Real-World Outcomes in Older Adults With Triple-Class Exposed Multiple Myeloma

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Introduction

- Patients with multiple myeloma (MM) who are triple-class exposed (TCEx) have previously received treatment with an immunomodulatory agent (IMiD), proteasome inhibitor (PI), and anti-CD38 monoclonal antibody and represent a heavily pretreated population with limited remaining therapeutic options[1]
- Although older adults aged ≥ 70 years represent a large portion of patients with TCEx MM, data regarding their real-world treatment patterns and outcomes remain sparse[2]

Objective

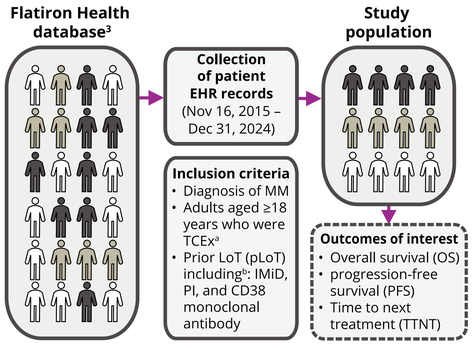
- This retrospective cohort study examines real-world outcomes of older adult patients with TCEx MM

Methods

Study design

- Data from Flatiron Health database derived from deidentified electronic health records (EHRs) were used to identify patients with MM who were TCEx (**Figure 1**)
  - The Flatiron Health database is a longitudinal data repository formed from a community of oncology practices and cancer centers across the United States (US)[3]
- The TCEx identification date was limited to November 16, 2015 (first date of US Food and Drug Administration approval of daratumumab) and the data cutoff date, December 31, 2024
- Index date was defined as the date where patients received a subsequent line of therapy after becoming TCEx, the first subsequent line was considered as the index line of therapy, and the index line start date was defined as the index date

Figure 1. Study design



[a]TCEx date was defined as the earliest line of therapy end date of the third treatment class where patients became TCEx.
[b]LoTs were IMiD including lenalidomide, pomalidomide, and thalidomide; anti-CD38 monoclonal antibody including daratumumab and isatuximab; protease inhibitor including bortezomib, carfilzomib, ixazomib. LoT, line of therapy.

Outcomes measured

- Patient characteristics were identified on or before the TCEx date
- OS was measured from the index date to death
- PFS was determined from the index date to death, documented progressive disease or the initiation of subsequent treatment, whichever occurred first
- Time to next treatment was defined as time from index date to initiation of subsequent line
- Outcomes were estimated using Kaplan-Meier methods

Results

Patient characteristics

- Among 6301 patients with TCEx MM (55.1% male; 62.4% white), 3099 (49.2%) were aged ≥ 70 years
- There were 3193 TCEx patients (50.7%) who received subsequent treatment
  - Of these patients 1426 (44.7%) were aged ≥ 70 years (**Table 1**)

Among patients who are TCEx, older patients aged ≥ 70 years experienced worse clinical outcomes as compared to younger patients aged < 70 years and exhibited worsening outcomes with increasing number of pLoT

Figure 2A. OS from the index date for patients with index therapy stratified by age at TCEx date

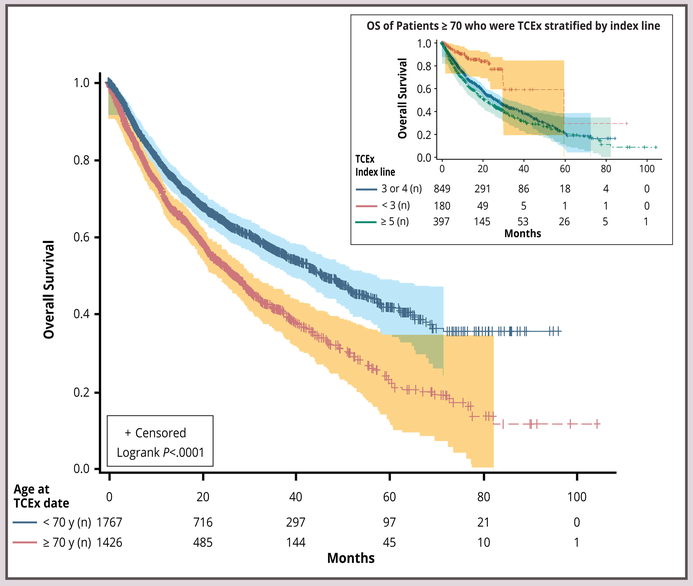
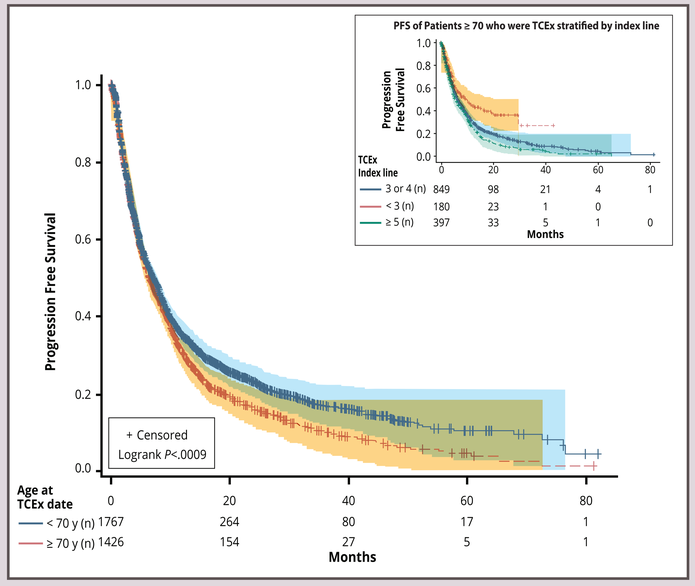


Figure 2B. PFS from the index date for patients with index therapy stratified by age at TCEx date



Data are represented as number of patients at risk and 95% Hall-Wellner Bands.

Table 1. Characteristics for patients with TCEx MM who received index therapy

Characteristic	Age <70 y (n = 1767)	Age ≥70 y (n = 1426)
Age at TCEx date,[a] median (range), y	61 (24-69)	76 (70-86)
Male, n (%)	996 (56.4)	755 (52.9)
Race		
White	1087 (61.5)	975 (68.4)
Black or African American	341 (19.3)	194 (13.6)
Asian	50 (2.8)	30 (2.1)
Other	135 (7.6)	101 (7.0)
Missing	154 (8.7)	126 (8.8)
ISS stage at baseline, n (%)		
I	429 (24.3)	265 (18.6)
II	378 (21.4)	325 (22.8)
III	392 (22.2)	344 (24.1)
Unknown	568 (32.1)	492 (34.5)
ECOG PS score,[b] n (%)		
0	495 (34.4)	338 (28.1)
1	701 (48.6)	581 (48.3)
2	188 (13.0)	241 (20.0)
3-4	57 (4.0)	44 (3.6)
CCI score,[b] n (%)		
0	788 (44.6)	514 (36.0)
1	168 (9.5)	187 (13.1)
2	204 (11.5)	198 (13.9)
3	92 (5.2)	77 (5.4)
4	36 (2.0)	51 (3.6)
≥5	479 (27.1)	399 (28.0)
High-risk cytogenetics,[c] n(%)	625 (35.4)	493 (34.6)

[a]Age was calculated as Year (TCEx date)–birth year. [b]Closest values on or before index date for patients who received index therapy and on or before TCEx date. [c]Defined as the presence of del(17p), t(4;14) or t(14;16) or +1q21.
CCI, Charlson Comorbidity Index; ISS, International Staging System; PS, performance status.

- Median (range) follow-up for patients who were TCEx and received index therapy was 15.3 (0.03-96.0) months and 12.7 (0.03-104.3) months for those aged < 70 years and ≥ 70 years, respectively
- Compared to the younger cohort, the older cohort who received a subsequent treatment exhibited increased comorbidity burden with a mean Charlson Comorbidity Index (CCI) of 3 vs 2
- Patients who were < 70 years of age had a median of 2 pLoT while patients aged ≥ 70 years had a median of 3 pLoT (**Table 2**)
- Older patients had lower rates of prior stem cell transplant (SCT; 29.0%) as compared to younger patients (64.0%)

Table 2. Treatment exposure and refractory status on or before index date

Treatment exposure/refractory status	Age < 70 y (n = 1767)	Age ≥ 70 y (n = 1426)
Prior LoTs, median (range)	2 (1-13)	3 (1-16)
Number of LoTs prior to index treatment, n (%)		
1	420 (23.8)	180 (12.6)
2	556 (31.5)	508 (35.6)
3	354 (20.0)	341 (23.9)
≥4	437 (24.7)	397 (27.8)
Prior SCT, n (%)	1130 (64.0)	413 (29.0)
Prior treatment class refractory, n (%)		
Refractory to an IMiD	1541 (87.2)	1267 (88.8)
Refractory to a PI	1539 (87.1)	1241 (87.0)
Double-class refractory	1474 (83.4)	1177 (82.5)
Triple-class refractory	1341 (75.9)	1101 (77.2)
Penta-drug refractory	209 (11.8)	135 (9.5)

- Median time from MM diagnosis to initiation of index treatment was 26.9 months and 38.3 months for patients aged < 70 years and ≥ 70 years, respectively (**Table 3**)
  - The most common index regimen across cohorts was combined IMiD and CD38 monoclonal antibody, used in 16.6% of patients aged < 70 years and 17.9% of patients aged ≥ 70 years
- Among all TCEx patients identified (n = 6301), the chimeric antigen receptor T-cell (CAR T) therapy idecabtagene vicleucel (ide-cel) was administered to 119 (1.9%) patients and 130 (2.1) patients received ciltacabtagene autoleucel (cilta-cel) either as index or subsequent to index treatment
  - Among these patients CAR T therapy was received by fewer older patients (2.1%; n = 64) than younger patients (5.8%; n = 185)

Table 3. Post-TCEx index treatments

Post-TCEx index treatments	Age < 70 y (n = 1767)	Age ≥ 70 y (n = 1426)
Time from MM diagnosis to index treatment, median (range), mo	26.9 (1.5-159.1)	38.3 (1.2-162.3)
Duration of index treatment, median (range), mo	4.6 (0.03-79.8)	4.9 (0.03-81.2)
Index treatment type, n (%)		
IMiD + anti-CD38	294 (16.6)	255 (17.9)
PI + anti-CD38	200 (11.3)	172 (12.1)
IMiD + PI	182 (10.3)	150 (10.5)
PI + IMiD + anti-CD38	197 (11.1)	106 (7.4)
IMiD only	154 (8.7)	134 (9.4)
PI only	115 (6.5)	138 (9.7)
Anti-CD38 only	85 (4.8)	110 (7.7)
PI + alkylating agents	92 (5.2)	91 (6.4)
Investigational therapies	124 (7.0)	52 (3.6)

Efficacy

- Among patients who were TCEx, older patients exhibited worse clinical outcomes (PFS and OS) compared to those who were younger and outcomes for older patients worsened with increasing pLoT (**Figure 2**)
  - Older patients who were TCEx additionally spent a greater amount of time in disease (median, 38.3 months) compared to younger patients who were TCEx (median, 26.9 months) (**Table 3**)
- Median OS was 46.0 months for patients who were TCEx aged < 70 years and 27.3 months for patients aged ≥ 70 years (**Table 4**, **Figure 2**A)
  - Among patients aged ≥ 70 years who were TCEx, median OS varied according to initiating index therapy before third line (59.4 mo), as third or fourth line (26.5 mo) and in fifth line or beyond (20.6 mo)
- Median PFS was slightly longer for patients aged < 70 years who were TCEx (7.0 mo) compared to patients aged ≥ 70 years who were TCEx (6.5 mo) (**Table 4**, **Figure 2**B)
- Among patients who were TCEx, the median time to next treatment was 9.7 months for patients aged < 70 years and 11.7 months for patients ≥ 70 years

Table 4. Clinical outcomes and time to next treatment

Outcome	Age < 70 y (n = 1767)	Age ≥ 70 y (n = 1426)
OS, median (95% CI), mo	46.0 (42.2-51.5)	27.3 (24.3-29.6)
PFS, median (95% CI), mo	7.0 (6.3-7.6)	6.5 (5.8-7.1)
Time to next treatment, median (95% CI), mo	9.7 (9.0-11.0)	11.7 (10.4-12.5)

Conclusions

- Worse survival outcomes were observed in older adults with TCEx MM as compared to younger patients, though age-specific increases in mortality rates may contribute to the observed difference between age groups
  - Outcomes for older patients with TCEx MM further deteriorated with increasing pLoT
- Age-adjusted treatment strategies and novel therapeutic approaches are urgently needed to improve outcomes in the growing and vulnerable population of older adults with MM[1,2]

References

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Disclosures

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