Baseline characteristics and survival outcomes of patients with tri-exposed multiple myeloma in a German registry

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INTRODUCTION

- Multiple myeloma (MM) is a heterogeneous hematological cancer of variable clinical course and substantial clinical burden, accounting for 1% of all cancers worldwide and approximately 10% of hematological neoplasms.[1]
- Treatment options such as proteasome inhibitors (PI), immunomodulatory agents (IMiDs) and anti-CD38 antibodies have improved survival outcomes significantly.[2] However, as MM is an incurable disease, patients ultimately progress and may become refractory to these treatment classes in later years of treatment.
- Description of baseline characteristics and outcomes of patients who have been exposed to all three drug classes is limited, especially in the European setting.
- Data from European registries can provide valuable insights into patients' unmet needs.

OBJECTIVE

To assess baseline characteristics and outcomes in a population of patients with triple-class exposed multiple myeloma in a German patient registry.

METHODS

Data Source

- Data from the Oncology Information Service (OIs) registry includes longitudinal follow-up data from ~3,400 patients with relapsed and refractory MM (rrMM) followed since diagnosis. The registry includes data from a representative sample of 108 German centers between January 1, 2016 and March 31, 2020. Data collection is ongoing.
- A cohort of triple-class exposed patients with MM was defined according to the following criteria:
  - *ECOG performance score (PS) 0 – 1*
  - *Received ≥ 3 prior lines of therapy (LOTs)*
  - *Received ≥ 1 active therapies after meeting above criteria*
  - *Received a PI, an IMiD and an anti-CD38-antibody as part of their previous therapies*

Statistical Analysis

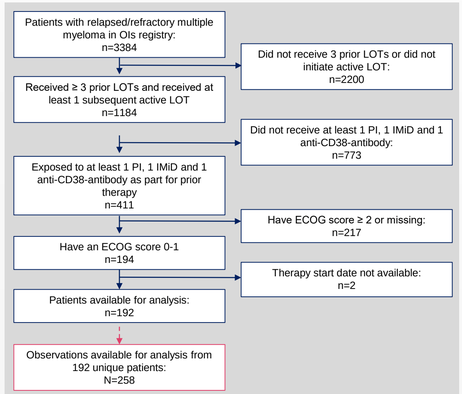
- Index dates were defined as the date of treatment initiation after meeting the selection criteria. Where patients fulfilled these criteria multiple times in their longitudinal follow-up, lines of therapy and their respective follow-up were included as separate observations. In such cases, correlation within patients was corrected by adjustment of the usual variance estimator.[3]
- Time to event analyses were performed for **Overall Survival (OS)** and **Time to Next Therapy (TTNT).**
  - *TTNT was defined as the time from the index date to the initiation of the next therapy line or death, whichever occurred first. Patients who were still alive and did not initiate a next therapy line at time of data-cut were censored at last date known to be alive.*
  - *TTNT may be interpreted as a proxy measure for progression-free survival, as the date of progression is not available in the OIs registry.*
- Univariate Cox proportional hazards (PH) models were fit to explore the prognostic value of available baseline characteristics, including ISS stage, refractoriness status, ECOG PS, prior LOTs, age, gender, hypercalcemia, creatinine levels, anemia status and bone involvement.
- Patient outcomes and findings from analysis are characterized in terms of tables, a forest plot, Kaplan Meier plots and a Sankey plot of treatment lines.

RESULTS

Study Population

- Among ~3,400 patients in the OIs registry, 258 treatment lines from 192 unique patients were available for analysis. **Figure 1** presents the process of patient identification.
- Median follow-up from index date was 10.9 months.

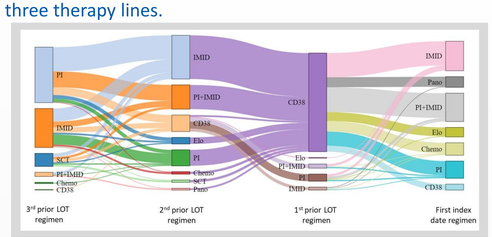
Figure 1. Identification of target study population within real-world database.



Treatment Regimens

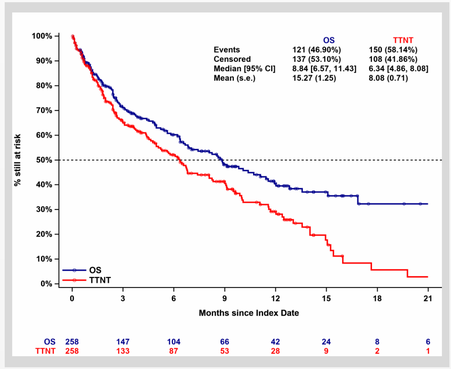
- In total, patients received 35 unique treatment regimens, with the most frequent being IxaRd (17%), followed by Pd, MP, Vd and PanoVd. No dominant regimen was observed in real world clinical practice.
- Most frequent regimens initiated at index date were PI+IMiD combinations (22%), IMiD only (23%), PI only (18%), and combinations with panobinostat (10%), elotuzumab (6%) and daratumumab (5%).
- **Figure 2** shows the treatment regimens used at first index date (most right column) and their previous three therapy lines:
  - Treatment classes were generally changed line-to-line.
  - 87% of patients were exposed to an anti-CD38 containing regimen in their 1st prior LOT (of which 65% are refractory to this line). Anti-CD38 antibody was rarely re-initiated
  - In the 2nd and 3rd prior LOT, patients received many different treatment regimens. Patients predominantly received IMiD and/or PI based regimens
  - For some patients, treatments received in earlier lines were used again in later lines of therapy.

Figure 2. Sankey plot showing treatment regimens used in first index date line (most right column) and the previous three therapy lines.



SCT: Stem cell transplantation regimens (auto and allo transplants); includes any induction, mobilization, high dose chemotherapy, consolidation and maintenance regimen; CD38: Any anti-CD38-antibody containing regimen, unless part of SCT; Pano: Any panobinistat containing regimen, unless part of regimens in SCT or CD38 groups; Elo: Any elotuzumab containing regimen, unless part of regimen in SCT, CD38 or Pano groups; PI: Any PI (bortezomib, carfilzomib, ixazomib) containing regimen, not containing any IMiD or part of SCT, CD38, Pano or Elo group; IMiD: Any IMiD (thalidomide, lenalidomide, pomalidomide) containing regimen not containing any PI or part of SCT, CD38, Pano, Elo group; PI+IMiD: Any PI (bortezomib, carfilzomib, ixazomib) and IMiD (thalidomide, lenalidomide, pomalidomide) containing regimen, not part of SCT, CD38, Pano, Elo group; CHEMO: Any other chemotherapy regimen, not part of previous groups

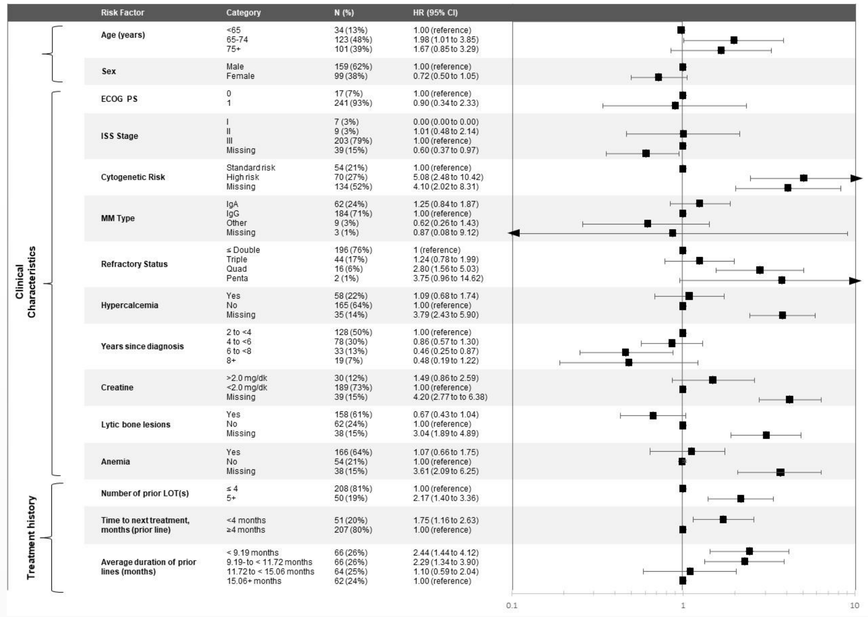
Figure 3. Kaplan-Meier estimates, OS and TTNT



OS, TTNT and Predictors of Outcome

- **Figure 3** presents a Kaplan Meier plot of OS and TTNT. Median OS was 8.84 months (95% CI 6.57 - 11.43) and median TTNT was 6.34 months (95% CI 4.86 - 8.08).

Figure 4. Patient Characteristics at Index Date and Predictors of Overall Survival



All patient characteristics are recorded at index date; N: number of observations (cf. methods section); HR: hazard ratio; CI: confidence interval; Hypercalcemia: >10,5 mg/dl or > 0,25 mmol/l higher than the upper norm; Anemia: hemoglobin <10.0 g/dl or >2.0 g/dl below the lower norm; High risk cytogenetics defined as carrier of any of the following abnormalities: Deletion of chromosome 13, Deletion of chromosome 17, Translocation t(4;14), Translocation t(6;14), Translocation t(11;14), Translocation t(14;16).

- At index date, 44 (17%) observations were triple-class refractory, 6% and 1% were quad- and penta-class refractory; 79% had ISS stage II and 93% had ECOG performance score 1.
- Most analyzed observations (87%) were in patients ≥65 years old. Approximately 19% had received 5 or more treatment lines.
- **Figure 4** presents findings from Cox PH analysis for OS and summary statistics of characteristics at index date.
- **OS:** Univariate Cox PH modeling suggested that higher degrees of refractory status, high cytogenetic risk, higher number of prior LOTs, shorter duration of prior LOTs and older age were associated with shortened OS (**Figure 4**). Anticipated significant effects were not observed for certain factors such as ISS Stage and MM subtype.
- **TTNT:** The impactful patient characteristics associated with shorter TTNT aligned closely with those identified for OS from Cox PH analysis.

CONCLUSIONS

- Analysis of a recent patient cohort from the German OIs MM disease registry showed poor OS and TTNT in patients with MM previously exposed to a PI, IMiD and anti-CD38-antibody.
- No single regimen was consistently used in this real world clinical practice population.
- Risk factors associated with shortened OS and TTNT included: higher degrees of refractory status, higher cytogenetic risk, later lines of treatment, older age and shorter duration of prior LOTs.
- Findings are comparable to those from earlier publications of similar US populations.[2,4,5]
- This study confirms high unmet need in triple-class exposed patients with MM in the European setting, which indicates that novel treatments with improved outcomes are needed for these patients.

ACKNOWLEDGEMENTS AND ADJUSTMENTS

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In this poster (presented at EHA-EBMT 3rd CAR T-cell meeting from February 4-6, 2021), labels for ISS stage in Figure 4 were incorrect. The labels were corrected in this version, made available online on March 7, 2021.

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