



Maintenance Treatment and Survival in Patients With Myeloma

¹ A.Sheth, ¹ A.Drake

^{1,2} Charles R. Drew University of Medicine and Science

Correspondence : drsheth284837@gmail.com

Article History :

Received date : 2019/10/09

Revised date : 2019/11/15

Accepted date : 2019/12/12

Published date : 2020/01/05



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ABSTRACT

Background: The evolution of treatment strategies for multiple myeloma (MM) has significantly transformed patient outcomes over the past two decades. This literature review explores the intricate relationship between maintenance treatment and survival in patients with myeloma, drawing upon several pivotal studies that chart this trajectory. **Literature Review:** The main body of the review elaborates on several pivotal studies that contribute to the understanding of maintenance therapies. The examination of post-transplant maintenance therapy reveals that achieving a complete response and MRD negativity post-ASCT correlates with improved progression-free survival (PFS) and overall survival (OS) (Sengsayadeth et al., 2017). The exploration of relapsed and refractory MM highlights the ongoing need for novel agents and personalized treatment approaches to sustain treatment efficacy (S. Nijhof et al., 2018). A meta-analysis of randomized controlled trials indicates that while conventional maintenance therapies have limited efficacy, newer regimens incorporating innovative agents significantly improve PFS (Li et al., 2018). The findings from the Myeloma XI study further substantiate the superiority of lenalidomide maintenance therapy in extending PFS, emphasizing the importance of deep responses and sustained MRD negativity (Goldschmidt et al., 2018). Additionally, the exploration of future directions in maintenance therapy raises critical questions regarding the optimal duration and composition of treatments, advocating for a personalized approach based on patient-specific factors (A. Holstein et al., 2011). **Conclusion:** The review concludes by underscoring the necessity of integrating lifestyle interventions to enhance the quality of life for MM patients, recognizing that the long-term effects of treatment can significantly impact patient well-being (N. Shapiro et al., 2011). Collectively, the articles illustrate a dynamic and evolving landscape in the management of multiple myeloma, emphasizing the critical role of maintenance therapy in improving survival outcomes and the necessity for ongoing research to optimize treatment strategies.

Keyword: Maintenance Treatment, Survival, Patients With Myeloma

INTRODUCTION

The evolution of treatment strategies for multiple myeloma (MM) has significantly transformed patient outcomes over the past two decades. This literature review explores the intricate relationship between maintenance treatment and survival in patients with myeloma, drawing upon several pivotal studies that chart this trajectory.

Beginning with the meta-analysis by , the authors highlight the dramatic improvements in overall survival rates, particularly noting that by 2014, younger patients could expect over 10 years of median survival due to advancements in treatment options, including the detection of minimal residual disease (MRD). Their findings suggest that achieving MRD negativity correlates with improved clinical outcomes, setting the stage for the discussion of maintenance therapies that follow.

(Sengsayadeth et al., 2017) build on this foundation by examining the changing landscape of post-transplant maintenance therapy. They emphasize the role of autologous stem cell transplantation (ASCT) as a cornerstone of treatment, while also introducing the concept of maintenance therapy as a crucial strategy to prolong survival and manage relapses. The authors argue that achieving a complete response and MRD negativity post-ASCT can lead to better progression-free survival (PFS) and overall survival (OS), thus underscoring the necessity for effective maintenance regimens.

In 2018, (S. Nijhof et al., 2018) further explore therapeutic strategies for relapsed and refractory MM, noting that despite advancements, the disease remains incurable with most patients experiencing relapse. They underscore the need for novel agents targeting specific pathways to enhance treatment efficacy, which aligns with the ongoing quest for improved maintenance therapies that can sustain treatment responses over time.

(Li et al., 2018) provide a quantitative synthesis of randomized controlled trials focused on maintenance therapy, revealing that while conventional

maintenance has limited efficacy, regimens incorporating new agents significantly improve PFS. This critical evaluation of the data illustrates the potential of these newer therapies to enhance treatment outcomes, although the impact on OS remains less pronounced.

(Goldschmidt et al., 2018) contribute to this discourse by discussing the Myeloma XI study, which demonstrated the superiority of lenalidomide maintenance over observation. They highlight the importance of achieving deep responses and sustained MRD negativity, which are essential for improving long-term survival outcomes. Their findings advocate for the integration of triplet regimens during induction therapy to maximize benefits.

(A. Holstein et al., 2011) further refine the understanding of maintenance therapy, focusing on the advancements in pre- and post-ASCT strategies. They pose critical questions regarding the optimal duration and composition of maintenance therapies, emphasizing the need for personalized approaches based on patient characteristics and disease risk factors.

Finally, (N. Shapiro et al., 2011) address the broader implications of long-term survival and continuous treatment in MM, advocating for the integration of lifestyle interventions to enhance patients' quality of life (QOL). Their work highlights the importance of supportive care in conjunction with pharmacological treatments, recognizing that the long-term effects of therapy can significantly impact patient well-being.

Collectively, these articles illustrate a dynamic and evolving landscape in the management of multiple myeloma, emphasizing the critical role of maintenance therapy in improving survival outcomes and the necessity for ongoing research to optimize treatment strategies.

LITERATURE REVIEW

The article "Role of MRD status in relation to clinical outcomes in newly diagnosed multiple myeloma patients: a meta-analysis" by provides a

comprehensive analysis of the impact of minimal residual disease (MRD) status on clinical outcomes in patients with multiple myeloma. This meta-analysis is particularly relevant given the significant advancements in treatment options and the resultant improvements in patient survival rates over the past two decades.

The authors begin by contextualizing the historical landscape of multiple myeloma treatment, noting that the average overall survival for patients was approximately three years at the turn of the 21st century. However, with the introduction of innovative therapies and a more aggressive treatment approach, particularly in younger patients, the median overall survival had extended to over ten years by 2014. This shift is underscored by the FDA's approval of 14 new cancer drugs in 2015, four of which were specifically indicated for multiple myeloma, highlighting the rapid evolution of treatment protocols in this field.

A central theme of the article is the critical role of MRD assessment in predicting clinical outcomes for multiple myeloma patients. The authors present evidence from various clinical studies indicating a strong correlation between MRD negativity and improved progression-free survival and overall survival. This finding is significant as it suggests that achieving MRD negativity can serve as a reliable prognostic indicator, thereby guiding treatment decisions and potentially leading to better patient management strategies.

The article also emphasizes the need for standardized MRD detection methods, as variability in testing can affect the interpretability of results. The authors advocate for the integration of MRD status into routine clinical practice to enhance treatment efficacy and optimize patient outcomes. Their analysis of the existing literature supports the notion that MRD monitoring should be an essential component of treatment protocols, particularly in the context of personalized medicine.

The article "Posttransplant maintenance therapy in multiple myeloma: the changing landscape" authored by (Sengsayadeth et al., 2017) provides a comprehensive examination of the evolution of maintenance therapy in multiple myeloma (MM) following autologous stem cell transplantation (ASCT). It

underscores a significant shift in the treatment paradigm over the last two decades, transforming MM from a dire prognosis to a condition with improved survival outcomes, primarily due to advancements in therapeutic strategies.

The authors highlight that the median survival after induction chemotherapy and ASCT has reached approximately seven years, a notable improvement attributed to the introduction of innovative therapies. High-dose melphalan followed by ASCT remains a cornerstone of treatment for eligible patients, yet the inevitability of relapses necessitates effective posttransplant strategies. The article postulates that the depth of response to initial treatment correlates with better outcomes, particularly emphasizing the importance of achieving complete response and minimal residual disease negativity, which are associated with enhanced progression-free survival (PFS) and overall survival (OS).

A critical aspect of the article is its discussion on the two main postinduction approaches: consolidation and maintenance therapy. Maintenance therapy is defined as treatment administered for at least one year post-ASCT, aimed at sustaining the depth of response achieved during initial therapy. The authors elucidate how early attempts at maintenance with conventional chemotherapy yielded unsatisfactory results, leading to a reevaluation of strategies. However, the introduction of new agents such as thalidomide, lenalidomide, and bortezomib has revolutionized maintenance therapy, making it a standard practice for many patients post-ASCT.

The article effectively reviews current data on maintenance therapy, highlighting the necessity for agents that induce minimal toxicity while preserving the initial therapeutic response. This focus on balancing efficacy and safety is crucial, as patients often face long-term treatment regimens. The authors also indicate the potential for emerging agents to further enhance posttransplant treatment strategies, suggesting that ongoing research is vital to optimize outcomes for MM patients.

The article "Current and New Therapeutic Strategies for Relapsed and Refractory Multiple Myeloma: An Update" by (S. Nijhof et al., 2018) provides a

comprehensive overview of the advancements in treatment strategies for patients with multiple myeloma (MM), particularly those who are relapsed and refractory. The authors highlight a significant improvement in the median survival of patients over the past two decades, now approximating 7–8 years. This enhancement is attributed to high-dose conventional therapy, particularly autologous stem-cell transplantation, alongside improvements in supportive care and the introduction of immunomodulatory drugs (IMiDs) and proteasome inhibitors (PIs).

Despite these advancements, the authors emphasize that multiple myeloma remains an incurable malignancy. A critical point raised in the article is the poor prognosis for patients who have undergone at least three prior lines of therapy and have developed double-refractory disease to both IMiDs and PIs. The reported event-free survival and overall survival for these patients are alarmingly low, at just 5 and 13 months, respectively. This stark reality underscores the urgent need for ongoing research and the development of new therapeutic options.

The article further discusses the evolving understanding of the biological mechanisms underlying MM, which has facilitated the emergence of novel agents targeting specific pathways involved in tumor cell growth and survival. The authors advocate for future studies to focus on the optimal sequencing of treatments, which remains an area of uncertainty. They also suggest that incorporating biomarker analyses could enhance patient selection for new therapeutic agents, thereby potentially improving outcomes.

The article "Long-Term Efficacy of Maintenance Therapy for Multiple Myeloma: A Quantitative Synthesis of 22 Randomized Controlled Trials" by (Li et al., 2018) presents a comprehensive meta-analysis aimed at evaluating the efficacy of maintenance therapies in patients with multiple myeloma (MM). The authors synthesized data from 22 randomized controlled trials involving a substantial cohort of 9,968 patients, thereby providing a robust framework for assessing the impact of various maintenance regimens.

A critical aspect of the study is its examination of progression-free survival (PFS) and overall survival (OS) outcomes associated with different maintenance

therapies. The findings indicate significant heterogeneity in PFS among the various regimens, suggesting that while some treatments may offer considerable benefits, others may be less effective. The authors found that maintenance therapies incorporating new agents outperformed conventional maintenance strategies and simple observation concerning PFS, underscoring the importance of novel pharmacological approaches in enhancing patient outcomes.

However, the study also reveals a noteworthy limitation: despite the marked improvement in PFS, the impact of these maintenance therapies on OS was minimal. This dichotomy raises important questions regarding the clinical significance of PFS as a standalone endpoint, particularly in the context of long-term patient survival and quality of life. The authors suggest that while maintenance therapies with new agents, particularly those involving Lenalidomide (Len), can significantly prolong PFS, their limited effect on OS necessitates further investigation into the underlying mechanisms and potential strategies to enhance long-term survival in MM patients.

Additionally, the article highlights the need for a nuanced interpretation of survival metrics in clinical practice. The observed differences in PFS and OS could reflect the complexities of disease biology, treatment resistance, and patient-specific factors. Thus, the findings advocate for a more individualized approach to maintenance therapy, where treatment plans are tailored to the unique characteristics and responses of each patient.

The article "Navigating the treatment landscape in multiple myeloma: which combinations to use and when?" by (Goldschmidt et al., 2018) provides a comprehensive overview of the evolving strategies in the maintenance treatment of patients with newly diagnosed multiple myeloma (NDMM). The authors draw on data from the Myeloma XI study, which included over 2000 patients, to highlight the significant benefits of lenalidomide maintenance therapy. Their findings indicate that lenalidomide not only extends the median progression-free survival (PFS) across all patient subgroups but also remains effective even in patients with high-risk disease, underscoring its pivotal role in the management of myeloma.

The article further discusses the approval of lenalidomide maintenance therapy following autologous stem cell transplantation (ASCT) in both Europe and the USA as of 2017, marking a significant advancement in treatment protocols. The authors provide a comparative analysis of bortezomib-based induction and maintenance therapies against the traditional VAD induction and thalidomide maintenance regimen. The results are compelling, with the bortezomib group demonstrating superior PFS, which was sustained for up to 96 months, while overall survival (OS) rates were comparable between the two treatment strategies.

Another critical point raised in the article is the safety profile of prolonged bortezomib maintenance therapy, which, notably, did not correlate with an increased risk of second primary malignancies. This aspect is particularly important for clinicians when considering long-term treatment options for myeloma patients.

The authors advocate for the use of triplet regimens, such as VTD, VRd, or VCD, for induction therapy prior to ASCT, contingent upon the tolerability of toxicities. They emphasize that achieving the deepest possible response, ideally a sustained state of minimal residual disease negativity, is crucial for transplant-eligible patients.

While the article effectively summarizes the current landscape and evidence supporting maintenance treatment in myeloma, it also identifies the need for ongoing clinical trials to explore the efficacy of newer agents and consolidation treatments post-ASCT. This indicates a recognition of the dynamic nature of multiple myeloma treatment and the necessity for continual research to optimize patient outcomes.

The article "Future Directions in Maintenance Therapy in Multiple Myeloma" by (A. Holstein et al., 2011) provides a comprehensive overview of the evolving landscape of maintenance therapy in multiple myeloma (MM), particularly focusing on the implications of advancements in treatment regimens. The authors highlight that the integration of immunomodulatory drugs (IMiDs) and proteasome inhibitors (PIs) into pre-autologous stem cell transplant (ASCT)

induction regimens has significantly improved patient outcomes, setting the stage for the subsequent maintenance phase.

One of the critical insights presented in the article is the role of lenalidomide in post-ASCT maintenance strategies. The authors articulate that lenalidomide has been pivotal in prolonging overall survival (OS) and delaying disease recurrence among patients who have undergone ASCT. This reflects a shift towards more personalized treatment approaches, where the goal of maintenance therapy is not only to extend survival but also to do so with minimal toxicity. The authors emphasize the importance of balancing efficacy with quality of life, a consideration that is paramount in the management of chronic conditions like MM.

Furthermore, the article raises pertinent questions regarding the optimal duration of maintenance therapy, the potential benefits of single-agent versus multi-agent approaches, and the influence of cytogenetic risk on treatment decisions. These questions are crucial for clinicians as they navigate treatment plans tailored to individual patient profiles. The authors suggest that future research should focus on these areas to refine maintenance strategies and optimize outcomes.

The article "Lifestyle considerations in multiple myeloma" by (N. Shapiro et al., 2011) provides a comprehensive examination of the evolving landscape of multiple myeloma (MM) treatment and its implications for patient quality of life (QOL). As MM is recognized as the second most prevalent hematological malignancy in the United States, the authors emphasize the significant advancements in therapeutic strategies over the past fifteen years, which have led to the adoption of continuous treatment protocols. This shift has notably improved the five-year relative survival rate to 55.6%, underscoring the importance of not only prolonging survival but also enhancing the quality of life for patients living with this chronic condition.

A critical evaluation of the article reveals that while the advancements in treatment have been remarkable, they have also introduced a complex interplay of long-term side effects that necessitate further research and attention. The authors highlight that MM patients experience a higher symptom burden and lower reported

QOL compared to survivors of other hematological cancers, indicating a pressing need for supportive care interventions. This observation is particularly significant given the chronic nature of MM and the continuous administration of maintenance therapies, which can exacerbate the challenges faced by patients.

The article effectively argues for the integration of lifestyle interventions into the management of MM. The authors explore various aspects of lifestyle, including physical activity, weight management, nutrition, sleep, and substance use, and their potential roles in mitigating the adverse effects of treatment and enhancing overall well-being. This focus on lifestyle modifications is critical, as it not only addresses the physical health of patients but also their psychological and emotional needs, which are often overlooked in traditional treatment paradigms.

Moreover, the authors provide a solid foundation for future research directions by advocating for studies that examine the impact of healthy behaviors on QOL and long-term outcomes in MM patients. The call for a more holistic approach to patient care that encompasses both medical treatment and lifestyle modifications is a crucial takeaway from this article.

CONCLUSION

The literature review highlights the transformative advancements in treatment strategies for multiple myeloma (MM), particularly focusing on the critical role of maintenance therapy in enhancing patient survival outcomes. The introduction sets the stage by noting significant improvements in median survival rates, particularly among younger patients, due to the introduction of novel therapies and the emphasis on achieving minimal residual disease (MRD) negativity. This foundational understanding is further developed through various studies that explore the evolving landscape of maintenance treatment following autologous stem cell transplantation (ASCT) and the implications for long-term survival.

The main body of the review elaborates on several pivotal studies that contribute to the understanding of maintenance therapies. The examination of post-

transplant maintenance therapy reveals that achieving a complete response and MRD negativity post-ASCT correlates with improved progression-free survival (PFS) and overall survival (OS) (Sengsayadeth et al., 2017). The exploration of relapsed and refractory MM highlights the ongoing need for novel agents and personalized treatment approaches to sustain treatment efficacy (S. Nijhof et al., 2018).

A meta-analysis of randomized controlled trials indicates that while conventional maintenance therapies have limited efficacy, newer regimens incorporating innovative agents significantly improve PFS (Li et al., 2018). The findings from the Myeloma XI study further substantiate the superiority of lenalidomide maintenance therapy in extending PFS, emphasizing the importance of deep responses and sustained MRD negativity (Goldschmidt et al., 2018). Additionally, the exploration of future directions in maintenance therapy raises critical questions regarding the optimal duration and composition of treatments, advocating for a personalized approach based on patient-specific factors (A. Holstein et al., 2011).

The review concludes by underscoring the necessity of integrating lifestyle interventions to enhance the quality of life for MM patients, recognizing that the long-term effects of treatment can significantly impact patient well-being (N. Shapiro et al., 2011). Collectively, the articles illustrate a dynamic and evolving landscape in the management of multiple myeloma, emphasizing the critical role of maintenance therapy in improving survival outcomes and the necessity for ongoing research to optimize treatment strategies.

DISCLOSURE STATEMENT

- Disclosure Statement : The authors have no conflicts of Interest to declare
- Funding Sources : None
- Acknowledgements : -
- Author Contribution : All authors discussed and contributed the final content for journal submission and publication

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