From Under the Microscope

Multiple Myeloma

Multiple myeloma is a plasma cell neoplasia, which accounts for more than 10% of all hematological malignancies and 1.4 percent of new cancer cases in this country each year. While the disease is incurable, it can be treated. The current five-year survival rate of people with multiple myeloma is 47%.

Multiple myeloma is characterized by clonal proliferation of plasma cells in the bone marrow microenvironment and subsequent organ damage. The WHO 2008 criteria of diagnosis of multiple myeloma requires 10% or more clonal plasma cells on bone marrow examination or a biopsy proven plasmacytoma plus evidence of associated end-organ damage (known by the acronym CRAB, which stands for: increased calcium; renal insufficiency; anemia and bone lesions).

In 2014, the International Myeloma Working Group (IMWG) updated their guidelines.The new guidelines try to identify a group of patients who have a risk of progression to symptomatic myeloma within 2 years of 80% or greater. There are three differences or additions to the previous CRAB criteria to fit those new definitions. The first is, if the patients have greater than 60% plasma cells in the bone marrow, there is an 80% risk that the patients are going to progress to myeloma within 2 years. The second is the patients with a free light chain ratio greater than a 100 or less than 0.01 who also have a greater than 80% risk of progression within 2 years. The third is that the patient has greater than one focal bone lesion by MRI. If the patients have two of these, then the risk of progression to myeloma is greater than 80%, those patients are considered to be symptomatic.

Over the last decade, the treatment of multiple myeloma has been rapidly evolving. Historically, the treatment and thought process for patients with symptomatic myeloma has been "first do no harm," and so the definition of patients with symptomatic myeloma has been limited to the patients who clearly have evidence of end-organ damage. What you are seeing in the revised guidelines is an attempt by the myeloma community to begin to try and get ahead of the problem, anticipate some of these patients who we know are at very high risk, and intervene early. The new guidelines from IMWG really tried to identify a group of patients with very high risk, what we call ultra-high-risk smoldering. So that, the idea was not to make it more complicated for who take care of patients, but really to try and say these are patients you should probably go ahead and embark on therapy early.

Currently, cytogenetic analysis plays a very important role in the management of multiple myeloma. In the absence of concurrent trisomies, patients with 17p deletion, t(14;16), and t(14;20) are considered to have high-risk to progress to myeloma. Patients with t(4;14) translocation are considered intermediate-risk. All others are considered as standard-risk. Standard-risk patients can be treated with lenalidomide plus low-dose dexamethasone, or a bortezomib-containing triplet such as bortezomib, cyclophosphamide, dexamethasone. Intermediate-risk and high-risk patients require a bortezomib-based triplet regimen. In eligible patients, initial therapy is given for approximately 4 months followed by autologous stem cell transplantation (ASCT).

New therapies for multiple myeloma have dramatically improved life expectancy. Thus far, monoclonal antibodies, immunotherapy, histone deacetylase inhibitors, and the new proteasome inhibitor ixazomib show promise. Investigators are in hot pursuit of new therapies that will extend remissions and improve survival. It is an exciting and very promising time to treat myeloma patients with unprecedented outcomes!

Reference:Am J Hematol. 2014 Oct;89(10):999-1009, http://www.managingmyeloma.com, Lancet Oncology, 2014, volume 15, No.12: e538-548

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