Rapidly evolving treatment landscape in multiple myeloma - leveraging a living systematic literature review (SLR)

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CONCLUSIONS

- → The daily maintenance of the REAL-SLR allowed real-time analysis of trends in reported outcomes, intervention categories, and subgroups of interest in multiple myeloma
- → In the rapidly evolving therapeutic landscape in multiple myeloma REAL-SLR is well suited to ensure decision makers are properly informed and novel therapies and practices are quickly adopted
- → Given the large amount of evidence published in the last years, traditional SLRs and living SLRs updated every few months may not keep up with emerging trial results and industry trends
- → Comprehensiveness, evidence stratification, and daily updating of the REAL-SLR provide valuable insights for decision-making, in a faster and more easily accessible way compared to static ad-hoc SLRs

BACKGROUND

- Systematic literature reviews (SLRs) are critical to healthcare stakeholder decision-making but are labor intensive while quickly becoming outdated, especially in fast evolving research areas
- Living SLR process aims to address this challenge by conducting regular updates, typically every few months[1]
- Despite this continuous update process, critical emerging evidence might not be captured and disseminated efficiently, which can impact the adoption of novel findings into practice
- Moreover, dissemination of results from updates is more challenging compared to traditional reviews, with more than half of published living SLRs not publishing an update[2,3]

OBJECTIVES

- → To develop a REal-time AI-assisted Living SLR (REAL-SLR), that addresses the challenges of existing living SLR frameworks in the rapidly evolving areas of oncology clinical research, by employing daily updates and results dissemination through an online platform
- → To use REAL-SLR to analyze trends in population characteristics, reported outcomes, and novel therapies approved, recommended or investigated in multiple myeloma clinical trials

METHODS

- A daily-updated REAL-SLR was created in multiple myeloma, compliant with PRISMA guidelines, using the Population, Intervention/Comparators, Outcomes, and Study design (PI/COS) framework (**Table1**)
- Clinical trials from PubMed published in English since 2020, and conference abstracts from American Society of Hematology, International Myeloma Society, and European Hematology Association (2024-2025), were identified and reviewed
- In addition, trials supporting regulatory approvals and guideline recommendations without publication timeframe restrictions, were identified and reviewed
- A proprietary artificial intelligence model was employed during first title and abstract review. Second review and conflict resolution were conducted by human researchers
- Evidence was stratified by treatment pathways and interventions, outcomes, and subgroups categories

Table 1. PICOS statement

Element	Inclusion
Patient population	• Patients diagnosed with symptomatic multiple myeloma or smoldering myeloma
Intervention and Comparators	• Any pharmacological intervention (including biologics, cell treatments, vaccines, etc.) and stem-cell transplant used for the treatment of myeloma
Outcomes measures	• Overall survival and mortality • Progression-free survival • Other progression measures (such as duration of response, time to progression, time to next treatment) • Response rates (such as complete response, very good partial response, objective response rate, minimal residual disease) • Quality of life (measures such as EORTC QLQ-C30, EORTC MY-20, and EQ-5D utility) • Safety (treatment-related adverse events [AEs], grade ≥3 and serious AEs, AEs of special interest and discontinuations)
Study design	• Prospective interventional studies including randomized and non-randomized trials, any phase • Pooled analyses of trials • External control trials
Restrictions	• English language

Figure 1. Distribution of multiple myeloma (MM) trials (2020–2025) in the REAL-SLR database

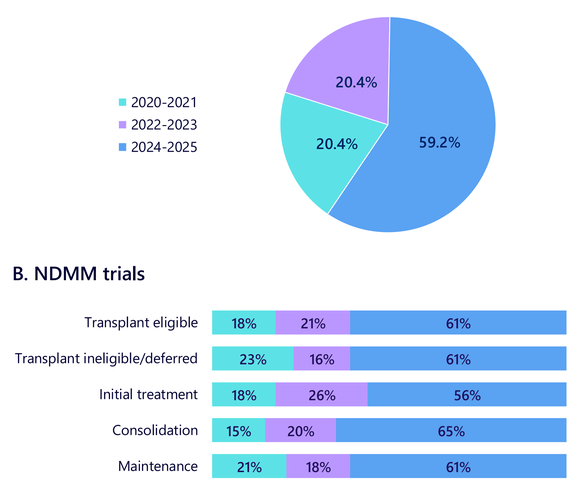


Figure 2. Temporal trends in drug classes investigated in multiple myeloma between 2020 to 2025

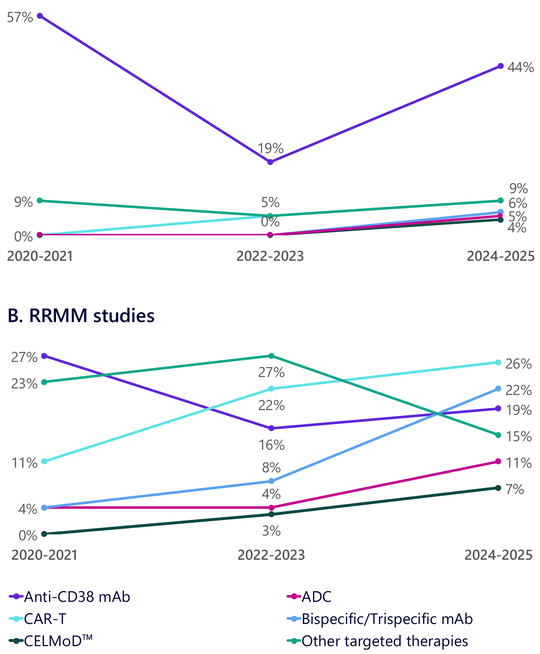
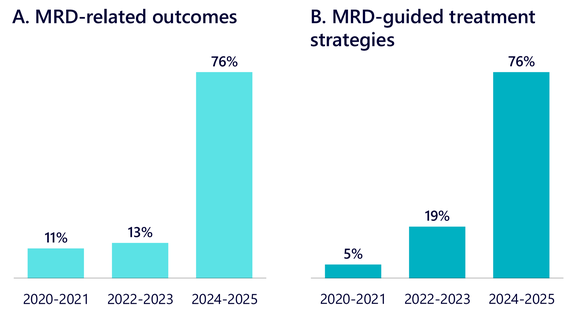


Figure 3. Temporal trends in the use of MRD negative rates in multiple myeloma



RESULTS

- As of March 17, 2026, REAL-SLR included 737 studies in multiple myeloma: 301 (40.8%) in newly diagnosed (NDMM), 416 (56.4%) in relapsed/refractory (RRMM), and 20 (2.7%) in smoldering myeloma populations
- When analyzing publications from 2020 to 2025, a larger proportion of trials were published in 2024-2025 (59%), compared to 2021-2022 and 2020-2021 with 20% each (**Figure 1A**)

Trends in population characteristics

- In 2024-2025 there has been an increase in trials in NDMM including transplant ineligible/deferred patients. The distinction by transplant eligibility is rapidly blurring with more patients reserving transplant to later lines (**Figure 1B**)
- Consolidation therapies are gaining more attention in recent years, compared to induction and maintenance (**Figure 1B**)
- Among RRMM studies, an increased interest in recent years was observed for patients who were anti-CD38 refractory and triple-class refractory, in line with the introduction of anti-CD38 monoclonal antibodies (**Figure 1C**). Similarly, recent studies account now for patients with prior CAR-T therapies and BCMA-targeted therapies with 84% and 80% of these studies being published in 2024 and 2025 alone, respectively

Trends in investigated therapies

- Temporal trends of interventions in NDMM showed a growing interest towards quadruplet combinations, antibody-drug conjugates (ADCs), bispecific/trispecific antibodies, CELMoDs™, and CAR-Ts (**Figure 2A**)
- A similar trend can be observed in RRMM, except for therapies designed for various other molecular targets (ie, XPO1-targeted, BRAF-targeted, ALK-targeted, CD47-targeted, histone deacetylase inhibitors, BCL2 inhibitors, etc.) which showed a decreasing interest in 2024-2025 (**Figure 2B**)
- Studies of ADCs and CELMoDs™ represented similar proportions of the total studies in NDMM compared to RRMM. However, CARTs, bispecific/trispecific antibodies and other targeted therapies had higher proportions of the total studies in RRMM compared to NDMM (**Figure 2**)
- Therapies generally reserved for heavily pre-treated patients such as CAR-Ts, bispecific/trispecific antibodies, and ADCs, have been recently investigated in earlier lines of therapy for RRMM

Trends in outcomes

- Minimal residual disease (MRD)-related outcomes were included in 205 studies. Of the studies published between 2020 and 2025, 76% published in 2024-2025 alone included MRD related-related outcomes (**Figure 3A**)
- MRD-guided treatment strategies received increased attention, with 76% of the MRD-guided trials published in 2024-2025 (**Figure 3B**)

ABBREVIATIONS

ADC, antibody-drug conjugate; CAR-T, chimeric antigen receptor T-cell therapy; IMiD, immunomodulatory drug; LOT, line of therapy; mAb, monoclonal antibody; PI, proteasome inhibitor

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