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Time needed to complete: 1h 07m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Multiple Myeloma At First Relapse: Is My Patient Refractory to Lenalidomide?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Biran:
Hi, my name is Noa Biran from Hackensack, New Jersey, and today we're going to discuss Multiple Myeloma at First Relapse: Is My Patient Refractory to Lenalidomide?

So we have to first define what is the difference between relapsed and refractory myeloma. And these patients represent a diverse group. Patients can relapse while being off of therapy. And these patients may have been discontinued from treatment for various reasons, including toxicity, not necessarily progression. Patients can relapse while on active therapy. And there are a subset of patients which perhaps represent the most high-risk and difficult-to-treat patients who are considered primary refractory, and these are patients who never achieve a response to their primary appropriate therapy. Relapse disease is disease that's been previously treated and then progresses. And refractory disease is progressive disease while on active therapy or within 60 days of last treatment.

Disease progression is defined by IMWG criteria, and it can be defined by clinical relapse which is really an end-organ symptom, hypercalcemia, anemia, a new bone lesion, symptoms related to hyperviscosity, or renal dysfunction that is attributed to the monoclonal gammopathy.

Or IMWG defines a biochemical relapse, which is a 25% or greater increase in paraprotein parameters, M spike, urine M spike, or in the case of free light chains, it's defined by more than 10 mg/dL difference between the involved and the uninvolved free light chain in the serum or urine. A relapse from CR doesn't necessarily need to be treated. It represents appearance of the serum or urine M spike, but does not yet meet the definition of progression of disease. These patients really just have to have more frequent monitoring. And a relapse from MRD negativity is similar in that a bone marrow which once showed MRD negativity now shows MRD positivity, represents reemergence of the disease, but at this point, does not represent a need for change in therapy.

IMWG definition of progression is defined similarly, in that progression of disease represents an increase of 25% from the lowest value and a serum M spike has to be at least 0.5 g/dL, or above. Refractory disease and primary refractory disease we defined prior.

So, how do we really define patients who are lenalidomide-refractory? Because many of our patients who are on lenalidomide maintenance are on sub-therapeutic dose. So there are three things we can possibly do in these situations, increase the lenalidomide dose, add weekly dex, or switch to an alternative regimen, either a new IMiD, or a totally different monoclonal antibody or proteasome inhibitor-based regimen. We know that to be fully considered lenalidomide-refractory, patients have to have progression or less than a partial response on a full dose of lenalidomide.

When we look at patients who receive treatment on clinical trials, it's very important to define those who are lenalidomide-refractory, and that's because they have significantly different response to various therapies compared to lenalidomide exposed patients. And that's because their disease is much more refractory and has acquired many more mutations.

In this study, you can see that when compared to bortezomib and dex, patients who were LEN-refractory have inferior outcomes compared to those who are lenalidomide exposed. And various treatment regimens were explored to evaluate response in these lenalidomide-refractory patients. And in sequential order, you can see that combination of dara/bortezomib/dex, carfilzomib/dara/dex, and cetuximab, carfilzomib/dex are excellent treatment options in patients who are lenalidomide-refractory.

So to summarize, we know that relapse myeloma is previously treated myeloma that's progressed after prior therapy and requires a change in treatment. The definition of progression of disease is a 25% increase in the tumor burden from the lowest documented value. And in the case of an M spike, it needs a 0.5 g/dL increase or above from the nadir. We know that in our lenalidomide-refractory patients response rate is significantly reduced and it is important to choose triplet-based combinations with a change in two agents.

Thank you for joining me today, and I hope you learned something about lenalidomide-refractory myeloma.

Announcer:
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