Managing Myeloma

Is there a role for Bcl-2 directed treatment for patients with translocation 11;14?

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Welcome to *Managing Myeloma.* I am Dr. Sagar Lonial. I am frequently asked, “Is there a role for Bcl-2 directed treatment for patients with translocation 11;14?” I think that this is really an important and exciting question. For years we have been talking about using biomarker-directed therapy in all of cancer, and in myeloma, we do not really have biomarker-directed therapy. What we know about the Bcl-2 inhibitor venetoclax* is that it does seem to have preferential activity in the context of patients with the 11;14 translocation. There is a lot of really good biology to evaluate this and try and understand *why* this is. If one looks at a single-agent response rate of venetoclax in relapsed/refractory myeloma for 11;14 translocated patients, the overall response rate is about 40%. If you add dexamethasone to that (venetoclax-dexamethasone for 11;14 translocated myeloma), the response rate jumps to 60%.

We at Emory have a system where we do BH3 profiling and can identify whether that response rate can even be higher based on sensitivity to venetoclax in vitro using assays. With that approach, we have been able to significantly and effectively predict almost all of our patients responding versus not responding to a Bcl-2 directed therapy like venetoclax. I think clearly there is a role for 11;14 directed therapy with Bcl-2 inhibition; the question is, can we expand it even beyond that? There is very exciting data coming from Philippe Moreau and another collaborative group evaluating venetoclax in combination with bortezomib and dexamethasone, suggesting that even in non-11;14 patients, you may be able to overcome bortezomib resistance by adding in venetoclax in a small subset of patients. I think there is more to the story here to come. The use of bortezomib and venetoclax is clearly very active. Venetoclax-dexamethasone in 11;14 positive patients does represent a biomarker-driven therapy and one that I think we are all very excited about. Thank you for viewing this activity.

*Venetoclax has not been approved by the FDA for the treatment of multiple myeloma at any stage of the disease