

## Is the treatment landscape expanding for the front-line setting in multiple myeloma?

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The landscape of multiple myeloma treatment keeps increasing and it was only a few years back when we had approximately five drugs approved within a frame of a few weeks which was very interesting. What's happened now is that these same drugs are being used more in the upfront setting. Most recently, we saw approval of a drug which we have used quite a lot, daratumumab, in the upfront setting based on data which was presented at last year's ASH, the ALCYONE data. This was daratumumab in combination with melphalan, prednisone, and bortezomib (MPV) which showed a progression-free survival benefit in these patients and deep minimal residual disease (MRD). This is one of the first few trials in a randomized fashion comparing four drugs to three drugs. This is certainly widening the landscape of treatments available to us. Having said that, I do not think this regimen is that relevant to what we do in the United States, being an MPV-based data regimen. But it opens the door for approval in the upfront setting, which is a good thing. We are obviously eagerly awaiting the data from the MAIA trial which is more applicable to patients in the United States where lenalidomide-dexamethasone has been combined with daratumumab, and that is being compared to len-dex. Our hope is that we hear some of this data either later this year or early next year. All of those drugs which actually got approved in the relapsed setting – daratumumab, ixazomib, carfilzomib, elotuzumab – are all being studied more in the upfront setting. That is going to allow us to expand our horizon of what we have available for treatment. With that, I think the future for myeloma will be typically a quadruplet combination in the context of a clinical trial and that would be to drive down deep, deep responses. The depth of response hopefully is going to translate into survival benefit, which then is going to cure a subset of patients. Just having these drugs moved to the upfront setting is going to allow us a lot more flexibility, and our remission durations hopefully are going to continue to keep increasing to way beyond what they are today.