

What are the practical considerations in management of the most common adverse events with proteasome inhibitors?

Ajay K. Nooka, MD, MPH, FACP

Assistant Professor
Department of Hematology and Medical Oncology
Winship Cancer Institute of Emory University
Atlanta, Georgia

Welcome to *Managing Myeloma*. I am Dr. Ajay Nooka. I am frequently asked, “What are the practical considerations in management of the most common adverse events with proteasome inhibitors?”

The three proteasome inhibitors that are currently approved are bortezomib, carfilzomib, and ixazomib. Bortezomib has been used for myeloma therapies for the last 15 years. The main side effects that you see with bortezomib are peripheral neuropathy as well as the risk for herpes zoster eruptions and some GI toxicity.

So, how do I manage the peripheral neuropathy? Again, it is very crucial to identify the at-risk patient who has a prior history of peripheral neuropathy from the disease itself, or when you are using it in patients who have prior history of other neurological disorders, a prior history of diabetes which predisposes patients to have diabetic neuropathy. These are all things that need to be taken into consideration even before starting the dosing, and appropriate dose reductions are extremely crucial. Making the dose reduction at the first sign of grade 2 toxicity would certainly prevent any further progression of this peripheral neuropathy. Also, what we had seen over the last 5 years is when we change from the IV administration of bortezomib to subcutaneous administration of bortezomib, the rates of grade 3 peripheral neuropathy have significantly come down almost from 16% to 6%. So, appropriately identifying those symptoms and giving them vitamin B certainly can help the scenario of peripheral neuropathy.

The second proteasome inhibitor is carfilzomib. The main side effects of carfilzomib are fatigue and anemia, and I would appropriately treat these patients by giving them stimulants if needed, for anemia by giving them transfusions as needed, taking off any offending agent that is causing anemia, and making sure that the other causes of anemia are taken care of. All those things are very, very appropriate, and one most important side effect with carfilzomib, not the most common side effect, is rate of cardiac events. Uncontrolled hypertension, cardiac failure, and dyspnea, these all need to be watched for very, very closely when you are using a carfilzomib-based regimen.

The third proteasome inhibitor that was recently approved is ixazomib. Ixazomib is one of the easiest drugs to take. The main side effects that you see are the GI side effects as well as rash. Rashes are not very common; these occur in fewer than 10% of the patients. The GI side effects are seen in a lot of patients, but the grade 3 side effects are seen in close to 6% of patients. So, appropriately giving them the right antiemetics, properly giving them the right PPI would certainly help mitigate these toxicities.