Managing Myeloma

Efficacy of Ixazomib Maintenance in Myeloma Patients

Shaji K. Kumar, MD
Professor of Medicine
Mayo Clinic College of Medicine
Consultant, Division of Hematology
Medical Director, Cancer Clinical Research Office
Mayo Clinic
Rochester, Minnesota

Welcome to *Managing Myeloma*. My name is Shaji Kumar. I am a Consultant in Hematology at Mayo Clinic in Rochester, Minnesota. Today, I will be reviewing the results of the data that looked at the deep and durable responses with weekly ixazomib, lenalidomide, and dexamethasone in patients with newly diagnosed multiple myeloma, a long-term followup of patients who did not undergo stem cell transplant.

The combination of a proteosome inhibitor and immunomodulatory drug is one of the current standards of care for patients with newly diagnosed multiple myeloma. Bortezomib in combination with lenalidomide was studied in a phase 3 trial comparing it to lenalidomide in patients with newly diagnosed multiple myeloma. It was shown that the combination of the proteosome inhibitor and immunomodulatory drug not only improved the progression-free survival, but also improved overall survival in newly diagnosed multiple myeloma.

Ixazomib is the first oral proteosome inhibitor to be introduced in the clinic and, in combination with lenalidomide and dexamethasone, has proven to be an effective regimen in patients with relapsed myeloma. This particular phase 2 study was the initial study to look at this combination in newly diagnosed multiple myeloma. Overall, 65 patients were enrolled in this phase 1/2 study. In the initial part of the study, dose escalation of ixazomib was performed in combination with lenalidomide and dexamethasone used at standard doses. Ixazomib was given orally once weekly for 3 weeks with 1 week off, and lenalidomide was given daily for 3 weeks with 1 week off, along with weekly doses of dexamethasone. Patients were allowed to collect stem cells after 3 cycles of therapy and proceed to stem cell transplant after 6 cycles, if they so desired. The overall results of the study had previously been published. We found that the regimen was quite effective in the initial therapy of previously untreated multiple myeloma.

This particular analysis is looking at the group of patients who did not go to a stem cell transplant, but continued on therapy often with maintenance using ixazomib. The study was designed to look at ixazomib maintenance as a single agent after completing 12 cycles of induction therapy with the combination. What we found was, among the 42 patients who did not go to a stem cell transplant, the overall response rate was 88%. In this group of patients, 25 of the 42 patients actually continued on maintenance therapy with single-agent lenalidomide. In those patients, the depth of response continued to

deepen on single-agent ixazomib, with 8 out of those 25 patients having deepening responses. The vast majority of these patients went on from a very good partial response (VGPR) to obtain a complete response (or a stringent complete response) with single-agent ixazomib.

Overall, the trial results essentially tells us two things. One, the combination of ixazomib, lenalidomide, and dexamethasone provides an attractive all-oral regimen for newly diagnosed myeloma that can be continued as a maintenance regimen, with ixazomib alone given on a weekly basis. The toxicity is manageable. In fact, among the patients who continued on maintenance therapy with ixazomib, emergence of new grade 3 toxicity occurred in very few patients. No patients discontinued therapy due to adverse events during the maintenance phase of the study. The key point again is that this particular triplet regimen, which is all-oral and convenient, is an effective regimen that can be continued for a long period of time in patients who do not go to a stem cell transplant, with continued improvement in the response rate. Clearly, this is a regimen that needs to be studied further. There is a phase 3 trial that has completed accrual and we are awaiting the results. Now, this also provides an attractive platform for combining it with other treatments, especially monoclonal antibodies. Right now, there are phase 2 studies that are looking at combining daratumumab with the combination of ixazomib, lenalidomide, and dexamethasone, thus maximizing the benefit of an all-oral regimen but also incorporating the efficacy of a new generation of agents like monoclonal antibodies. Thank you for viewing this activity.