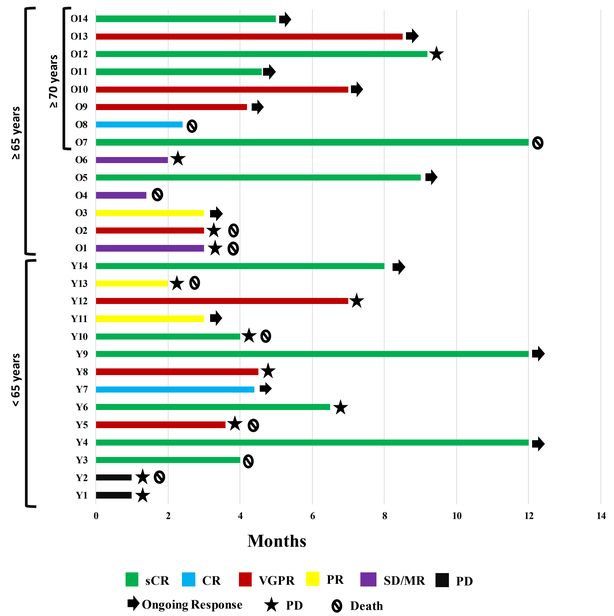

Table 5. KarMMa Study Ineligibility Criteria Stratified by Age Groups

	< 65 years	≥ 65 years	≥ 70 years
Number evaluable	17	16	8
Overall	13 (76%)	12 (75%)	6 (75%)
ECOG ≥ 2	4 (23%)	2 (12%)	0
Cardiac (Cardiomyopathy, LVEF<45%)	2 (12%)	4 (25%)	3 (37%)
Neuro/CNS (Seizure, Stroke, CNS bleed, Delirium, Tremor, Parkinson's)	3 (18%)	3 (19%)	0
Renal (Renal failure, CrCl<45ml/min)	1 (6%)	2 (12%)	2 (25%)
Infections (HepB, CMV, Cystitis)	2 (12%)	1 (6%)	0
Malignancies (Bladder, PCL)	2 (12%)	1 (6%)	0
Others	4 (23%)	2 (12%)	1 (12%)

Results

Table 6. Ide-cel Related Adverse Events

Event and Grade	< 65 years (n=14)	≥ 65 years (n=14)	≥ 70 years (n=8)
CRS			
Any	13 (93%)	13 (93%)	8 (100%)
Grade 1	8 (57%)	10 (71%)	7 (87%)
Grade 2	4 (28%)	3 (21%)	1 (12%)
Grade 3-4	0	0	0
Grade 5	1 (7%)	0	0
ICANS			
Any	2 (14%)	2 (14%)	1 (12%)
Grade 1	1 (7%)	2 (14%)	1 (12%)
Grade 2-3	0	0	0
Grade 4	1 (7%)	0	0
Grade ≥ 3 Hematologic Toxicity at Day 30			
Anemia	3 (21%)	2 (14%)	1 (12%)
Neutropenia	6 (43%)	5 (36%)	4 (50%)
Thrombocytopenia	6 (43%)	2 (14%)	2 (25%)

CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome; CTCAE v5 : Grade ≥ 3 = Anemia < 8 g/dL; Platelets < 50,000/mm^3; Neutrophil < 1000/mm^3

- At data cutoff, 6/16 (37%) of patients < 65 years had died – four from progressive myeloma, one from AKI + Septic shock, and one from grade 5 CRS/HLH with superimposed infection.
- At data cutoff, 5/14 (36%) of patients ≥ 65 years had died – two from progressive myeloma, one from possible cardiac arrest, one from AKI + Bacteremia + MDS + AML, and one from Covid-19 pneumonia/ARDS. The later two (25%) were > 70 years old patients.

Conclusions

- In this real-world analysis of older patients including septuagenarians and octogenarians robust clinical response and tolerable toxicities were observed s/p ide-cel.
- Despite high prevalence of polypharmacy, comorbidities, falls, neuropathy, and organ dysfunction, geriatric patients achieved excellent outcomes.
- The robust clinical outcomes observed in this small group of older patients could be associated with an indolent disease and/or bias in older patient selection.
- The ORR for > 70 years old patients were higher than the ORR observed in the pivotal KarMMa study.
- A multi-center retrospective analysis of outcomes for older patients receiving ide-cel is ongoing and may help provide further insight into older patient outcomes.

References

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2. Kumar S, et al. Lancet Oncol 2016;17:e328-46
3. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625-638
4. Common Terminology Criteria for Adverse Events (CTCAE) Version5. Published: November 27. US Department of Health and Human Services, National Institutes of Health, National Cancer Institute.

Presented as a poster in Tenth Annual Meeting of the Society of Hematologic Oncology (SOHO), September 28-October 1, 2022, Houston, TX.