Randomized Open-Label, Non-Inferiority, Phase 3 Study of Subcutaneous Versus Intravenous Daratumumab Administration in Patients with Relapsed or Refractory Multiple Myeloma: COLUMBA Updates

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Welcome to *Managing Myeloma*. I'm Dr. Saad Usmani, and I'm live at the 61st ASH conference in Orlando, Florida. Today, I will be reviewing the results of the study titled "Randomized Open-Label, Non-Inferiority, Phase 3 Study of Subcutaneous Versus Intravenous Daratumumab Administration in Patients with Relapsed or Refractory Multiple Myeloma: COLUMBA Updates."

Why is this study important? Daratumumab was originally approved as an IV formulation back in 2015, and many of us in the clinic struggled initially with the IV formulation because of the duration it takes to administer that therapy. We were all impressed with the efficacy, but this was a clinical issue that's probably more practical for the community physicians. With that in mind, its subcutaneous formulation was prepared and tested in a phase 1 study where recombinant hyaluronidase enzyme was combined with daratumumab, and it was given as a subcutaneous injection. That original phase 1 was first reported back in 2016 at ASH, and since then that subcutaneous formulation has now become a premixed more concentrated formulation that only requires 15 mL that can be given over 5 minutes as a subcutaneous formulation. So, now the objective of this particular study was to see if the IV and the subQ formulations are comparable. In the phase 1 study, the overall response rate in the relapsed/refractory patient population was almost 50%.

So, let's review the salient features of the COLUMBA trial. This trial randomized 522 patients to receive either the subQ or the IV formulation in a minus to one randomization. The median age of patients enrolled was 67, and median baseline body weight was 73 kilos.

Patients had received four prior lines of treatment and all the patients were previously treated with both PI and IMiD; 82% of the patients were refractory to the last line of treatment and 49% were refractory to both PIs and IMiDs; 26.3% and 17.3% of the patients had high-risk cytogenetics at baseline in the subQ and IV Dara arms, respectively.

So, after median follow up of 13.8 months, the median duration of treatment was about 5.5 months and it was similar between the subQ and the Dara IV formulations. A significantly lower rate of IRR was observed with the Dara subQ versus Dara IV, roughly 12% versus roughly 30-odd percent, and at the time of data cut off, 118 patients continued to stay on treatment. If you look at the overall response rate compared with the IV and the subQ, for the IV formulation with the updated data, it's 39.4%, whereas with the subQ data set, it's 43.7%. And the depth of response continues to improve over time. Bottom line, overall response rates were comparable across all subgroups, including body weight.

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So, what do these data mean? The clinical practice implication is that the subQ formulation is equal to IV formulation and hopefully, an FDA approval will be forthcoming. And from a clinical standpoint, I think, out in the community, subcutaneous daratumumab will provide a better administration strategy for patients. It's convenient and eventually it will be utilized in combination with other platform drugs in early relapse and even on the frontline setting.

Thank you for your attention.

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