blood® Editorial

Introduction to a How I Treat series on plasma cell dyscrasias

The aim of this How I Treat series is to propose updates to the management of plasma cell dyscrasias in the era of anti-CD38 monoclonal antibodies. During the last 20 years, the prognosis of patients diagnosed with these entities, and especially multiple myeloma, has been totally changed because of the availability of new drugs with novel mechanisms of action. However, many challenges remain, such as the management of high-risk myeloma or stage 3B amyloid light-chain (AL) amyloidosis. The following 4 papers each summarize current knowledge on a key topic and provide guidance to physicians in the therapeutic management of these patients.

- Aurore Perrot: "How I treat frontline transplantation-eligible multiple myeloma"
- Elena Zamagni, Simona Barbato, and Michele Cavo: "How I treat high-risk multiple myeloma"
- Efstathios Kastritis, Evangelos Terpos, and Meletios A. Dimopoulos: "How I treat relapsed multiple myeloma"
- Giovanni Palladini and Giampaolo Merlini: "How I treat AL amyloidosis"

Perrot deals with the treatment of standard risk transplant-eligible patients with multiple myeloma at diagnosis. For 25 years, autologous stem cell transplantation has been the standard of care for patients eligible (ie, patients under the age of 70 years with low comorbidities). The current strategy is to use a quadruplet induction, combining an anti-CD38 antibody, a proteasome inhibitor, an immunomodulatory drug, and dexamethasone, and maintenance with lenalidomide. The optimal goal of this strategy is no longer simple achievement of complete remission but obtainment of deep minimal residual disease (MRD) negativity. With the availability of such effective combinations, an ongoing question is whether transplant should remain the standard in the future.

Zamagni et al address the difficult situation of high-risk newly diagnosed patients with multiple myeloma, transplant eligible or not. High risk is mainly defined by cytogenetics, but other conditions such as primary plasma cell leukemia or extramedullary disease also fall into this category. Furthermore, the current cytogenetic definition of high risk is probably not optimal, and a consensus definition requires updating. Regardless, these patients have a high unmet need. Although tandem transplant could be an option for eligible patients, management of older patients is difficult. For this category of patients (about 15% to 20% of total patients), achievement of MRD negativity is probably crucial if longer survival is to be obtained.

Kastritis et al propose strategies for the most common clinical state: patients with multiple myeloma that has relapsed. With the use of quadruplet therapy frontline and a long maintenance with lenalidomide, many patients are thus lenalidomide resistant at relapse. The main question is whether myeloma in those patients is also resistant to antibodies and proteasome inhibitors. If not, these drugs can be used at relapse, with various responses. This highlights the need for novel therapies with different mechanisms of action. High hopes are being placed in novel immunotherapies for these patients.

Palladini and Merlini outline the current management of AL amyloidosis. This condition is unusual as the malignant clone is usually small, but the biochemical properties of the immunoglobulin light chain lead to a devastating disease, particularly in cases with heart involvement. In contrast to multiple myeloma, AL amyloidosis requires an early diagnosis and a close evaluation of response to adapt treatment from as early as the second course of treatment. Here again, anti-CD38 monoclonal antibodies are significantly improving the outcome for patients. Indeed, in contrast to multiple myeloma, many patients are currently being cured.

I hope that this series will help physicians optimize management of their current patients. The development of best therapy will definitely not stop with these recommendations. The preliminary results for immunotherapies, such as chimeric antigen receptor T cells and/or bispecific antibodies (or T-cell engagers), are very exciting. Immunotherapy will probably be the next revolution in treatment for plasma cell malignancies. A novel How I Treat series will probably be necessary in the next few years.

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