

# Is There More to Myeloma Than the Plasma Cell?

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**W**e don't treat disease, we treat patients." Perhaps in no disease more than multiple myeloma is it true that we have to treat the whole patient. It is true that stem cell transplant remains the cornerstone of therapy in eligible patients. However, there is more to myeloma therapy than just attacking the plasma cell. This year's Education Session on Multiple Myeloma made us all realize the wide scope of caring for patients with this disease.

Despite the overwhelming evidence for survival benefit of high-dose therapy in myeloma, many patients are simply not candidates for transplant, or do not wish to undergo transplant. For decades, this large group of patients was most commonly treated with melphalan and prednisone. In this session, Dr. Robert Orłowski introduced a new way of initially treating patients who are not eligible for transplant. He reviewed the data for the use of MPT (melphalan-prednisone-thalidomide), demonstrating its progression-free and overall survival benefit over MP. Newer combinations such as MP-lenalidomide, MP-bortezomib, and thalidomide-dexamethasone-doxorubicin were also reviewed with encouraging results. "We conclude, therefore, that MP is no longer the standard of care," said Dr. Orłowski. Furthermore, he emphasized that not all "non-transplant" patients are the same — further risk stratification based on age, cytogenetics, albumin, and beta-2 microglobulin will influence the choice of therapy in these patients.

Dr. Jeffrey Zonder discussed the thrombotic complications of myeloma, both from the disease itself and from its therapy. Even untreated, there is a high malignancy-associated risk of thrombosis in patients with myeloma, due to various genetic, biologic, and clinical factors. This is further exacerbated when patients are treated, especially with dexamethasone-based regimens. However, the greatest risk seems to be in patients treated with novel agents such as thalidomide and lenalidomide.

Why is this? What is the clinician to do to reduce the risk? Dr. Zonder addressed these questions head on by providing helpful, practical advice. He reminded us of the complex network of immunomodulatory drugs and the proposed mechanisms of thrombosis generation at a molecular level. Initial studies have demonstrated that low-dose warfarin therapy does not seem to adequately reduce the risk of thrombosis, whereas full-dose anticoagulation does. A complicating feature is the benefit observed from aspirin therapy — although one may not intuitively think aspirin may be of benefit, some studies have validated its use. Finally, the use of low-molecular-weight heparins (LMWH) was reviewed. It appears that when LMWH is used as full dose, patients have lower incidence of thrombosis. However, whether or not LMWH should be "standard prophylaxis" remains unclear. Dr. Zonder emphasized that patients undergoing these therapies require careful assessment, close monitoring, and some form of anticoagulation.

Finally, Dr. Bhoomi Mehrotra discussed side effects of bisphosphonates, which have been incorporated into myeloma treatment for almost ten years. Now, most patients with myeloma, even if they have moderate renal insufficiency, are treated with a bisphosphonate. Although this is based on solid evidence, an emerging complication of this therapy has dampened enthusiasm for these medications — osteonecrosis of the jaw (ONJ). The incidence of this complication is not fully known, but reports range from 1.8 to 12.8 percent, and seem to increase with time on therapy. Dr. Mehrotra reviewed the possible mechanisms of this condition, including the most significant predisposing factor, dental trauma; unfortunately, there is still no clear and validated definition of ONJ, but efforts are underway to standardize its classification and staging. He went on to provide practical tips to manage ONJ, including stage-specific cleansing techniques, dental interventions, and antibiotic use. Among his recommendations were careful dental assessment prior to the use of bisphosphonate therapy, the avoidance of invasive dental procedures while on bisphosphonates, and rapid attention to jaw pain, the hallmark symptom of ONJ. Dr. Mehrotra concluded by addressing the issue of renal insufficiency and reminded the audience of the need to monitor renal function and alter therapy if it worsens.

This Education Session emphasized that there is more to myeloma than the plasma cell. If we include the whole patient in therapeutic plans, the results will include improved survival and enhanced quality of life.