

## Four-drug combination regimen now approved in multiple myeloma

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Welcome to *Managing Myeloma*, I am Dr. Shaji Kumar. Today I would like to discuss the possible changes in the myeloma treatment landscape that may result from the recent FDA approval of a four-drug combination regimen now including daratumumab (bortezomib-melphalan-prednisone or VMP plus dara).<sup>1</sup>

As more drugs have become available for treating myeloma, we have focused on developing highly effective multidrug combinations. We already know that the combination of bortezomib, lenalidomide, and dexamethasone has improved the overall survival for the newly diagnosed myeloma patient. Phase 2 trials have shown that combinations that include newer proteasome inhibitors (such as carfilzomib-lenalidomide-dexamethasone) can be highly effective, and ongoing phase 3 trials are comparing these different triplets. With the addition of monoclonal antibodies (such as daratumumab and elotuzumab) we have a new class of drug that can potentially be combined with these triplets without significant overlapping toxicity, and potentially enhancing the benefit of using these regimens.

There are phase 2 trials that are already looking at adding daratumumab to combinations such as bortezomib-lenalidomide-dexamethasone, carfilzomib-lenalidomide-dexamethasone, and bortezomib-thalidomide-dexamethasone. Based on these phase 2 trials, phase 3 trials are being designed to look at adding daratumumab to the combinations that we typically use for the transplant-eligible patient population. Meanwhile, the ALCYONE trial has already been published and demonstrates that adding daratumumab to VMP regimen and continuing on daratumumab maintenance after the initial cycles of VMP regimen can lead to improved progression-free survival.<sup>2</sup> Clearly the data demonstrates that we can safely add the monoclonal antibody to the three-drug combination in these older patients. However, we still do not have the long-term data demonstrating that there is an improved overall survival, which I think is critical if we were to adopt this as a standard of care regimen for every transplant-ineligible patient with multiple myeloma.

For the transplant-eligible patient population, we really need to wait and see what the data is from the phase 3 trials before we uniformly adopt a four-drug combination. This is important because as we combine more drugs, we could certainly start seeing more toxicities. Also, importantly, we are enhancing the cost of therapy as well. The value

proposition for the four-drug regimens comes from the possibility that we can actually give these therapies for a limited duration and not continue on therapy until disease progression. I think it is important we have more data with these four-drug regimens in the upfront setting, and the depth of response that we can get, before we uniformly adopt four-drug combinations for patients with newly diagnosed disease.

Thank you for viewing this activity.

### References

1. The ASCO Post, May 25, 2018.  
<http://www.ascopost.com/issues/may-25-2018/fda-approves-daratumumab-vmp-combination/>
2. Mateos M-V, Dimopoulos MA, Cavo M, et al. *N Engl J Med*. 2018;378:518-528.  
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