Abstract 691

Depth of Response to Daratumumab, Lenalidomide, Bortezomib and Dexamethasone Improves Over Time in Patients with Transplant-Eligible Newly Diagnosed Multiple Myeloma: GRIFFIN Study Update

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Welcome to *Managing Myeloma*. I'm Dr. Sagar Lonial, and I'm live at the 61st ASH conference in Orlando, Florida. Today, I will be reviewing the results of the oral presentation titled "Depth of Response to Daratumumab, Lenalidomide, Bortezomib and Dexamethasone Improves Over Time in Patients with Transplant-Eligible Newly Diagnosed Multiple Myeloma: GRIFFIN Study Update."

The GRIFFIN study, I think, is a really important trial that is really asking the question about the addition of daratumumab to newly diagnosed myeloma most commonly used regimen, the RVd regimen. We've seen data from the CASSIOPEIA trial in the European group about the addition of Dara to VTd as a potential induction therapy regimen, as well as consolidation and Dara in the maintenance phase.

This trial was designed slightly different to use the U.S. version of VTd, which is RVd, and happens to be the most common induction regimen we use in the U.S. The rationale again for investigating this combination, we know that Dara is very well tolerated. We have data from ALCYONE as well as MAIA bringing daratumumab to early myeloma treatment, both combining with a proteasome inhibitor and an immunomodulatory agent. And so it was only natural to add daratumumab to RVd to really study in a randomized fashion what the potential additive benefits of Dara in this setting are. Dr. Voorhees has presented some of this data previously and has nicely demonstrated a significant improvement in overall response rate, which is the primary endpoint as well as stringent CR, but we actually have additional data being presented at this ASH meeting.

In this trial, 207 patients were randomized to receive either Dara-RVd or RVd. Baseline demographics and disease characteristics were balanced. This was a transplant-eligible patient population with a median age of 60 years, and patients were well balanced amongst the risk groups, and there were about 15% of patients who had high risk by FISH assessment.

The primary endpoint was the improved SCR rate at the end of consolidation, which was 42.4% for the RVd plus Dara group versus the RVd group, with a significant hazard ratio and *P* value that was also significant as well. This improvement was seen pretty much in all subsets of patients with the exception of a very small subset of high-risk genetics patients, but this was not really powered to ask a genetics question.

The response rate was noted to deepen over time, more so in the Dara arm than in the non-Dara arm, with CR going from 12% at the end of induction therapy to 21% at the end of transplant, and 50% at the time of the end of consolidation, with a median follow up of about 13.5 months. Again, higher overall response rate of 99% versus 92%. VGPR or better was 91% versus 73%, and greater than or equal to CR 52% versus 42% at the end of consolidation. Again, this data is consistent with what we expected to see: Dara is very easy to add into the other agents in both lenalidomide and bortezomib. There was a slight reduction in the number of collected stem cells of eight versus nine for the Dara arm versus the RVd arm. Median time to platelet engraftment and neutrophil engraftment after transplant was the same for both groups.

When we begin to look at adverse events, again, nothing that we're not unused to seeing in patients who are receiving Dara or lenalidomide-based induction therapies. Neutropenia, lymphopenia, thrombocytopenia, and leukopenia, slightly higher in the Dara arm compared to the no Dara arm, and no significant difference in grade 3 or grade 4 infections between the two arms.

One of the important pieces I think that we're seeing is that there are now hints towards an improvement in progression-free survival. It's important to realize that this trial is not powered to give you a difference in progression-free survival. But certainly, very early on, with a relatively short median follow up, we're starting to see the PFS curves begin to separate, suggesting this is not just a response issue; it really may be a durability of overall depth of response.

So, I think in terms of take-home messages, this is really important. I can tell you at our center for standard-risk myeloma, we have now adopted RVd/Dara as our standard induction therapy based on the very encouraging results from this trial, as well as the CASSIOPEIA trial, which added Dara to VTd. I think the addition of Dara to induction therapy is a really important question.

One of the questions that our group is really asking, however, is how long do we need to continue the Dara? In our own treatment algorithm, in the absence of a clinical trial, we are adding Dara for just the first four cycles of therapy, and then holding off on consolidation and maintenance decisions until we see additional follow-up from this trial, from the CASSIOPEIA trial, and from other trials asking maintenance daratumumab questions.

Thank you for your attention.

Link to Abstract #691: https://ash.confex.com/ash/2019/webprogram/Paper123465.html