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Carfilzomib-Based Regimens for Early Relapse Multiple Myeloma

Announcer:
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Dr. Biran:
Hi everybody, this is Noa Biran from Hackensack Meridian Health. Today I'll be discussing Carfilzomib-Based Regimens for Early Relapse Multiple Myeloma.

So we'll start off with a case. This is a case of a 55-year-old man with history of IgA kappa myeloma, intermediate risk, presenting with L3 compression fracture, hypercalcemia, 50 to 60% kappa-restricted plasma cells, and his FISH showed 1p deletion and 13q deletion consistent with high risk. Patient has underlying peripheral neuropathy from diabetes and well-controlled hypertension. He received 4 cycles of carfilzomib, len, and dex, followed by an auto transplant and then lenalidomide maintenance. His lenalidomide was reduced after 2 years because of diarrhea. While on dose-reduced lenalidomide, his markers achieved biochemical progression of disease 2 years and 5 months after auto transplant.

How do we decide what we're going to use next? And these are - we need to think about a combination of factors when determining the next regimen. One is the biology of relapse. Is this a quick relapse? Is the patient high risk? What comorbidities does the patient have? Will the peripheral neuropathy guide our treatment so as not to give the patient more risk of peripheral neuropathy? What about organ damage? Do we need to achieve quick remissions? Is there hypercalcemia? Renal infections? Is the patient in pain? And the other thing to consider is what was the response to prior therapy? Is the patient LEN-refractory or are we likely to achieve a response with lenalidomide-based therapy moving forward?

This patient would be a great candidate for carfilzomib-based therapy. Carfilzomib would be an option so as to avoid peripheral neuropathy. It has effective - it is effective in high-risk disease, and the patient has responded to carfilzomib in the past.

This is the CANDOR study, which shows that the combination of carfilzomib, daratumumab, and dex prolongs PFS, compared to carfilzomib and dex alone. And here you can see that a large subset of the patients were lenalidomide-refractory and high risk. And despite this, we see a significant improvement in median PFS compared to the doublet with a hazard ratio of 0.59. And if you look at the subset analysis, patients with high-risk disease in particular, benefited from the combination of carfilzomib, daratumumab, and dex. The IKEMA study evaluated the combination of isatuximab, carfilzomib, and dex, compared to carfilzomib and dex alone in patients with early relapse. Again, you can see that with us high amount of LEN-refractory patients, we see a significant improvement in median PFS, 35.7 versus 19.2 months, with a hazard ratio of 0.58. And you can see that in patients with high-risk subset including 1q21 gain, we see that the benefit of the triplet combination is maintained.

The ENDEAVOR study was a head-to-head study comparing two proteasome inhibitors, carfilzomib and dex, versus bortezomib and dex in patients with relapsed or refractory myeloma. And you can see that even when looking at overall survival, which is a difficult endpoint to achieve, we see a significant benefit in the carfilzomib group compared to the bortezomib group, hazard ratio of 0.79. And here you see almost all patients had prior IMiD, a little bit less than a quarter were high risk, and the amount of patients who had prior

bortezomib was the same in both groups. Again, you can see that in subset analysis, the high-risk subset continued to benefit from carfilzomib-based therapy.

So to summarize, when selecting a therapy for patients with relapsed myeloma, please consider the biology of the disease, the risk status of the patient, comorbidities of the patient, and their prior treatment response. The combination of carfilzomib with a monoclonal antibody, whether it is dara or isa, in combination with dex for patients who have had one to three prior lines, has shown absolutely beneficial median PFS rates of 28.6 to 35.7 months. And in multiple myeloma patients who have had one to three prior lines of therapy, we did see an OS benefit with carfilzomib/dex, compared to bortezomib and dex.

Thank you very much for joining me today, and I hope you learned something about the use of carfilzomib in patients with early relapsed myeloma.

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