Transcript Details
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Advancing Multiple Myeloma Treatment: The Role of Immunotherapy and Personalized Care

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. Shaji Kumar, who's a consultant in the Division of Hematology and Mark and Judy Mullins Professor of Hematological Malignancies at Mayo Clinic in Rochester, Minnesota. He'll be discussing treatment strategies for newly diagnosed multiple myeloma. Here's Dr. Kumar now.

Dr. Kumar:
The treatment of myeloma has changed dramatically over the past two decades and in particular over the past few years. We have had the immunomodulatory drugs, the proteasome inhibitors, and the monoclonal antibodies introduced over the last two decades, and these have significantly changed the outcomes of patients with multiple myeloma, with survival having almost tripled over this time period. Now, this is the result of these drugs being used in very effective combinations that allowed us to get deep responses in patients with multiple myeloma that often lasted for a long period of time.

Now, in the past five years or so, we have seen an influx of immunotherapies, particularly chimeric antigen receptor T-cells and bispecific antibodies, broadly referred to as T-cell redirection therapies. These two classes of drugs, as well as antibody drug conjugates targeting BCMA, have really changed the treatment paradigm again over the past few years. These new therapies are very effective even when used by themselves and can lead to deep responses in people for whom the myeloma is well controlled with traditional drugs, including some of the new drugs that came along during the past two decades. So the expected survival in patients with myeloma who are deceased—who became resistant to immunomodulatory drugs, proteosome inhibitors, and the monoclonal antibodies—was less than a year only about five or six years ago, and with the advent of immunotherapies, we are seeing those patients live two, three, or more years with some of the therapies, especially the CAR T-cell therapy.

There are several characteristics that we use in order to decide what kind of treatment a patient with myeloma should receive, whether it be at the time of diagnosis or at the time of disease relapse. Especially at the time of diagnosis, there have been several phase III trials, especially in the recent years, that have demonstrated that four-drug combinations can lead to deep, very durable disease responses, sometimes to the tune of 10 or more years.

Now, patients with myeloma have very different outcomes, primarily driven by two factors. One is the genetic changes that we can see in the myeloma cells, and the other is the overall frailty status of the patients, which in turn can be decided by age, comorbidities, impact of the tumor on the host, and a variety of other factors. Now, these two are the main characteristics that allow us to decide on a particular regimen. There are several high-risk factors that have been identified over time in addition to genomics, and the more of them you have, the higher the disease risk is, and the higher the disease risk, the more intense we want the treatment to be. This is because we know that outcomes can be significantly influenced by the depth of response, particularly if you are able to get them to be minimal residual disease negative. But at the same time, how intense a therapy a patient can tolerate depends to a large extent on the frailty, so it's a balance between the risk and the frailty that, in a sense, determines the intensity of therapy by which we can use a quadruplet, triplet, or doublet for a given patient.

In addition, we also want to think about—more importantly—the comorbidities. Even though the frailty status gives an overall picture, there might be specific comorbidities that can be adversely influenced by the specific drugs we use. So if you have someone who has neuropathy at baseline, we may want to avoid bortezomib; if somebody has cardiac disease, we may want to avoid carfilzomib; if someone has significant diabetes, maybe we want to use less steroids or avoid them altogether, a possibility that we are increasingly able to do because of the new therapies like immunotherapy.

The important thing is the survival of patients with myeloma continues to improve. We want to use the best possible therapies in the beginning to give the patients the best response and rapid reversal of some of the complications, particularly renal insufficiency, but at the same time also provide them with good supportive care, particularly prophylaxis against infection as well as bone health improvement. Such a coordinated approach using the best tools available at any given time when the patients need therapy will allow the patients to have a maximum survival but at the same time not suffer from undue toxicity from the therapies.

Announcer:
That was Dr. Shaji Kumar discussing the role of doublet, triplet, and quadruplet regimens in treating newly diagnosed multiple myeloma. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!