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Clinical Evidence for Anti-CD38–Based Frontline Regimens in Transplant-Eligible Patients With Multiple Myeloma

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Dr. Callander:
Welcome to this educational activity with GLC. I'm Dr. Natalie Callander. Today, I'm going to review pivotal data from anti-CD38-containing frontline programs for transplant-eligible patients.

The first one of these is one that was first presented about 2 years ago at ASH. This is the PERSEUS trial. So this is a very large trial, over 700 patients. And these were transplant-eligible individuals, they had to be younger than age 70. And they were randomized to receive bortezomib, lenalidomide, dexamethasone with or without daratumumab, for four cycles, then they went on to an autologous stem cell transplant, then two consolidation cycles, and then they were put on maintenance with respect to their previous arm. So patients on dara stayed on dara. Patients without received lenalidomide. And the data that was presented 2 years ago that I think is probably familiar to many people, the 48-month PFS was 84.3% for those receiving daratumumab versus roughly 68% for those receiving just the triplet.

And I think what has also been very exciting about this study which was recently updated at ASCO this year is we now know with a later analysis that about 35% of the patients did meet the definition of high-risk myeloma based on this new IMWG working definition. And what we were able to see then is that if you look at not just response but MRD negativity in both high-risk and standard-risk individuals, the benefit remains. And so that in standard-risk individuals, at 10^{-5}, about 76% of patients in standard risk were MRD negative versus only 54% not receiving daratumumab, versus in that high-risk group, almost the same results, 73% were MRD negative at 10^{-5} versus 45.7% in those high-risk patients.

And furthermore, if we look even deeper at patients receiving MRD at 10^{-6}, same benefits. And we know now that attainment of MRD negativity is so important in keeping patients from progressing, and so this is why this bar is so important.

So similarly, we have seen recently the GMMG-HD7 trial from Germany. Similarly, a phase 3, large, randomized trial, 662 patients. And in this design, patients received bortezomib, lenalidomide, dexamethasone with or without isatuximab. And in this case, they received three 6-week cycles. They went on to single or double autologous stem cell transplant. The choice was based on whether patients appeared to be in CR at that step, and then they were re-randomized to maintenance with either isatuximab, lenalidomide, dexamethasone, or lenalidomide, dexamethasone. So there was a second randomization.

The primary endpoint here was MRD negativity, and the preliminary study was presented some time ago, showing again a big advantage for the inclusion of isatuximab. Now, this was MRD determined only at the end of induction, and so what this showed was the MRD at 10^{-5} rate was 50% in those receiving isatuximab versus only 35.6%. And furthermore, what they were able to show is the inclusion of isatuximab improved response rates, whether you were looking at the CR rate, the VGPR rate, or the overall response rate. So this was really an important inclusion.

And furthermore, now because of that second randomization, there's been some updated data that's going to suggest that the inclusion of isatuximab, in any step is helpful, but for those individuals who receive isatuximab both as part of their induction and then part of their maintenance, probably will benefit the most. And that would actually sustain data that was seen in a recent update in CASSIOPEIA showing that daratumumab, both as part of induction and then maintenance, was beneficial. So we expect we're going to see the same thing from the GMMG-HD7 once it's a little bit more mature.

So I think in summary, it's fair to say that the introduction of anti-CD38 antibodies has made a big difference. We think for those transplant-eligible patients, it certainly improves the rate of MRD negativity, which we think is such an important surrogate. It seems to benefit high-risk patients as well, and I think we are looking just for confirmation that the inclusion of anti-CD38 antibodies as part of maintenance regimens is going to be as important as we think it is.

Well, my time is up. I hope you found this brief overview useful. Thank you very much for listening.

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