Review

Identifying Professional Education Gaps and Barriers in Multiple Myeloma Patient Care: Findings of the *Managing Myeloma* Continuing Educational Initiative Advisory Committee

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Abstract

Advances in the past decade and a half have led to unprecedented improved outcomes for patients with multiple myeloma (MM), and this disease appears to be transitioning to one more characteristic of a chronic disease in large part due to rapid translation of clinical insights into practice at the community level. Although evidence-based guidelines and consensus recommendations remain an important resource for managing cancer patients, they do not fill the gap between the principles of disease management today and the translation of tailoring treatment for individual patient needs. Thus, there is a continuing need for concise, focused educational activities and resources that facilitate improved knowledge and understanding of appropriate, individualized therapeutic strategies for assessing and caring for patients with MM. The next several years will truly be a time of shifting paradigms in the treatment of MM in which new agents will be approved, response criteria will be updated, and new approaches to risk assessment and monitoring minimal residual disease will evolve and enter practice. New groundbreaking therapeutic approaches, such as immunotherapy, might result in significant changes in how MM is treated and managed over the entire life cycle of the disease. Even the definition of the disease might be further amended as insights grow regarding who should be treated and who might benefit more from observation. As such, oncology clinicians will have to carefully review and update their management approaches accordingly even as they begin to focus even more on the survivorship needs of their MM patients.

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Introduction: Where Are We Now?

A Rapidly Changing Treatment Landscape

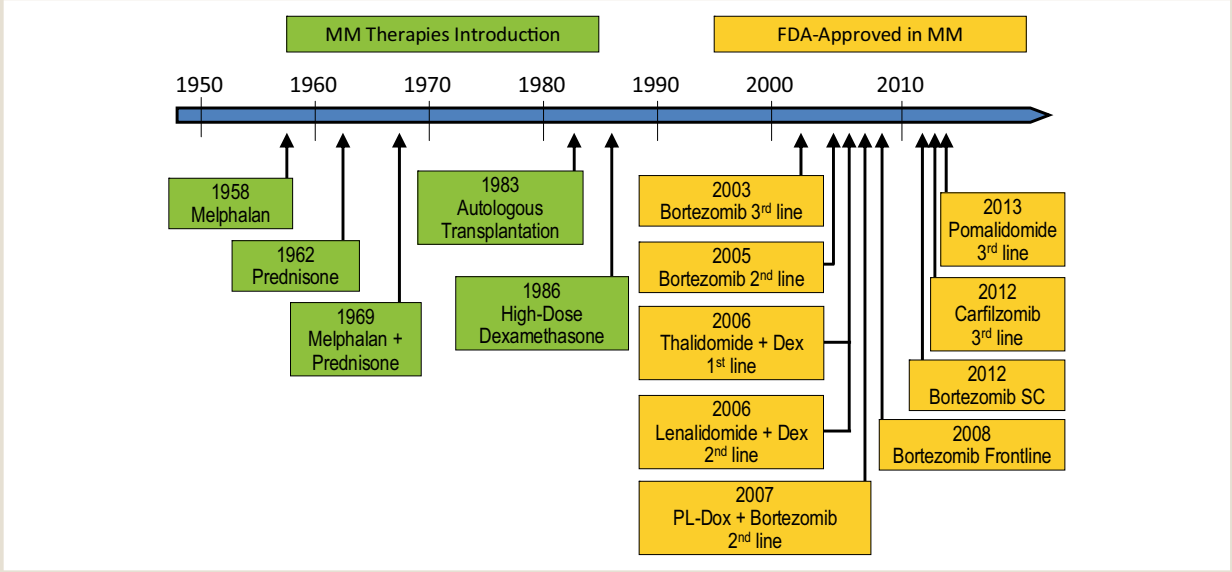
The treatment of multiple myeloma (MM) has changed dramatically within the past 15 years beginning with the introduction of the first novel agent into practice. Thalidomide saw widespread off-label use for MM in response to the initial results of the Arkansas study, which were confirmed by many other centers in all phases of the disease life cycle.[1-3] Treatment options continued to expand dramatically in the immediate years that followed, beginning with the approvals by the Food and Drug Administration (FDA) of bortezomib, thalidomide (with dexamethasone), lenalidomide (with dexamethasone), and pegylated liposomal doxorubicin (with bortezomib). Indeed, at the time of the publication of the highlights of the first annual National Comprehensive Cancer Network (NCCN) hematologic malignancies congress in 2006, it was noted that, "A 'dazzling array' of agents in combination represents a new treatment paradigm in MM," in a commentary addressing the progress made in primary therapy options as a consequence of a growing understanding of cellular mechanisms, proteins, and key signal transduction factors associated with this disease.[4] The pace of new drug approvals accelerated in the past 2 years, starting with FDA approval of subcutaneous administration of bortezomib and carfilzomib in 2012 followed by pomalidomide in 2013 (Figure 1). Additional novel agents are currently being investigated for use as single agents or in combination based on the scientific developments and clinical experiences to date.[5] As clinical experience with approved agents and clinical trials data mature, the treatment paradigm for MM will continue to evolve with what is expected to be a continued and steady pace. The *Managing Myeloma* Continuing Educational Initiative Advisory Committee met in February 2013 to identify current professional educational gaps in MM and barriers to care. In addition, there was a discussion of how the treatment paradigm will continue to change within the next 2 to 5 years and how these changes will affect future educational needs. The findings were subsequently reviewed for publication in the latter part of 2013. This white paper presents the findings and opinions of the committee.

Significantly Improved Survival

Although MM remains incurable, considerable progress has been made in extending survival.[6-15] Increased use and optimization of high-dose therapy (HDT) with autologous stem cell transplant (ASCT) support[16-18] was largely responsible for the trend in improved survival noted just up to the turn of the new millennium (Figure 2).[14] However, the significant increase in life expectancy seen in the past decade is attributed to the rapid and early incorporation of novel agents[14,19,20] including thalidomide,[2] bortezomib,[9,21] and lenalidomide[8,22] into treatment protocols in conjunction with improvements in supportive care.[23-25]

Landmark data from the Mayo Clinic[14] showed significantly improved median overall survival from time of relapse in patients whose disease relapsed after 2000 compared with those whose disease relapsed before that date (23.9 vs. 11.8 months; $P < .001$), and patients treated with one or more novel agents had significantly longer survival from time of relapse (30.9 vs. 14.8 months; $P < .001$). Similarly, at the Vancouver Hospital, the availability of lenalidomide- or bortezomib-based therapy for relapse after transplant doubled overall survival for patients with late relapse and tripled survival in patients with early relapse over that seen with patients treated before the introduction of novel agents.[19] Perhaps more importantly, the Mayo data showed that patients diagnosed after 2000 had experienced a 50% improvement in overall survival over that in the previous 2 decades (44.8 vs. 29.9 months; $P < .001$), suggesting that the use of novel therapies improves the

Figure 1 Multiple Myeloma (MM) Therapy Introduction Timeline



Abbreviations: FDA = Food and Drug Administration; PL-Dox=pegylated liposomal doxorubicin; SC = Subcutaneous.