HSD10

TRUST-MM | Translating US Real-World Data to UK Practice: Treatment Patterns and Outcomes in First Line Relapsed/ Refractory Multiple Myeloma

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Aim

To demonstrate an initial proof of concept for methods to use US real-world data from patients with relapsed/refractory multiple myeloma (RRMM) to support health technology assessment decision-making in the UK and European Union.

Background

- Multiple myeloma (MM) is an incurable haematological malignancy associated with substantial morbidity and symptom burden[1]. A key feature of MM is the development of resistance to multiple treatment classes as the disease progresses[2].
  - Consequently, there remains a substantial unmet need for therapies with novel mechanisms of action for patients with relapsed or refractory disease. As a result, there is meaningful development in this treatment setting.
- The efficacy of a given MM therapy largely depends on prior exposure to MM drugs, particularly those from within the same class[3,4]. Therefore, the treatment of choice at second line (2L) is strongly influenced by the standard of care (SoC) at first line (1L), which can vary across geographic and clinical contexts.
- This creates an opportunity to consider whether emerging real-world data from one country can be used to inform regulatory and clinical decision-making in another.

Objectives

- Describe treatments received in 1L by the study cohort.
- Describe treatment patterns for the index treatment line (2L) and the subsequent LOT, as defined by treatment sequencing and regimens received, time to treatment discontinuation and total duration of post-index treatment.
- Estimate real-world overall survival (rwOS) after index.

Methods

Study design and data source

- This retrospective cohort study included adults with multiple myeloma (MM) who experienced relapsed or refractory disease after 1L therapy and subsequently initiated 2L systemic anticancer therapy.
- The analysis was conducted using the COTA real-world database (now Verana Health), a HIPAA-compliant longitudinal oncology database comprised of academic and community oncology practices from the United States.
  - The database includes detailed information regarding patient demographic attributes, cancer diagnosis, molecular/ genomic testing, comorbidities, performance status, treatment, toxicities and outcomes.
- The analysis included data for patients diagnosed between 1 January 2015 and 30 April 2025.

Study population and follow-up

- The study included adults with MM who received a regimen consistent with UK SoC in 1L and subsequently initiated 2L treatment following relapsed or refractory disease.
- Individuals were excluded if they had:
  - missing age or sex information; or
  - Another primary malignancy in the 5 years before MM diagnosis
- The index date was the date of first administration of 2L therapy after evidence of relapsed or refractory disease following 1L therapy.
- End of follow-up was defined as the earliest of:
  - Date of death
  - The end of the study period
  - Initiation of CAR T-cell therapy or investigational products
  - Lost to follow-up

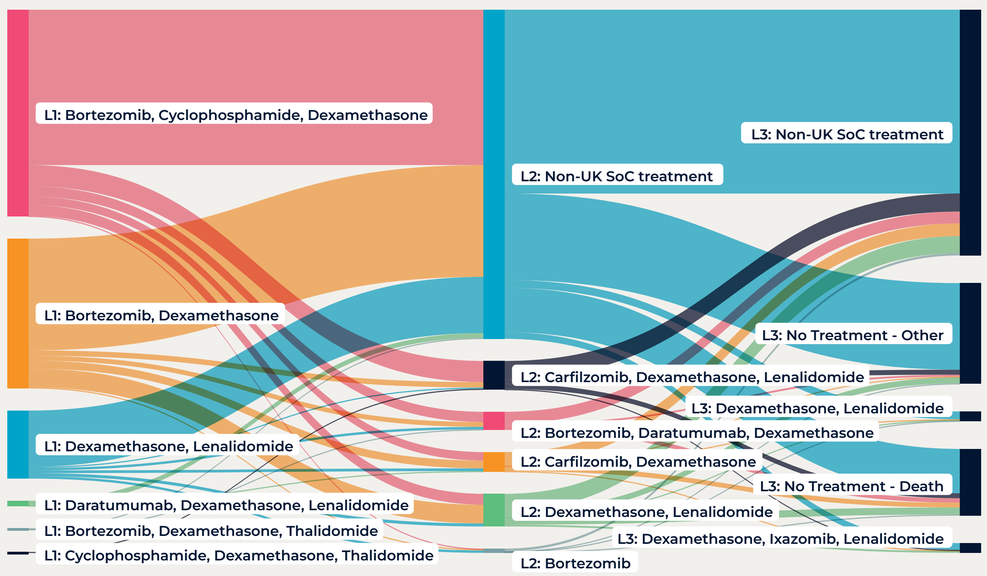
Statistical analysis

- Demographic and clinical characteristics were summarised using frequency counts and percentages for categorical variables, and measures of distribution (mean, standard deviation, median, interquartile range) for continuous variables.
- Treatment patterns were characterised using Sankey plots, with regimens grouped according to a predefined line-of-therapy (LOT) algorithm.
- rwOS was measured from initiation of 2L therapy (the index date) until death from any cause. Patients were censored at the end of the study period, loss to follow-up, or initiation of CAR T-cell therapy or an investigational product. rwOS was estimated using time-to-event methods and summarised by median survival time and time point-specific survival rates, with 95% confidence intervals (CIs).

Results

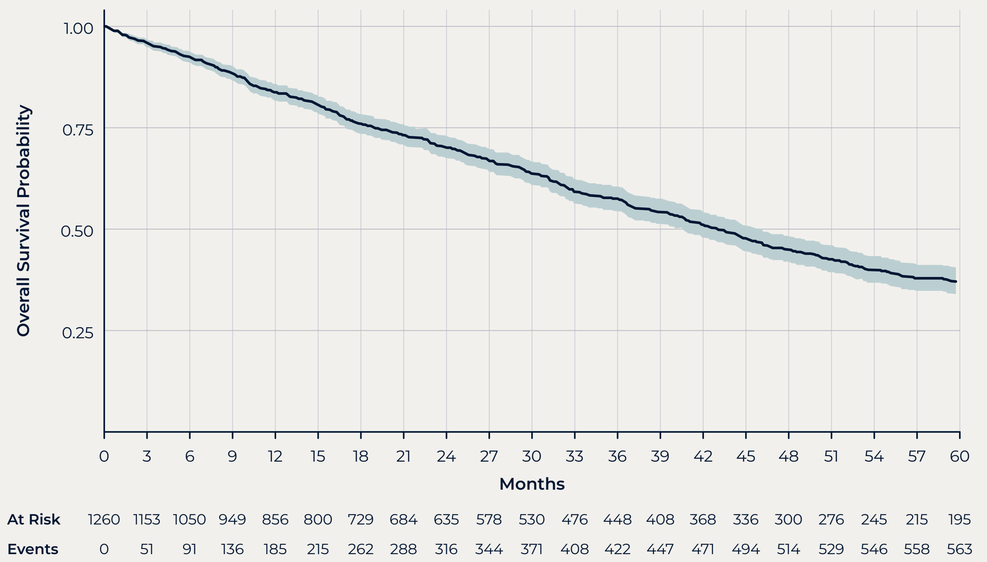
- The inclusion and exclusion criteria were applied, resulting in the following attrition:
  - Patients aged 18+ diagnosed with Primary Multiple Myeloma between 1 Jan 2015 and 30 April 2025; N = 6,664
  - Patients with complete age/sex information and no diagnosis of another primary malignancy in the five years prior to diagnosis with multiple myeloma; N = 6,013
  - Patients with RRMM who initiated 2L; N = 3,562
  - 43.0% of RRMM patients received UK-SoC treatment in 1L, resulting in a final cohort of **1,532 individuals**

Figure 1. Sankey plot documenting LOTs from UK 1L SoC



- Among the 1,532 patients who received a UK-SoC-compatible regimen in 1L, bortezomib plus dexamethasone, with or without cyclophosphamide, was the most common 1L treatment.
- In 2L, lenalidomide-containing regimens were most common, followed by carfilzomib-containing and bortezomib-containing regimens.

Figure 2. Kaplan-Meier for rwOS from initiation of 2L therapy following relapsed or refractory disease after 1L therapy using a UK SoC treatment



- rwOS was analysed in 1,260 patients. A total of 272 patients were excluded because the available records did not permit reliable determination of the index date and/or follow-up time.
- Median rwOS from 2L initiation was 43.0 months (95% CI, 40.3–46.2). Estimated 1-year, 3-year and 5-year survival probabilities were 84.7%, 57.4% and 36.8%, respectively.

Outcome	Estimate	95% CI
1-year Survival	84.7%	81.6, 85.9
3-year Survival	57.4%	54.4, 60.7
5-year Survival	36.8%	33.6, 40.4
rwOS (Months, Median)	43.0	40.3, 46.2

Table 1. Cohort baseline demographic and clinical characteristics

Characteristic	
Overall cohort	**1,532**
Age, Mean (SD)	66.45 (11.28)
Female, n (%)	706 (46.08%)
Age Band, n (%)	
18 – 49	120 (7.83%)
50 – 59	309 (20.17%)
60 – 69	445 (29.05%)
70 – 79	458 (29.90%)
80+	200 (13.05%)
Ethnicity, n (%)	
Asian	37 (2.42%)
Black	259 (16.91%)
White	920 (60.05%)
Mixed	116 (7.57%)
Other	130 (8.49%)
Missing	70 (4.57%)
Multiple Myeloma Stage, n (%)	
I	199 (12.99%)
II	362 (23.63%)
III	529 (34.53%)
Unknown	442 (28.85%)
Multiple Myeloma Subtype, n (%)	
IgG	801 (52.28%)
Non-IgG	351 (22.91%)
Others / Missing	380 (24.80%)
ECOG Performance Status, n (%)	
0 – 2	1,073 (70.04%)
3+	35 (2.28%)
Missing	424 (27.68%)
Charlson Comorbidity Index, n (%)	
0 – 3	578 (37.73%)
4+	66 (4.31%)
Missing	888 (57.96%)
High-Risk Cytogenetics, n (%)	
Multiple High-Risk Cytogenetics	51 (3.33%)
del(17p)	133 (8.68%)
t(4;14)	95 (6.20%)
t(14;16)	34 (2.22%)
No high-risk cytogenetics	1,219 (79.57%)

ECOG, Eastern Cooperative Oncology Group Performance Status; IgG, Immunoglobulin G

Conclusions

- In healthcare decision-making, it is increasingly common to consider real-world evidence from one region (e.g. the United States) to inform decisions in another (e.g. the United Kingdom or European Union).
- By assessing overlap in UK and US 1L MM treatments, we identified a comparable US cohort and estimated key real-world outcomes. This approach is an important step in identifying UK-relevant comparator populations for real-world evidence studies and serves as the foundation for future evidence generation on the effectiveness of therapies not currently available in the UK.
- However, rigorous methods are required to ensure that such “borrowed” evidence is fit for purpose and truly addresses the research question. Leading agencies, such as NICE, EMA, FDA, among others, have all emphasised structured approaches for using RWE across jurisdictions.
- This proof-of-concept study successfully identified a US real-world cohort with 1L treatment patterns aligned with UK SoC and described subsequent treatment patterns and rwOS following 2L initiation. These findings provide an initial foundation for a structured and auditable framework to assess the relevance, transportability and appropriate use of international real-world evidence in UK and EU healthcare decision-making.

References

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