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MULTIPLE MYELOMA IN THE ERA OF PRECISION MEDICINE: RECENT ADVANCES IN PATHOGENESIS, DIAGNOSIS, AND TREATMENT

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ABSTRACT

Background: Multiple myeloma (MM) is the second most common hematologic malignancy worldwide, with rising incidence due to population aging and improved recognition of precursor conditions such as MGUS and SMM. Despite significant therapeutic advances, including proteasome inhibitors, immunomodulatory drugs, and anti-CD38 antibodies, MM remains incurable, highlighting the need for continued research into novel diagnostics and treatment strategies.

Aims: The aim of this review is to critically analyze recent advances in molecular diagnostics, minimal residual disease monitoring, and immunotherapeutic strategies in multiple myeloma, with emphasis on their clinical applicability and future perspectives.

Methods: A narrative review of the English-language literature (2020–2025) was conducted in PubMed and Google Scholar. Eligible studies included clinical trials, systematic reviews, meta-analyses, observational studies, and international guidelines involving adult patients (≥19 years). Articles addressing molecular diagnostics, novel biomarkers (e.g., ctDNA, serum BCMA), or systemic therapies (including proteasome inhibitors, CAR-T cells, and bispecific antibodies) were considered. Priority was given to randomized phase II/III trials, real-world evidence, guidelines, and emerging technologies such as liquid biopsy and AI-assisted prediction models.

Results: Global incidence and prevalence continue to rise, driven by population aging and improved detection, while mortality has stabilized or declined in high-income regions. Genomic profiling confirms heterogeneous driver mutations (e.g., KRAS, NRAS, TP53, BRAF), high-risk cytogenetic abnormalities [del(17p), t(4;14)], and dysregulated pathways (NF-κB, JAK/STAT, PI3K/AKT/mTOR). Diagnostics have advanced through refined IMWG criteria, highly sensitive MRD assays using next-generation flow or sequencing (10^{-5}-10^{-6}), and emerging biomarkers such as circulating tumor DNA and serum BCMA. Frontline outcomes have improved with quadruplet regimens combining proteasome inhibitors, immunomodulatory agents, and anti-CD38 antibodies.

In relapsed/refractory disease, BCMA-targeted CAR-T cells and bispecific antibodies, including GPRC5D-directed agents, achieve high response rates, though challenges remain in durability, toxicity, and treatment access.

Conclusions: Integration of molecular diagnostics, sensitive MRD monitoring, and potent immunotherapies is extending remissions for many patients with MM. Priorities include overcoming resistance, mitigating toxicity, optimizing MRD-guided treatment sequencing, and reducing global disparities in access to advanced therapies. Precision medicine strategies offer a promising pathway to improve survival and quality of life.

Keywords: Multiple myeloma, plasma cell malignancy, epidemiology, pathogenesis, genomic profiling, diagnostic biomarkers, Minimal residual disease (MRD), CAR-T cell therapy

1. INTRODUCTION

Multiple myeloma (MM) is a malignant disorder characterized by the clonal proliferation of plasma cells within the bone marrow [1]. It is the second most common hematologic cancer worldwide, accounting for approximately 1% of all cancer diagnoses and up to 15% of blood cancers [2].

According to GLOBOCAN estimates, the global number of new multiple myeloma cases increased from approximately 148,000 in 2021 to 188,000 in 2022, primarily driven by population aging and improved detection of precursor conditions such as monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) [3]. The age-standardized incidence rate (ASR) during this period remained around 2.1 per 100,000 worldwide, with the highest rates observed in Australia, North America, and Northern Europe (3.8-4.9 per 100,000), and the lowest in regions such as Melanesia and West Africa (0.8-1.0 per 100,000) [4]. In Poland, the incidence of multiple myeloma increased from approximately 6.4 per 100,000 inhabitants in 2009 to 8.3 per 100,000 in 2017, based on National Health Fund (NFZ) registry data. During the same period, prevalence rose from 13.6 to 23.9 per 100,000 (a ~76% increase), while the mortality-to-prevalence ratio decreased from 78% to 22.8%, reflecting both earlier diagnosis and improved survival outcomes. One-, three-, and five-year survival rates improved from 70.5%, 51.5%, and 40.2% (for patients diagnosed in 2009) to 78.4%, 60.3%, and 48.3% (for patients diagnosed in 2013), respectively [5].

In high-income countries, mortality rates have stabilized or slightly declined, reflecting the impact of novel therapies such as proteasome inhibitors, immunomodulatory agents, and autologous stem cell transplantation [6].

Despite these advances, MM remains incurable. The disease and its complications, including bone lesions, renal impairment, anemia, and increased susceptibility to infections, continue to impose a substantial global burden. This is particularly evident in middle- and high-income countries experiencing rapid demographic change and increasing prevalence of lifestyle-related risk factors such as obesity and diabetes. These trends highlight the urgent need for continued research into the pathogenesis, diagnostic strategies, and emerging treatment approaches that can deliver sustained remissions and improved outcomes [6].

This review provides a comprehensive and up-to-date summary of recent advances in the molecular basis, clinical presentation, and therapeutic innovations in MM, with a focus on clinical applicability and future directions.

The aim of this review is to critically analyze recent advances in molecular diagnostics, minimal residual disease monitoring, and immunotherapeutic strategies in multiple myeloma, with emphasis on their clinical applicability and future perspectives.

2. METHODS

This study is a structured narrative review aiming to synthesize the most relevant and recent clinical evidence on multiple myeloma from January 1, 2020 to August 5, 2025. A systematic search was performed in PubMed/ MEDLINE and Google Scholar (for supplementary references), using predefined terms including "multiple myeloma" OR "BCMA" OR "CAR-T" OR "bispecific antibodies" OR "minimal residual disease" OR "genomic profiling". Eligible studies were full-text, peer-reviewed publications in English involving adult patients (≥19 years), including clinical trials, meta-analyses, original research, systematic reviews, and international guidelines. Abstracts, case reports, preprints without peer review, and studies with insufficient methodological detail were excluded.

The initial search yielded 1097 records; after removal of duplicates and screening of titles and abstracts, 95 full texts were assessed, and 34 studies were included in the final synthesis: 12 randomized controlled trials, 6 systematic reviews or meta-analyses, 5 clinical guidelines or consensus statements, 7 observational registry-based studies, and 4 original research articles focusing on biomarkers or novel diagnostic approaches. Additional narrative reviews (n=8) were consulted to provide epidemiological and contextual background but were not part of the formal synthesis. No formal risk-of-bias assessment or quantitative meta-analysis was

undertaken, as the aim was to provide a clinically oriented qualitative synthesis.

3. RESULTS

3.1. EPIDEMIOLOGY AND RISK FACTORS

Multiple myeloma (MM) represents a growing global health burden, with approximately 148,000 new cases in 2021 and over 116,000 deaths worldwide, corresponding to an age-standardized mortality rate of 1.37 per 100,000 population. Between 1990 and 2021, incidence, prevalence, and disability-adjusted life years (DALYs) have steadily increased [3, 8]. This trend is most pronounced in high-income countries, particularly among older adults, although the growth of the global population and improved diagnostic capabilities have also led to increases in lower- and middle-income regions [9].

Established risk factors for MM include advanced age (median age at diagnosis ~69 years), male sex, and African American ethnicity. A personal or family history of plasma cell disorders, such as MGUS or SMM, significantly increases the risk of progression to symptomatic disease [10]. MGUS affects approximately 3.2% of individuals over age 50 and carries a consistent annual risk of progression of about 1%. In contrast, progression from SMM to active myeloma is highest within the first five years after diagnosis, at roughly 10% per year.

Obesity is a notable modifiable risk factor. An increased body mass index (BMI) correlates with a higher likelihood of developing MGUS and with progression to overt MM. Meta-analyses and large cohort studies, including the PLCO trial and the AGES-RS cohort, suggest that each 5 kg/m² increase in BMI is associated with an ~11% increase in MM risk [11]. Mechanistic studies indicate that adipose tissue promotes chronic inflammation, cytokine dysregulation, and altered adipokine signaling, which collectively support plasma cell proliferation and survival.

Occupational and environmental exposures may also contribute to MM pathogenesis. For example, exposure to benzene derivatives has been associated with increased risk in agricultural and certain industrial settings. Although hereditary predisposition is rare, familial clustering of plasma cell disorders suggests a possible genetic susceptibility.

3.2. PATHOGENESIS AND MOLECULAR MECHANISMS

Multiple myeloma develops through a complex interplay between genetic alterations in plasma cells and signals from the bone marrow microenvironment. Chromosomal translocations such as t(4;14) activate FGFR3 and stabilize the c-MYC oncoprotein in approximately 15–20% of cases, promoting proliferation and resistance to oxidative stress. This FGFR3–c-MYC axis represents a promising therapeutic target in aggressive disease subtypes [12].

Cytokines, particularly interleukin-6 (IL-6) and insulin-like growth factor-1 (IGF-1), activate the PI3K/AKT/mTOR pathway in plasma cells, enhancing survival, migration, and chemotaxis [13]. Although PTEN loss is uncommon, pathway activation is widespread due to cytokine-driven signaling [14]. Aberrant NF-κB activation, present in myeloma and stromal cells in about 80% of patients, supports cell proliferation, angiogenesis, and therapy resistance, particularly to proteasome inhibitors [15].

Mutations in KRAS, NRAS, and BRAF, along with persistent IL-6 signaling, also stimulate the MAPK and JAK/STAT pathways, reinforcing transcriptional programs that promote cell growth and resistance to apoptosis.

The bone marrow niche, especially mesenchymal stem cells (MSCs), plays a critical role in disease maintenance. Aberrant PI3K/AKT/mTOR activation in MM-associated MSCs enhances their tumor-supportive functions and contributes to drug resistance. Targeting PI3K in these niche cells has been shown to disrupt tumor–microenvironment interactions, offering a potential therapeutic avenue [16].

In summary, MM pathogenesis is driven by deregulated signaling cascades , including PI3K/AKT, NF-κB, MAPK, JAK/STAT, and FGFR3/c-MYC, working in concert with microenvironmental cues. These molecular abnormalities enable malignant plasma cell survival, expansion, and therapy resistance, while also providing multiple targets for precision-based treatment strategies.

3.3. CLINICAL MANIFESTATIONS AND COMPLICATIONS

Multiple myeloma most commonly presents with skeletal pain, particularly in the spine, ribs, and pelvis, due to osteolytic lesions present in approximately 80% of patients at diagnosis. These lesions can lead to pathological fractures, spinal cord compression, and hypercalcemia, collectively reducing quality of life and survival outcomes [17].

Anemia affects about 70% of patients at diagnosis and typically worsens over time due to cytokine-mediated suppression of hematopoiesis and bone marrow infiltration [17]. Renal impairment occurs in roughly 30% of cases, caused by mechanisms such as light chain cast nephropathy, hypercalcemia, amyloid deposition, and dehydration.

Immunodeficiency is a hallmark of MM, with patients having up to a twofold increased risk of severe infections compared with matched controls. Common pathogens include respiratory bacteria, urinary tract organisms, and opportunistic fungi. In advanced disease, infections such as Cryptococcus may occur [18].

Neurological complications, although less common, may include peripheral neuropathy or rare paraneoplastic syndromes such as leptomeningeal or optic nerve involvement, which in some cases precede MM diagnosis. Extramedullary disease is also relatively uncommon but clinically significant, presenting as hepatomegaly, splenomegaly, lymphadenopathy, or soft tissue plasmacytomas. These features are generally associated with more aggressive disease biology and poorer prognosis [19].

In summary, the major complications of MM include bone destruction, anemia, renal impairment, heightened susceptibility to infection, and neurological events, all of which contribute significantly to morbidity and mortality in affected patients.

3.4. DIAGNOSTIC CRITERIA AND BIOMARKERS

The diagnosis of multiple myeloma (MM) requires meeting at least one of the following two criteria: Clonal bone marrow plasma cells ≥10%, or Biopsy-proven plasmacytoma, and at least one myeloma-defining event (MDE) or biomarker as specified by the International Myeloma Working Group (IMWG) guidelines [20].

The classic CRAB criteria - C: hypercalcemia, R: renal impairment, A: anemia, B: bone lesions, remain central to MM diagnosis. Additional biomarkers defining active MM include: Bone marrow plasma cell infiltration ≥60%, Involved/uninvolved serum free light chain (FLC) ratio ≥100, At least one focal lesion ≥5 mm on MRI [20].

The diagnostic work-up should include serum protein electrophoresis (SPEP), serum immunofixation, free light chain assays, bone marrow aspiration and biopsy with cytogenetic and fluorescence in situ hybridization (FISH) analysis, and imaging with low-dose whole-body CT or PET-CT. MRI is particularly recommended for detecting focal lesions in patients with smoldering MM who do not yet meet CRAB criteria.

Common cytogenetic abnormalities with prognostic significance include t(4;14), t(11;14), t(14;16), del(17p), and trisomies [20]. The key IMWG diagnostic criteria and myeloma-defining events are summarized in Table 1.

Table 1. IMWG diagnostic criteria and myeloma-defining events.

Criterion	Parameter	Threshold/ definition	Clinical note
CRAB features	Hypercalcemia; renal impairment; anemia; bone lesions	-	Core end organ damage features per IMWG criteria
MDE	Clonal plasma cells in bone marrow	≥60%	Biomarker defining active MM
MDE	Serum free light chain (involved/uninvolved) ratio	≥100	Biomarker defining active MM
MDE	MRI focal lesion	≥1 lesion ≥5 mm	Biomarker defining active MM

Abbreviations: IMWG - International Myeloma Working Group; MDE - myeloma defining event; CRAB - hyperCalcemia, Renal impairment, Anemia, Bone lesions; FLC - (involved/uninvolved) serum free light chain; MRI - magnetic resonance imaging; BM - bone marrow.

For disease monitoring, minimal residual disease (MRD) assessment has become a critical biomarker. Next-generation flow cytometry (NGF) and next-generation sequencing (NGS) enable detection sensitivity down to 10^{-5}-10^{-6} cells. Achieving MRD negativity is strongly associated with longer progression-free survival (PFS) and overall survival (OS) across multiple clinical settings [21].

Emerging biomarkers, such as serum BCMA (sBCMA), show promise in early disease detection and treatment monitoring, particularly in patients with non-secretory MM or renal impairment. sBCMA levels correlate with tumor burden and treatment response and are only minimally affected by renal function, making this biomarker especially valuable in patients with impaired kidney function [22, 23]

Modern diagnosis and disease monitoring in MM therefore rely on the integration of CRAB criteria, validated biomarkers, advanced imaging, and highly sensitive MRD detection methods - enabling earlier detection, better risk stratification, and more individualized treatment planning.

3.5. CURRENT TREATMENT MODALITIES

Treatment strategies for multiple myeloma (MM) have advanced substantially between 2021 and 2025. For transplant-eligible patients, frontline therapy often consists of quadruplet regimens such as daratumumab, bortezomib, lenalidomide, and dexamethasone (D-VRd), now recommended as a preferred induction option following the PERSEUS trial. For transplant-ineligible patients, isatuximab, bortezomib, lenalidomide, and dexamethasone (Isa-VRd) has received a Category 1 recommendation based on the IMROZ trial. Isatuximab, carfilzomib, lenalidomide, and dexamethasone (Isa-KRd) is listed as a Category 2B option in selected cases according to NCCN v2.2025 guidelines [24].

In the relapsed/refractory setting, CAR-T cell therapies have transformed outcomes: Idecabtagene vicleucel (ide-cel): Overall response rate (ORR) 73%, median PFS 8.8 months in heavily pretreated patients. The KarMMa-3 trial reported a superior median PFS of 13.3 months vs 4.4 months with standard of care [25].

Ciltacabtagene autoleucel (cilta-cel): ORR 97%, stringent complete response (sCR) in 67% of patients, with median PFS not yet reached. In the CARTITUDE-4 trial, 12-month PFS was 76% compared to 49% with standard regimens [26].

Bispecific antibodies targeting BCMA, such as teclistamab and elranatamab, as well as GPRC5D-directed agents like talquetamab, have demonstrated ORRs of up to 63% in triple-class refractory disease, with cytokine release syndrome (CRS) as a common but generally manageable adverse event [27].

In 2025, combinations of belantamab mafodotin with bortezomib and dexamethasone (BVd) or with pomalidomide and dexamethasone (BPd) were approved in the European Union, the United Kingdom, Canada, and Japan. In the United States, in July 2025, the FDA's ODAC committee voted against the proposed BVd regimen, and regulatory review is still ongoing. In the randomized DREAMM-7 trial, median PFS for BVd was 36.6 months compared with 13.4 months for DVd (HR 0.51), and interim analyses also demonstrated an overall survival (OS) benefit. [28]

Treatment selection is increasingly guided by patient eligibility for transplantation, cytogenetic risk stratification, prior therapies, and treatment tolerance, with an emphasis on balancing depth of response with safety and quality of life.

Selected frontline and relapsed/refractory regimens with their reported efficacy and clinical notes are summarized in Table 2.

Table 2. Selected frontline and RRMM regimens and outcomes

Setting	Regimen/target	Efficacy	Clinical note
Frontline	Daratumumab + bortezomib + lenalidomide + dexamethasone (D VRd)	-	Recommended frontline quadruplet in eligible patients
Frontline	Isatuximab + bortezomib + lenalidomide + dexamethasone (Isa-VRd)	-	Category 2B recommendation

RRMM	Idecabtagene vicleucel (BCMA CAR T)	ORR 73%; median PFS 8.8 mo; updated PFS 13.3 vs 4.4 mo (vs SOC)	CRS/neurotoxicity noted as class concerns
RRMM	Ciltacabtagene autoleucel (BCMA CAR T)	ORR 97%; sCR 67%; median PFS not reached; 12 mo PFS 76% vs 49%	CRS/neurotoxicity noted
RRMM	Bispecific antibodies (e.g., teclistamab, elranatamab; GPRC5D directed talquetamab)	ORR up to 63% in triple class refractory	CRS common; management required
RRMM	Belantamab mafodotin + bortezomib + dexamethasone	Median PFS 36.6 mo vs 13.4 mo (DVd); HR 0.51; OS improvement in interim analyses (DREAMM-7)	Early access program noted

Abbreviations: RRMM - relapsed/refractory multiple myeloma; ORR - overall response rate; sCR - stringent complete response; PFS - progression free survival; CRS - cytokine release syndrome; AE - adverse event; NR - not reached; CAR T - chimeric antigen receptor T cell therapy; BCMA - B cell maturation antigen; GPRC5D - G protein coupled receptor, class C group 5 member D; D VRd - daratumumab, bortezomib, lenalidomide, dexamethasone; Isa VRd - isatuximab, bortezomib, lenalidomide, dexamethasone.

3.6. ADVANCES IN PERSONALIZED AND PRECISION MEDICINE

Recent years have witnessed substantial progress in tailoring multiple myeloma (MM) treatment through advanced diagnostics and next-generation immunotherapies. Bispecific T-cell engagers (BsAbs) have emerged as effective "off-the-shelf" agents targeting either B-cell maturation antigen (BCMA) or G protein–coupled receptor class C group 5 member D (GPRC5D) on malignant plasma cells, redirecting endogenous T cells to attack tumor cells. Teclistamab and elranatamab, both BCMA-directed, have achieved durable responses with median progression-free survival (PFS) of approximately 12 months in heavily pretreated patients, while maintaining manageable toxicity profiles. Talquetamab, targeting GPRC5D, has demonstrated high activity in relapsed/refractory MM and offers an alternative for patients resistant to BCMA-targeted agents [29].

Bridging strategies using BsAbs before BCMA-directed CAR-T cell therapy are gaining traction. In a retrospective, single-center cohort study of 52 patients with relapsed/refractory MM, BsAb bridging achieved a 100% overall response rate (ORR) prior to leukapheresis, improved T-cell clonality in leukapheresis products, and facilitated deeper responses following idecabtagene vicleucel or ciltacabtagene autoleucel infusion. After CAR-T cell therapy, the day-30 ORR was 78%, underscoring the potential benefit of BsAb bridging in enhancing subsequent CAR-T efficacy [30].

Parallel advances in minimal residual disease (MRD) detection and artificial intelligence (AI) are enabling earlier intervention and more precise risk assessment. In a preprint study by Chen et al. (2024), an AI-based MRD evaluation and prediction model achieved an area under the receiver operating characteristic curve (AUROC) of approximately 0.88 for forecasting disease progression up to 12 months in advance. In a peer-reviewed study by Ferle et al. [31] models based on routine blood work predicted progression events with AUROC values ranging from 0.80 to 0.87. Highly sensitive MRD assessment using next-generation flow cytometry or sequencing can now detect malignant plasma cells at levels as low as 10^{-6}, refining risk stratification and treatment monitoring.

Integration of these advances with genomic profiling enables a truly personalized approach to MM management, supporting evidence-based therapy selection, optimized sequencing, and dynamic monitoring tailored to each patient's disease biology and risk profile [32].

3.7. CHALLENGES AND LIMITATIONS

Despite remarkable progress, multiple myeloma (MM) management faces persistent challenges in diagnosis, treatment, and equitable access to care.

Treatment resistance remains the most significant obstacle, particularly in patients with disease refractory to multiple drug classes. Clonal evolution and tumor heterogeneity allow resistant subclones to emerge, often leading to triple-class refractory disease (refractory to proteasome inhibitors, immunomodulatory drugs, and anti-CD38 monoclonal antibodies) with a median overall survival of less than six months [33].

Clinical trial limitations also hinder generalizability of results. Stringent eligibility criteria frequently exclude older patients and those with comorbidities, meaning trial populations may not reflect real-world patient demographics. Consequently, real-world outcomes can be significantly worse than those reported in trials.

Health disparities exacerbate these challenges. Older patients, racial and ethnic minorities, women, and individuals from lower-income households often experience delays in diagnosis, lower rates of stem cell transplantation, and reduced access to novel therapies such as CAR-T cells and bispecific antibodies [34]. Geographic and socioeconomic barriers contribute to higher mortality in rural and underserved areas.

Treatment-related toxicities, including cytokine release syndrome (CRS) and neurotoxicity from CAR-T cell therapy, can be particularly challenging to manage in elderly or frail patients, limiting the broader application of these therapies.

Finally, the high cost of emerging treatments, coupled with regulatory delays and restrictive reimbursement policies, limits timely and equitable access to potentially life-prolonging therapies.

Addressing these issues will require coordinated efforts to expand clinical trial inclusivity, improve access to innovative treatments, optimize toxicity management strategies, and reduce financial and systemic barriers to care.

4. DISCUSSION

Multiple myeloma (MM) remains a major hematologic malignancy with a rising global incidence, primarily driven by aging populations and improved diagnostic capabilities [4,9]. Higher prevalence among men and individuals of African ancestry is consistently reported, and the integration of genetic and environmental risk factors has enhanced modern risk stratification models [2]. Despite earlier detection, disparities in time to diagnosis and access to advanced therapies persist, particularly in resource-limited regions [34]. Molecular studies have significantly deepened our understanding of MM pathogenesis, confirming the heterogeneity of driver mutations, including KRAS, NRAS, TP53, and BRAF, and high-risk chromosomal abnormalities such as del(17p) and t(4;14) [7]. Single-cell RNA sequencing has revealed mechanisms of immune evasion, including checkpoint upregulation and suppression of natural killer cell activity [15], while dysregulated NF-κB, JAK/STAT, and PI3K/AKT/mTOR pathways play a central role in disease progression and resistance to therapy [15]. These findings underscore the value of molecular profiling for both prognostication and treatment selection.

Advances in diagnostics, particularly minimal residual disease (MRD) assessment using next-generation flow cytometry and sequencing, have redefined treatment endpoints [35]. Achieving MRD negativity correlates strongly with prolonged progression-free and overall survival, suggesting its potential as a surrogate endpoint for regulatory approval of new therapies. Emerging biomarkers, such as circulating tumor DNA and serum BCMA, offer promise for earlier detection and improved disease monitoring, especially in patients with non-secretory MM. On the therapeutic front, quadruplet regimens incorporating anti-CD38 antibodies have improved first-line outcomes in both transplant-eligible and -ineligible patients [7]. BCMA-directed CAR-T cell therapies, including idecabtagene vicleucel and ciltacabtagene autoleucel, have achieved deep responses in heavily pretreated populations, although durability, toxicity management, and manufacturing timelines remain challenges [26]. Bispecific antibodies such as teclistamab and elranatamab provide “off-the-shelf” alternatives with high response rates in triple-class refractory disease, while GPRC5D-targeted agents like talquetamab expand therapeutic options for patients relapsing after BCMA-directed therapy [29].

The integration of molecular diagnostics, MRD-guided monitoring, and novel immunotherapies is moving MM management toward a precision medicine paradigm, enabling risk-adapted treatment sequencing, earlier identification of resistance, and potentially shorter fixed-duration regimens for patients achieving sustained MRD negativity. Nonetheless, this review is based on a narrative synthesis, and heterogeneity in study designs, patient populations, and endpoints limits direct comparison of trial outcomes. Clinical trial cohorts often underrepresent older adults and patients with significant comorbidities, leading to possible differences between trial efficacy and real-world effectiveness. Additionally, access to innovative therapies remains uneven across regions due to geographic, socioeconomic, and regulatory constraints.

Addressing these issues will require strategies to overcome resistance and improve the durability of CAR-T and bispecific antibody responses. Standardization and wider adoption of MRD-guided treatment, expansion of equitable access through cost reduction and infrastructure development, and the integration of artificial intelligence with multi-omics profiling will be essential to refine prognosis and optimize therapy selection.

This review has several limitations. The included studies were heterogeneous in design, follow-up, and outcome definitions, which complicates direct comparison. Discrepancies between clinical trial data and real-world practice, as well as regional disparities in access to novel therapies, further limit generalizability. In addition, as this is a narrative review without a formal risk-of-bias assessment or quantitative meta-analysis, the analytical rigor is inherently reduced.

5. CONCLUSION

Multiple myeloma remains an incurable malignancy, but substantial advances in molecular diagnostics, MRD monitoring, and novel immunotherapies have markedly improved outcomes. Quadruplet frontline regimens, CAR-T cell therapy, and bispecific antibodies are reshaping treatment standards, while biomarkers such as ctDNA and sBCMA enhance disease monitoring. Future research should focus on optimizing therapy sequencing, managing long-term toxicities, and broadening access to innovative treatments to further improve survival and quality of life.

DISCLOSURE

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The authors deny any conflict of interest.

USE OF AI

Declaration of the use of generative AI and AI-assisted technologies in the writing process.

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