Managing Myeloma

Phase 2 Trial of Ixazomib, Lenalidomide, Dexamethasone and Daratumumab in Patients with Newly Diagnosed Multiple Myeloma

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Welcome to *Managing Myeloma*. I am Dr. Shaji Kumar and I am live at the 60th ASH Conference in San Diego, California. Today, I will be reviewing the data that I presented for the Phase II trial of ixazomib, lenalidomide, dexamethasone, and daratumumab in patients with newly-diagnosed multiple myeloma.

The treatment approach to newly-diagnosed myeloma has significantly changed over the past few years with the introduction of several new drugs, including new drug classes such as monoclonal antibodies. Previous studies have clearly demonstrated that a triplet containing a proteasome inhibitor and then immunomodulatory drug along with dexamethasone significantly improves overall survival in patients with newly-diagnosed myeloma compared to a doublet.

The current standard of care for the initial therapy of a patient with newly-diagnosed myeloma is a combination of bortezomib, lenalidomide, and dexamethasone. Ongoing trials are looking at the combination of carfilzomib, lenalidomide, and dexamethasone, comparing this to bortezomib, lenalidomide, and dexamethasone. With the introduction of the monoclonal antibodies and its demonstration of its efficacy in a variety of different triplet regimens, there has been intense interest in adding the monoclonal antibodies to the initial therapy of multiple myeloma. This has taken two forms. One is combining the monoclonal antibody with an immunomodulatory drug, so combinations of daratumumab with lenalidomide-dexamethasone, and elotuzumab with lenalidomide-dexamethasone. Both are being studied in Phase III trials. At this ASH, we will be hearing the results of the daratumumab, lenalidomide, and dexamethasone.

We have previously shown that the ixazomib-lenalidomide-dexamethasone is an effective triplet for management of multiple myeloma. We wanted to examine if adding the monoclonal antibody to a triplet would be a better approach in patients with newly-diagnosed myeloma to examine the efficacy of this quadruplet regimen. This is consistent with what is happening in the field, where there are several clinical trials that are ongoing looking at combining daratumumab with triplets that are currently in use. We already have results from the ALCYONE trial which looked at adding daratumumab to bortezomib, melphalan, and prednisone demonstrating an improved progression-free survival. There are early results from the CASSIOPEIA trial that added daratumumab to bortezomib, thalidomide, and dexamethasone, showing an improvement in stringent complete response.

In this particular ASH meeting, we will also be hearing the results of daratumumab added to bortezomib, lenalidomide, and dexamethasone from the Griffin trial and also addition of daratumumab to bortezomib, cyclophosphamide, and dexamethasone in the LYRA trial. This current Phase II trial is looking at adding daratumumab to ixazomib-lenalidomide-

dexamethasone, an all oral triplet. We enrolled 14 newly-diagnosed patients to this Phase II trial–38 of these patients went on to get treatment. The overall response rate for the regimen was about 96%. There was one patient who did not achieve a partial response and could only get a 43% reduction in the serum M-spike. Among the patients who had a partial response or overall response to the therapy, we had 67% of these patients who had a very good partial response or better. There are nine patients who stopped treatment and went on to a stem cell transplant. There were three patients who actually progressed on therapy and have since gone off. There have been no discontinuations due to toxicity. The regimen has been overall well-tolerated with most of the adverse events related to hematological adverse events, and also will have some GI toxicity related to ixazomib and infusion-related reactions related to daratumumab. The patients continue on therapy and we anticipate that the depth of response will continue to improve on this current regimen. We also looked at 21 patients who went on to collect stem cells. We did not see a significant impact on the stem cell collection with the use of the four-drug regimen.

Overall, our conclusion is that this quadruplet is clearly an effective regimen. It is well-tolerated. It does not interfere with the ability to collect stem cells and we need to look at the long-term results to see what the maximum depth of response that can be attained on this four-drug regimen. Thank you for watching this.

Reference

Kumar S, Kapoor P, Laplant B, et al. Phase 2 Trial of Ixazomib, Lenalidomide, Dexamethasone and Daratumumab in Patients with Newly Diagnosed Multiple Myeloma. ASH 2018. Abstract 304.