CURRENT SECOND-LINE TREATMENT OF PATIENTS WITH MULTIPLE MYELOMA

FIRST OUTCOME DATA OF ROUTINE CARE TREATMENT OF PATIENTS WITH MULTIPLE MYELOMA IN GERMANY – RESULTS FROM THE MYRIAM REGISTRY

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INTRODUCTION

The recent approval of new treatments for patients with multiple myeloma (MM) has broadened therapeutic options. Research will now shift focus on the identification of the most effective sequential treatments. Non-interventional cohort studies can investigate how quickly new treatments are adapted in routine care and what their impact will be on sequential treatments and outcome.

CONCLUSION

The recent interim analysis of the MYRIAM registry reveals that currently daratumumab-based regimens dominate second-line treatment in patients with MM in Germany, because most patients starting second-line have not yet received this drug in first-line treatment. As daratumumab is now frequently used in newly diagnosed MM, focus will shift to effective daratumumab-free second-line therapies in patients relapsed or refractory after first-line daratumumab. Future analysis will allow evaluation of sequential treatment strategies after first-line daratumumab.

PATIENTS AND METHODS

MYRIAM (NCT03308474) is a prospective, intersectoral, national, multicenter cohort study that documents patients' and disease characteristics, treatment, clinical and patient-reported outcomes of patients with MM in Germany. Between 2017 and 2023, about 2,200 patients with MM at begin of first-, second- or third-line systemic treatment will be recruited in 150 sites (university/community hospitals, office-based practices) and followed for a maximum of 5 years. Data are collected in electronic case report forms, regularly quality controlled by data managers and randomly monitored on site.

Outcome data with short follow-up

Due to ongoing recruitment and the comparatively long survival of patients with MM, many treatments are not yet completed and patients with early progression may still be overrepresented in the current analysis.

To increase the length of minimum follow-up and reduce bias in outcome data, the sample for analyses of outcome parameters was defined as all patients with start of first-line treatment at least one year prior to database cut ("outcome sample"). This results in lower patient numbers for outcome analyses as compared to the total sample.

Here, we present data from the 5th interim analysis (database cut: 2021-SEP-30) and an update on frequencies of second-line regimens as of 2021-DEC-31. As daratumumab (DARA) was approved for patients with newly diagnosed MM in August 2018, this date was taken as cut-off to compare choice of treatment pre- and post-approval.

RESULTS

We identified 554 patients with documented first- and second-line treatment (not planned for stem cell transplantation (SCT) in second line). Of these 554 second-line treatments, 78 (14%) had started pre-approval of daratumumab (2017-08/2018) and 476 (86%) post-approval (09/2018-2021).

Patient characteristics

Key patient characteristics of the outcome sample (n=513; see Outcome data with short follow-up) are shown in **Table 1**. At the start of second-line treatment, patients not receiving SCT were median 75 years old, 22 % had an ECOG performance status of 0 and 85 % had comorbidities.

Prior first-line treatment

Patients with second-line treatment and no planned treatment with SCT, had previously received a first-line bortezomib-based regimen (BOR, n=459/554, 83%) or a lenalidomide combination (LEN, n=155/554, 28%); and 6% (n=33) of patients received daratumumab in first-line (**Figure 1**).

Second-line treatment

As second-line treatment 253/554 (46%) patients received daratumumab. While this share was 17% (n=13/78) in the pre-approval era (2017-08/2018), it increased to 50% (n=240/476) in the post-approval era (09/2018-2021). The most frequent second-line regimen was DARA+LEN+dexamethasone (DRd) (n=113/554, 20%; **Figure 3**). 101/554 (18%) of patients received carfilzomib (CARF), 312/554 (56%) lenalidomide-containing regimens (**Figure 2**).

Treatment sequence

The most frequent sequential treatment in patients without planned SCT starting second-line prior to approval of daratumumab was Vd (BOR/Dexa) → Rd (LENA/Dexa) in 9% (7/78) or VCd (BOR/CYC/Dexa) → KRd (CARF/LENA/Dexa) in 6% (5/78) in our sample. In patients starting second-line treatment post approval of daratumumab, the most frequently used sequential treatment was VCd (BOR/CYC/Dexa) → DRd (DARA/LENA/Dexa) in 10% (49/476) of the patients.

Outcome

The 1-year progression-free survival rate in patients without SCT was 49% (95% CI: 44-54%; **Figure 4**), and the 1-year overall survival rate was 80% (95% CI 75-83%; **Figure 5**) from start of second-line treatment.

Abbrevations:
CI: confidence interval | ECOG: Eastern Cooperative Oncology Group | MM: multiple myeloma | OS: overall survival|PFS: progression-free survival | SCT: stem cell transplantation.
BOR: bortezomib | CARF: carfilzomib | CYC: cyclophosphamide | DARA: daratumumab | Dexa: dexamethasone | LEN: lenalidomide.
DRd: daratumumab + lenalidomide + dexamethasone | DVd: daratumumab + bortezomib + dexamethasone | KRd: carfilzomib + lenalidomid + dexamethasone | Rd: lenalidomid + dexamethasone | VCd: bortezomib + cyclophosphamide + dexamethasone | Vd: bortezomib + dexamethasone.

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Conflicts of interest, general
MYRIAM is designed, managed and analysed by iOMEDICO and receives continuous financial support from AMGEN GmbH, Bristol Myers Squibb GmbH & Co. KgaA, GSK Research and Development Limited, Janssen-Cilag GmbH and Oncopeptides AB (publ). None of the funders had any role in study design, data collection and analysis, interpretation of results, decision to publish, or preparation of the abstract. The funders were provided the opportunity to review a preliminary version of this poster, but the authors are solely responsible for final content and interpretation.

Conflicts of interest
Einsele H: Advisory Role or Expert Testimony: BMS/Celgene, Janssen-Cilag, Novartis, Amgen, Takeda, Sanofi, GSK; Honoraria: BMS/Celgene, Janssen-Cilag, Novartis, Amgen, Takeda, Sanofi, GSK; Financing of Scientific Research: BMS/Celgene, Janssen-Cilag, Amgen, Sanofi, GSK | **Nusch A:** Financing of Scientific Research: Roche, Novartis, AstraZeneca | **Kiewe P:** Honoraria: Pfizer, Roche, BMS, Janssen, BeiGene, AstraZeneca, Novartis | **Knauf W:** Advisory Role or Expert Testimony: Amgen, BMS/Celgene, Janssen; Honoraria: Amgen, BMS/Celgene, Janssen | **Engelhardt M:** Financing of Scientific Research: Amgen, BMS, Janssen-Cilag, Sanofi, Takeda

No Conflicts of interest:
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Table 1

	non-SCT Second-line treatment (2L)
Patients (N)	**513**
Age at start of treatment (years)	
N	513
Median	74.9
ECOG performance status	
ECOG 0 n (%)	111 (21.6%)
Comorbidities	
Yes n (%)	438 (85.4%)
Progression -free survival (months)	
Events n (%)	266 (51.9%)
1-year PFS rate [95% CI]	48.6% [43.5, 53.6]
Overall survival (months)	
Events n (%)	128 (25.0%)
1-year OS rate [95% CI]	79.5% [75.1, 83.2]

Table 1 Second-line treatment of patients not planned for SCT: Patient characteristics and survival data

N: Patients with start of first-line treatment at least one year prior to database cut ("outcome sample").

Figure 1

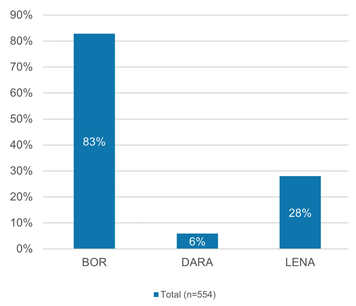

Figure 1: First-line treatment (non-SCT): Frequencies of substances (TOP3)

Figure 2

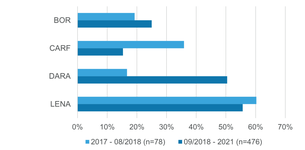

Figure 2: Second-line treatment (non-SCT): Frequencies of substances by time of first-line approval of daratumumab

Figure 3

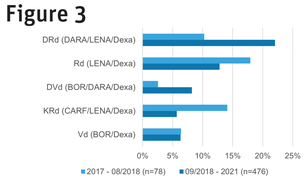

Figure 3: Second-line treatment (non-SCT): Frequencies of most frequent regimens by time of first-line approval of daratumumab

Figure 4

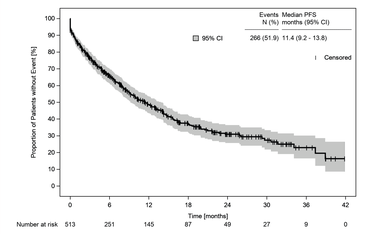

Figure 4: Progression-free survival (PFS) from start of second-line treatment

Figure 5

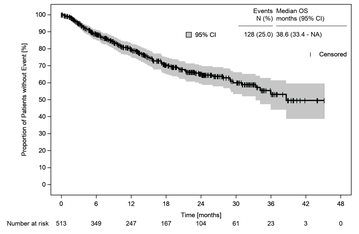

Figure 5: Overall survival (OS) from start of second-line treatment