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EDITORIAL

Advances in current treatment for patients with newly diagnosed multiple myeloma

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INTRODUCTION

Multiple myeloma (MM) is a hematologic malignancy characterized by the proliferation of monoclonal plasma cells at multiple sites in the bone marrow, with accompanying alterations in the bone marrow microenvironment, and suppression of the host antitumor immune response, resulting in the uncontrolled accumulation of malignant plasma cells and excess secretion of immunoglobulins (paraproteins). MM, in almost all cases, is preceded by a premalignant phase, monoclonal gammopathy of undetermined significance (MGUS).[1] MGUS is present in ~3% of the population aged >50 years and progresses through asymptomatic smoldering myeloma to symptomatic MM at a rate of 1% annually.[2] MM is usually diagnosed when the disease becomes symptomatic, classically presenting with bone pain, anemia, renal insufficiency, hypercalcemia and recurrent infections due to immune deficiency. MM has an annual age-adjusted incidence of 5.8 cases per 100 000 of the population and predominantly affects older individuals; the median age at diagnosis is 69 years.[3,4]

MM is an incurable disease and the survival prognosis for patients diagnosed with MM has historically been poor. The introduction of high-dose chemotherapy (HDT) followed by autologous stem cell transplantation (ASCT) in the 1980s improved response rates and progression-free survival (PFS), but median overall survival (OS) remained at <3 years throughout the 1990s.[5] However, treatment options for patients with newly diagnosed MM (NDMM) have increased during the past decade with the introduction of novel therapies using thalidomide, lenalidomide and bortezomib. As a consequence, survival outcomes for patients with NDMM have greatly improved.[6,7] An analysis of survival trends in a large cohort in the United States identified that patients treated with one of the novel agents had significantly better OS and better survival time from relapse compared with patients who received conventional treatments.[6] Patients aged <65 years at diagnosis now have a median survival time of 56 months; however, outcomes remain poor in NDMM patients aged >65 years for whom OS is only 26 months.[8] The treatment of MM in elderly patients remains a clinical challenge—they are usually ineligible for stem cell transplantation and are unable to tolerate the toxicity of intense chemotherapy. Besides age at diagnosis and disease stage, prognosis is also adversely affected by the presence of several 'high-risk' genetic markers, including deletions of chromosome 13, hypodiploidy and deletions of chromosome 17p, t(4;14) or t(14;16).[2]

Significant improvements in response rates, PFS and OS have been seen in patients with NDMM treated with combination regimens based on immunomodulatory drugs (thalidomide and lenalidomide) and proteasome inhibitors (bortezomib).[9–16] These advances, coupled with an improved understanding of the disease, have shifted the treatment paradigm in MM. The current aim of this therapy for patients with NDMM is to achieve deep and long-term clinical remissions with early and continued use of regimens that are effective and safe to maintain disease control and extend OS.

The purpose of this supplement is to review current approaches to the treatment of NDMM, providing an update on the most recent developments and treatment regimens involving the novel therapies, and highlighting the key issues that clinicians face when devising a long-term management strategy for NDMM patients. In the first article, Drs Munshi and Girnius provide an overview of the current approaches related to the diagnosis and management of MGUS, smoldering MM and MM, highlighting the need for a long-term approach to optimize disease control and the importance of a risk-stratified approach to treatment. In the second article, Drs Giralt and Bensinger discuss the role of ASCT and the role of novel therapies in induction treatment. The question of how to optimize the response to ASCT using consolidation therapy with novel agents is then addressed by Drs Moreau and Touzeau, including a review of recent clinical evidence showing the benefit of post-transplantation maintenance treatment with novel agents to extend PFS. Finally, Professor San Miguel and Dr Mateos provide an overview of the treatment options available for NDMM patients ineligible for HDT–ASCT because of either advanced age or comorbid conditions. Again, the focus is on the way in which the novel therapies have transformed the treatment options available to this population, who represent the majority of NDMM patients. In this setting, early and continued treatment with novel agents appears to have the potential to extend survival times for elderly and frail patients for whom outcomes have remained poor.

Collectively, these articles illustrate how the introduction of novel agents, such as lenalidomide and bortezomib, has transformed the approach to treatment of NDMM and has provided a valuable clinical update for those working in this field.

CONFLICT OF INTEREST

SL is a consultant for Millennium, Celgene Corporation, Novartis, Merck, Bristol-Myers Squibb, Onyx and Johnson & Johnson, with honoraria.

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