Managing Myeloma

Should patients with cardiac history receive carfilzomib?

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Welcome to *Managing Myeloma*. I am Dr. Ajay Nooka. I am frequently asked, "Should patients with cardiac history receive carfilzomib?" Carfilzomib is an epoxy ketone-based proteasome inhibitor which is approved by the FDA for treating relapsed/refractory multiple myeloma patients who have seen more than one line of therapy. It is approved in combination with lenalidomide and dexamethasone in support in combination with dexamethasone. It is a very important proteasome inhibitor which has potency even among patients who have progression in the prior proteasome inhibitor, bortezomib. A main concern that we always have is the cardiac toxicity that is seen in less than 5% of the patients. The main side effects, or the manifestations of cardiac toxicity in patients receiving carfilzomib are cardiac failure, hypertension, and dyspnea. In my opinion, it is not an absolute contraindication to give carfilzomib among patients with cardiac history. What really helps is to identify those patients who are at risk. Did the patient have a prior history of an MI? Did the patient have any valvular disease? Did the patient have a prior history of systolic heart failure? All these things should be taken into consideration to make the right decision to give carfilzomib among these patients.

Especially, when we come to hypertension, this is the next group where it will be extremely crucial about identifying the patient to give carfilzomib. For patients with uncontrolled hypertension, my first goal is to bring the hypertension under control, take the help of a cardio-oncologist, and then administer the agent carfilzomib. Whenever I am using carfilzomib, I always go with a 30-minute infusion rather than a 10-minute infusion. It certainly decreases the rate of a lot of side effects including the dyspnea and hypertension. I suggest having a home-based diary and using the diary to keep track of the blood pressures before the carfilzomib administration and after the carfilzomib administration, and to keep strict hypertension guidelines of systolic not more than 140. If it goes more than 140 or goes beyond the 20% increase, we certainly have to hold off on the carfilzomib and make a one dose level reduction in the next cycle. What is needed to be conveyed clearly to the patient is, this dyspnea that is seen with carfilzomib-based therapies is non-cardiac, non-pulmonary, and does not have any long-term consequences. If they are seeing it, which is seen in almost half the patients, it should not frighten them. It is something that is expected 2 days or 3 days after receiving a carfilzomib-based infusion.

One other thing that I always talk about is we do see some patients who do have a real drop in the ejection fraction. Anecdotally, everybody has those patients, and this is not the common theme that you see across. An ejection fraction number should not withhold you to give carfilzomib if it is clinically indicated. There are certain subsets of patients to whom I will not give carfilzomib. Number one is in old, frail patients who have an ejection fraction of 30%, that probably is not the right person. The second group of patients are the patients who have uncontrolled hypertensions and systolics of 180s and 200s, and those are not the patients that typically should receive carfilzomib. Otherwise, it is a good tolerable agent and the toxicity that you see is in the range of less than 5% of patients. Thank you for viewing this activity.