Transcript Details
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Optimizing Multiple Myeloma Care: Advances for Newly Diagnosed Patients

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, we'll learn about treatment options for multiple myeloma with Dr. Morie Gertz, who's a hematology specialist at the Mayo Clinic Comprehensive Cancer Center in Rochester, Minnesota. Let's hear from him now.

Dr. Gertz:
The current treatment options for newly diagnosed multiple myeloma—I must say, we're immensely fortunate to have so many effective options. I think the key is that we're using multiple classes of agents in the initial therapy of multiple myeloma, and I think most investigators believe that the use of an anti-CD38 antibody, daratumumab or isatuximab, with an immunomodulatory agent, which would generally be lenalidomide, a proteasome inhibitor—and there have been trials looking at using both bortezomib and carfilzomib as well as dexamethasone. The use of a quadruplet for newly diagnosed myeloma I think is now the global standard, and the exception might be patients who are very frail. Perhaps the omission of the proteasome inhibitor would be reasonable. There may be dosing adjustments for those patients who have significant degrees of renal insufficiency. But I think that it's widely agreed that the use of a quadruplet induction regimen—antibody, IMiD, proteasome inhibitor, and steroid—would be the starting point for all newly diagnosed patients.

Novel agents have had a dramatic impact. If you go back a number of decades, we were using alkylating agents, we were using vincristine, we were using doxorubicin, and these are rarely considered in the initial management of patients with multiple myeloma with the exception of patients who have significant renal failure at presentation or are being treated in the hospital where there may be issues with acquisition of new agents. But the novel agents, the anti-CD38 antibodies, proteasome inhibitors, and immunomodulatory drugs, have gone from being novel agents to really the standard of care for newly diagnosed multiple myeloma.

The selection of a newly diagnosed regimen I think are determined by a number of factors: patient's age, probably more important frailty and how robust they are, and whether treatment is commencing in the hospital where it's very difficult to start an immunomodulatory drug or as an outpatient. Whether the patient presents with significant renal impairment would also have an impact.

One of the nice things about the toxicity of the therapies associated with multiple myeloma is that they tend to be dose related, and as a consequence, if patients are having side effects, one not need abandon a specific medication. Usually, dosing modifications will result in control.

I think from a patient's perspective, the most toxic agent is dexamethasone because of its neuropsychiatric effects, insomnia, mood swings, irritability, and personality changes. The dose that we use at 40 mg weekly has never been substantiated in a phase I/phase II maximum-tolerated dose trial, so there's a lot of flexibility in modifying the dose. And many patients are intolerant to 40 mg per week, but fortunately, you can have a lot of flexibility giving patients 20 mg a week, 12 mg a week, or 8 mg a week. Adjust it so that it's tolerable.

The second big problem with our induction therapy is chemotherapy-induced peripheral neuropathy, which are characteristic of bortezomib and thalidomide. This isn't consistently reversible, so one needs to be vigilant for the possibility that patients are developing neurotoxicity because as soon as they start developing paresthesias in our soles or in their toes, you really need to either half the dose or just discontinue the drug completely. Otherwise, you're going to have a patient with a long survival but intractable painful neuropathy.

For immunomodulatory drugs, the three big changes are fatigue, diarrhea, and venous thromboembolism. Fatigue is very difficult to manage without dose modification, but the diarrhea often has a bile acid component, and it can be treated by supplementing with

colestipol or cholestyramine, which will help reduce the diarrhea. At least in half the patients it will get better. Venous thromboembolism is really an issue of anticoagulation and is not a reason to discontinue the treatment. Even if the patient gets a serious VTE, such as pulmonary embolism, you would anticoagulate the patient and resume the immunomodulatory drug.

Finally, with anti-CD38 antibodies, the primary problem is upper respiratory infection. Sometimes you can manage this with prophylactic antibiotics, such as doxycycline, penicillin, sulfamethoxazole, and trimethoprim. Some patients get severe recurrent infections associated with very low IgG levels. In those patients, they may benefit from supplemental intravenous immunoglobulin. But at the very least, these toxicities are treatable and should not necessitate stopping.

Announcer:
That was Dr. Morie Gertz discussing treatment options for 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!