Sagar Lonial, MD
Professor
Vice Chair of Clinical Affairs
Department of Hematology and Medical Oncology
Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia

What new classes of therapy are emerging for multiple myeloma?

Welcome to *Managing Myeloma*, my name is Sagar Lonial, and I am from the Winship Cancer Institute of Emory University in Atlanta, Georgia. I am frequently asked, “What new classes of therapy are emerging for multiple myeloma?” After such a banner month in the area of myeloma with three new drug approvals, one might wonder what else is left? Well, as you know we are not curing everybody with myeloma, and so there are a number of drug classes in evolution that I think are worth talking about. The first is probably the checkpoint blockade group of drugs, the PD1, PDL1, CTLA4 axis of drugs. The work in that area has been really, really preliminary so far. But at the ASH 2015 meeting, there were actually two abstracts presented; one combining pembrolizumab with lenalidomide and dexamethasone, and another combining pembrolizumab with pomalidomide and dexamethasone. The reason these are important is that pembrolizumab alone really had no significant activity in myeloma in a phase 1/2 trial. However the combination with lenalidomide or pomalidomide was actually quite active with roughly a third to 40% of patients responding, and many of those responses occurred in patients who were resistant to either lenalidomide or pomalidomide coming into the trial. So it suggests that the checkpoint blockade inhibitors may be able to overcome IMiD resistance through mechanisms that we are now just beginning to learn about.

The other big category that is evolving is the nuclear transport export inhibitors, the SINEs, so-called SINE category of which selinexor is probably the furthest along. There are trials now looking at selinexor as a single agent as well as in combination with carfilzomib, all showing pretty promising activity. There has been some nausea associated with that, but it is early on, and I think with appropriate management, this can be minimized.

The third new class is sort of a big broad category that I think is worth talking about and that is the class of mutation-driven therapies. This includes things like BRAF, which occurs in about 4% to 5% of patients with myeloma. It can include IDH1, it can include IDH2, which are being specifically targeted by drugs and mutations. It can also include things like RAS, NRAS, KRAS and, MAP kinase, and there are a number of tryosine kinase inhibitors in this realm that are certainly exciting and are early in their days of being evaluated. And finally, to go after P53: MDM2 inhibitors are currently being explored in phase 1/phase 2 trials. Certainly through the MMRC,for patients who have one normal copy of P53, there are hopes that the MDM2 inhibitor might be able to help reverse that P53 abnormality. These are probably the biggest categories of drugs or classes that are emerging in the context of multiple myeloma.

Thank you for viewing this activity. For additional resources, please view the other educational activities on the *ManagingMyeloma.com* website.