What are the criteria used to determine patient candidacy for four-drug combination therapy?

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Hello and welcome to *Managing Myeloma*. I'm Dr. Muhamed Baljevic. Today, I am going to discuss the use of four-drug combinations that are available for use in newly diagnosed, transplant-eligible patients. Many of us are frequently asked: How have four-drug combinations been adapted in the medical community? What are the criteria used to determine who may be most appropriate to start with a four-drug combination? This is an excellent question.

We should start by saying that at this point in time, quadruplet regimens outside daratumumab/bortezomib/thalidomide/dexamethasone (dara-VTd) have not been approved for newly diagnosed multiple myeloma patients. Dara-VMP has been approved for newly diagnosed non-transplant-eligible patients and dara-VTd has been approved for newly diagnosed transplant-eligible patients. As we saw today, we have covered the CASSIOPEIA trial based on which this approval was made.

However, we are still in the process of conducting the PERSEUS phase 3 trial[1] that is evaluating whether or not the PFS benefits will be present with dara-VRd versus VRd alone. There are also innovative study designs that are accruing large numbers of patients with dara-KRd-based regimens. At this point in time, it may be challenging to try to give quadruplets outside dara-VTd because of limitations in terms of insurance coverage.

However, some have been choosing dara-VRd quadruplet and that is certainly not an unreasonable choice for high-risk patients as we outlined earlier. At this point in time, we also do not have any data to tell us whether or not we should preferably be considering this type of quadruplet option just for high-risk patients and omit it in standard risk patients. If the dara-VRd indeed shows PFS benefit and becomes fully approved, this is certainly something that we will want to know.

We can say that quadruplet therapy is something that is very attractive in terms of depths of responses. We do know that the deeper the responses, particularly to earlier lines of therapy, the better the long-term outcome can be expected, and this particularly goes for situations when we reach deep MRD-negative responses.

It is not unreasonable to consider a premise (as many of the centers are currently practicing) where if the patient does achieve these very, very deep MRD negative responses, that the stem cells can be collected, and the transplantation deferred until the time of relapse. There are study designs that are also asking this question in an MRD-adapted fashion and over the next few years, we hope to learn a lot more in terms of how these quadruplet regimens, as well as MRD-directed approaches, can help us achieve a better treatment decision for our patients that will maximize the efficacies while at the same time minimizing the toxicities.

Reference

1. ClinicalTrials.gov. Daratumumab, VELCADE (Bortezomib), Lenalidomide and Dexamethasone Compared to VELCADE, Lenalidomide and Dexamethasone in Subjects With Previously Untreated Multiple Myeloma (Perseus). NCT03710603.