DR. NOOPUR RAJE DISCUSSES HER RESEARCH INTERESTS IN MM

Please tell us about your medical background.

I received my medical degree from B.J. Medical College, Pune University, India. I trained in internal medicine at Massachusetts General Hospital (MGH) and completed a fellowship in hematology and medical oncology at the Dana-Farber Cancer Institute in Boston, MA. Currently, I hold a faculty appointment at MGH and am an associate professor of medicine at Harvard Medical School. At MGH, I am the director of the Multiple Myeloma Program, Medical Oncology. As a hematologist/oncologist, my primary focus is in multiple myeloma (MM), both as a clinician and researcher.

Noopur Raje, MD
Director, Multiple Myeloma Program,
Medical Oncology
Massachusetts General Hospital
Boston, MA

What are your research interests?

We pursue laboratory and clinical research in MM with the goal of translating these efforts to the improvement of patients' lives. My research focuses on understanding the biology of MM, the biology of bone disease in MM, tumor microenvironment and its role in MM pathogenesis, the development of novel therapeutics, as well as identifying and validating novel targets.

I have been involved with investigating the role of B-cell activating factor (BAFF) in MM using a neutralizing antibody and cyclin-dependent kinase inhibitors. All of these clinical trials are backed by translational research endpoints informed by our preclinical studies with the view to validating our data.

Despite the significant progress that has been made in the treatment of MM in recent years, substantial challenges remain. This is especially true for our high-risk MM patients, and for those with advanced drug-resistant MM. To address these challenges, we must identify novel classes of anti-MM agents and incorporate them into safe and effective regimens. We must also develop more efficient algorithms to help us select the most appropriate therapeutic options for each individual patient.

Is subcutaneous administration of Velcade® an example of the evolving use of existing novel therapies?

The standard administration of bortezomib (Velcade®) is intravenous (IV) injection, but subcutaneous (SQ) administration is now being studied as an alternative in MM. Prof. Philippe Moreau and colleague have published data from a randomized, Phase III, non-inferiority study of SQ versus IV administration of bortezomib in patients with relapsed MM. They compared the efficacy and safety at the standard dose (1.3 mg/m2) and twice per week schedule. No significant differences were found in time-to-progression (TTP) and 1-year overall survival (OS), and side effects – peripheral neuropathy (PN) in particular – were significantly less common with SQ than with IV administration. The data demonstrate that SQ bortezomib is feasible, resulting in equivalent bortezomib plasma exposure and similar efficacy, but with an improved systemic safety profile compared to standard IV administration. The data support the use of SQ bortezomib administration in the clinical setting where the safety and efficacy of IV bortezomib have been established.

Can you tell us about the SQ bortezomib clinical experience you have had with the MM patients you are treating?

In the United States, bortezomib is currently approved for the treatment of MM via IV administration. It has been a very effective part of the anti-MM arsenal for many patients, but data show that approximately a third of MM patients being treated with IV bortezomib experience PN, which can cause pain, numbness, and/or tingling in the extremities. To manage side effects, the dosage or frequency of administration can be decreased. Once weekly instead of twice weekly administration of IV bortezomib has become common since a clinical trial demonstrated the safety and efficacy of this approach, which significantly reduces side effects, including PN.

In the SQ route of administration for bortezomib, it is injected into the fat below the skin. This is not yet approved by the US Food and Drug Administration (FDA), but an application has been submitted. Some cancer centers are now using the SQ method, and patients can inquire if their treatment facility offers it. My patients who are on SQ bortezomib are doing very well. No patient has had significant issues with it.

For a patient, SQ administration makes bortezomib delivery more quick and comfortable. But convenience is not the only factor. Importantly, the SQ administration method makes it possible for us to use bortezomib in individuals with pre-existing PN who otherwise respond well to the therapy. In addition, with SQ administration, patients may tolerate bortezomib longer, which might improve the depth and duration of their response to therapy.

Unfortunately, insurance reimbursement remains an issue because SQ bortezomib is not yet FDA-approved. Of course, once the SQ route is approved, the next step would be to determine if combining weekly and SQ bortezomib administration can maintain efficacy while further reducing side effects. I would also be cautious about using SQ bortezomib in combination approaches as data to that effect are lacking.

Thank you. Any closing comments?

The outlook for patients with MM has improved significantly with the use of the immunomodulatory drugs thalidomide and lenalidomide (Revlimid®), and the proteasome inhibitor bortezomib. The progress continues, with advances being made in the discovery and development of new drug classes, the introduction of next-generation agents, and our ability to effectively treat MM with existing novel agents while reducing the potential for side effects and being watchful of the patients' quality of life. Overall, we are looking at the very realistic goals of further improving outcomes and expanding treatment options for patients with MM.

Editor's Note: Dr. Raje is a member of the American Medical Association (AMA), America Society of Hematology (ASH), American Society of Clinical Oncology (ASCO), and American Association of Cancer Research (AACR). She is also an *ad hoc* reviewer for several journals, including *Blood*, *Clinical Cancer Research*, *Leukemia*, and the *American Journal of Hematology*. Dr. Raje is the recipient of several awards and has published extensively in the field of MM research. **MT**