From Data to Decisions: The Role of Real-World Evidence in Recent Multiple Myeloma Drug Approvals in the US and EU

HPR136

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Background

- Multiple myeloma (MM) is a hematologic malignancy that remains incurable, necessitating continuous innovation in therapeutic strategies
- Integration of real-world data/evidence (RWD/E) for regulatory decision-making has gained momentum, particularly in oncology, due to patient heterogeneity and rapidly evolving treatment landscapes
- The European Medicines Agency (EMA) and US Food and Drug Administration (FDA) guidelines provide a framework for the use of RWE in marketing applications, postapproval studies, and label expansions
- Understanding how RWE influences approvals can inform future drug development and regulatory strategies

Objectives

For all MM drug approvals issued by FDA and EMA between January 2021 and November 2024:

- Identify and analyze common regulatory feedback themes on the use of RWE in marketing applications
- Assess the utilization of RWE and characterize its applications, including identification of the associated RWD sources

Methods

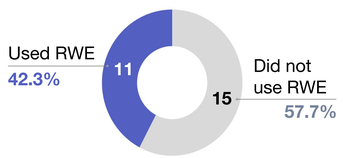
Publicly available FDA and EMA approval documents were identified and reviewed as follows:

Time Frame	Health Authority	Sources	Study Sample
January 2021 - November 2024	**FDA**	Drugs@FDA Review Documents (e.g., multidiscipline review, integrated review)	All original and supplemental New Drug Application (NDA) and Biologics License Application (BLA) approvals indicated for the treatment of MM
	EMA	European Public Assessment Reports (EPAR) database	All original and type II variation approvals indicated for the treatment of MM

Results*

- In total, 26 drug marketing applications indicated for the treatment of MM were approved **(Figure 1)**

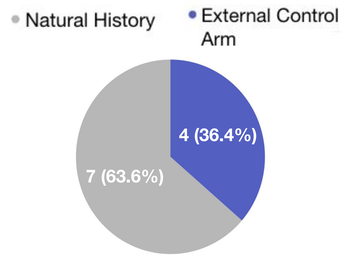
Figure 1. FDA & EMA MM Drug Approvals (2021-2024)



*Results presented hereinafter differ from those reported in the initial abstract due to additional data availability and updated analyses.

Results (continued)

Figure 2. Applications of RWE in MM Drug Approvals (2021-2024)



Main Findings/Key Takeaways

✓ In the past 4 years, **42%** of MM drug approvals issued by FDA and EMA included **RWE** as **supportive evidence**

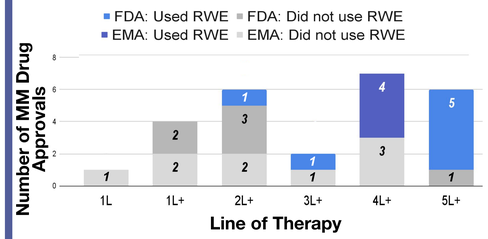
✓ RWE was used to generate **external control arms** and **natural history** studies

Common Regulator Feedback

- RWE-based comparisons provided valuable context to complement clinical trial data
- External comparisons using RWD were used to support benefit-risk assessments and offered important insights into real-world treatment outcomes, though they were not regarded as comprehensive for evaluating long-term efficacy and safety
- Heterogeneity of treatment options was evident in the RWE studies; however, RWD provided natural history and contextualization of the disease

Results (continued)

Figure 3. Number of MM Approvals With vs Without RWE by Health Authority and Line of Therapy (2021-2024)



Key Differences Between MM Marketing Applications That Used RWE vs Those That Did Not (Figure 3):

- RWE-supported approvals were often later-line therapies for relapsed/refractory multiple myeloma (RRMM), including chimeric antigen receptor T-cell (CAR-T) therapies and bispecific T-cell engagers (**Table 1**)
- Non-RWE–supported approvals included both newly diagnosed and earlier-line MM treatments: selinexor, daratumumab, carfilzomib, and isatuximab

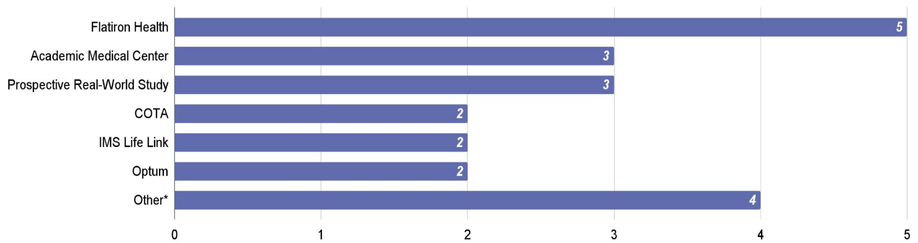
Table 1. RWE in MM Drug Approvals by Line of Therapy (2021-2024)

Approved MM Therapies	Line of Therapy				Grand Total
	2L+	3L+	4L+	5L+	
Ciltacabtagene autoleucel	X		X	X	3
Elranatamab			X		1
Idecabtagene vicleucel		X	X	X	3
Melphalan flufenamide				X	1
Talquetamab			X	X	2
Teclistamab				X	1
Grand Total	1	1	4	5	11

Abbreviations: 1L, first-line; 1L+, first-line or higher; 2L+, second-line or higher; 3L+, third-line or higher; 4L+, fourth-line or higher; 5L+, fifth-line or higher

Figure 4. Sources of RWD Used in MM Drug Approvals (2021-2024)

(Each data source may be used in multiple marketing applications)



*Note: "Other" includes 4 distinct RWD sources, each used in 1 marketing application.

Conclusions/Future Directions

- FDA and EMA have recognized RWE as supportive evidence in marketing applications for RRMM; **RWE can be relevant and reliable in addressing challenges associated with conducting large-scale trials for rare cancer populations**
- RWE can contextualize single-arm trials and/or establish an external control arm for rare cancers with significant unmet need in later-line and/or relapsed/refractory settings

Disclosures: This study was sponsored by Flatiron Health, Inc.—an independent member of the Roche Group. During the study period, AC, LP, and LT reported employment with Flatiron Health, Inc., and stock ownership in Roche.
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