LONG-TERM RESULTS FROM THE MYRIAM REGISTRY

MULTIPLE MYELOMA IN ROUTINE CARE: PATIENTS' PATHS AND OUTCOMES OF PATIENTS NOT SCHEDULED FOR STEM CELL TRANSPLANTATION

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INTRODUCTION

Triple class exposition (TCE), i. e. prior therapy with a proteasome inhibitor (PI), an immunomodulatory drug (IMiD) and an anti-CD38 monoclonal antibody (mAb), is a pre-requisite for treatment with most of the drugs recently approved for treatment of patients with relapsed and/or refractory multiple myeloma (MM).

The MYRIAM registry provides valuable insights into treatment under real-world conditions of patients with MM regarding long-term observation and sequential treatment. Here, we analyzed the paths of patients without stem cell transplantation in first line to characterize the subsequent lines of treatments.

METHODS

Between 2017 and 2026, 2,200 patients with MM starting their first- (1L), second- (2L) or third-line (3L) systemic therapy will be recruited in 150 sites (hospitals, office-based practices) and followed for up to 5 years. MYRIAM is a prospective, non-interventional, multi-center cohort study that collects patients' characteristics, treatment, clinical and patient-reported outcomes of patients with MM in Germany. It was approved by ethics committees and is registered at clinicaltrials.gov (NCT03308474).

Here we present data from the 8th interim analysis (data cut: 30-SEP-2024) on patients not scheduled for stem cell transplantation (non-SCT) in first line.

LIMITATIONS

As the primary recruitment goal of 1,500 patients starting first-line treatment was reached in October 2021, this cohort was closed; therefore, analyses are here restricted to patients who started first line between SEP-2017 and OCT-2021.

Eligibility for stem cell transplantation is not captured in MYRIAM as a specific parameter, instead initial intention and actual transplantation are collected. Here, the assignment to a subgroup followed the initial intention for a certain treatment option.

For patients scheduled for SCT, it can be assumed that patient and disease characteristics will be similar between transplant-eligible (TE) patients and patients scheduled for SCT. The non-SCT group in MYRIAM comprises patients who were never intended to receive an SCT, but also patients who – based on patient and disease characteristics – might have been theoretically eligible for SCT but for any reason the decision was not to choose SCT.

RESULTS

Out of 2,185 patients with MM recruited until data cut, 1,479 had been enrolled at start of 1L between SEP-2017 and OCT-2021, of which 60 % (883/1,479) were non-SCT.

Sequential treatment / number of lines

At data cut, 39 % (343/883) of patients had already received 2L treatment whereas 23 % (205/883) had died prior to 2L **(Figure 2)**.

Further 27 % (241/883) still had the "potential" to receive 2L treatment with longer follow-up: At the time of data cut, these patients were either in ongoing 1L treatment (14 %, 120/883) or in a therapy break (8 %, 69/883) or the regular five-year observation period had ended (2 %, 19/883) or they had switched to another onco-specialist (4 %, 33/883) **(Figure 2)**.

The remainder of 11 % (94/883) were lost to follow-up (LTFU) for observation in MYRIAM: e. g. treatment was continued at hospice/nursing home or documentation terminated for other reasons **(Figure 2)**.

This means, currently it can be estimated that between 39 % (treated in 2L) and 66 % (treated in 2L plus potential for 2L) of patients not scheduled for SCT in 1L will receive a 2L treatment. In contrast, the currently estimated attrition rate for 1L is between 23 % (death prior to 2L) and 51 % (death plus potential, if all patients in the potential group died without receiving 2L). With longer follow-up time, the estimation will become more concise.

Rates for treatments 2L to 5L can be deducted correspondingly from **Figure 2:** At data cut, 136 patients (15 %) had proceeded into 3L, 59 (7 %) had received 4L and for 20 (2 %) 5L had been as yet documented.

Triple class exposition (TCE)

Starting 2L, 3 % (10/343) of patients were TCE, while starting 5L this proportion had increased to 85 % (17/20) **(Table 1)**.

Outcome

While systemic treatment ended in 1L for 23 % (202/883) due to progression, this proportion increased to 50 % (10/20) in 5L. In contrary, remission as reason for end of line of treatment decreased from 9 % (81/883) to 0 % (0/20) in 5L **(Figure 1)**.

Median treatment duration in 1L was 8.1 months [95 % – CI 7.2, 9.1] and decreased to 2.0 months [95 % – CI 0.7, 7.9] in 5L **(Table 1)**. Median time to next treatment (TTNT) in 1L was 24.7 months [95 % – CI 22.2, 26.8] and decreased with higher line to 2.6 months [95 % – CI 1.9, 7.9] in 5L **(Table 1).** The difference between treatment duration and TTNT indicates that some treatments are discontinued (e.g. because of remission) and not continued until progression.

Status of follow-up

Overall, follow-up was completed for 66 % (586/883) of patients, with death as the most frequent reason in 40 % (355/883). For 7 % (66/883) the maximum follow-up of 5 years was reached and 18 % (155/883) were lost to follow-up. With 34 % (297/883) of patients still under observation, these data will provide a more precise estimation of attrition rates with longer follow-up.

CONCLUSION

Seven years after project start, MYRIAM provides a sound description of the current state of long-term routine care for unselected patients with MM in Germany.

Expectedly, treatment duration and time to next treatment decreased with subsequent treatment lines, while the proportion of patients with triple class exposition (TCE) increased within the course of treatment. This depicts the still unmet medical need for patients with MM without stem cell transplantation in first line and will help direct future focus towards sequential treatments and their effectiveness for future analyses.

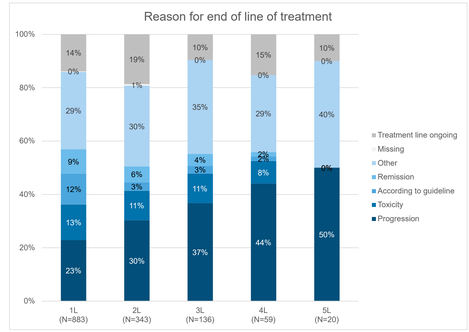
Table 1: Patients with 1L non-SCT: Treatment duration / time to next treatment (TTNT)

	First line	Second line	Third line	Fourth line	Fifth line
Patients (N)	**883**	**343[a]**	**136[b]**	**59[c]**	**20**
Median age at start of line of treatment [years] (25 % – 75 % quantiles)	78 (72 – 81)	79 (73 – 82)	79 (74 – 82)	78 (74 – 82)	76 (74 – 83)
Treatment duration (months) (Kaplan-Meier estimate)					
Events	761 (86.2 %)	276 (81.7 %)	119 (89.5 %)	50 (86.2 %)	18 (90.0 %)
Median	8.1 [7.2, 9.1]	8.8 [7.1, 10.2]	5.1 [3.5, 6.2]	3.0 [1.6, 4.0]	2.0 [0.7, 7.9]
25 % – 75 % quantile	3.3 – 24.9	3.2 – 21.9	2.1 – 9.6	1.1 – 12.0	0.7 – 27.9
Time to next treatment (TTNT) [months] (Kaplan-Meier estimate)					
Events	548 (62.1 %)	205 (60.7 %)	97 (72.9 %)	42 (72.4 %)	16 (80.0 %)
Median	24.7 [22.2, 26.8]	16.8 [12.9, 19.5]	7.4 [6.4, 9.5]	5.2 [3.1, 7.3]	2.6 [1.9, 7.9]
25 % – 75 % quantile	9.7 – 51.2	6.3 – 41.7	3.8 – 19.2	2.4 – 14.5	2.6 – 11.3
Triple class exposition (TCE)					
Prior treatment with PI & IMiD & CD38-mAB	N/A	10 (2.9 %)	58 (42.6 %)	39 (66.1 %)	17 (85.0 %)

N: Number of patients with documented treatment in the respective line, regardless of type of treatment (non-SCT / planned SCT / planned CAR-T). In 1L all the patients were not scheduled for SCT.
CD38-mAB: daratumumab, isatuximab | IMiD: lenalidomide, pomalidomide, thalidomide | PI: bortezomib, carfilzomib, ixazomib
CD: cluster of differentiation | IMiD: immunomodulatory drug | mAb: monoclonal antibody | PI: proteasome inhibitor | TCE: Triple class exposition | TTNT: Time to next treatment.

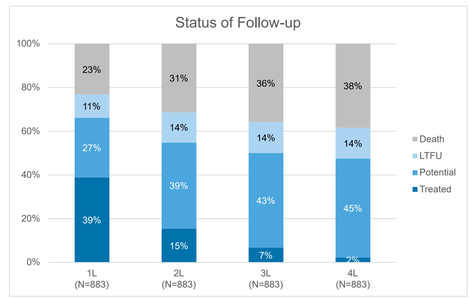
[a] 5 patients were scheduled for SCT | [b] 3 patients were scheduled for SCT | [c] 1 patient was scheduled for CAR-T.

Figure 1: Patients with 1L non-SCT: Reason for end of line of treatment



Other: including e.g. deterioration of general condition, death, stable disease, patient wish or patient lost to follow-up, referral to hospice/palliative care or other.

Figure 2: Patients with 1L non-SCT: Status of Follow-up



LTFU: Lost to Follow-up.

Abbreviations:

CAR-T: Chimeric antigen receptor T cell | IMiD: immunomodulatory drug | LTFU: lost to follow-up | mAB: monoclonal antibody | MM: multiple myeloma | PI: proteasome inhibitor | SCT: stem cell transplantation | TCE: triple class exposition | TE: transplant-eligible | TTNT: time to next treatment.

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