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Pomalidomide-Based Regimens in Early Relapse Multiple Myeloma

Announcer:
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Dr. Mikhael:
Hello, my name is Dr. Joseph Mikhael, and I'm going to be talking today about Pomalidomide-Based Regimens in Early Relapse Multiple Myeloma.

And when we think about early relapse in myeloma, we can divide patients into those who are LEN-refractory, and those who are LEN-sensitive. We can see here that the studies I'm going to highlight are primarily in lenalidomide-refractory patients.

Starting with the OPTIMISMM study, which is randomized study of adding pomalidomide with bortezomib and dexamethasone, versus bortezomib and dexamethasone alone. And this was an important study, because we definitely saw a significant improvement in progression-free survival in those patients that had the pomalidomide added to the bortezomib and dexamethasone, with a hazard ratio of 0.61. And so this is a commonly used regimen, even internationally.

The one that we see perhaps the greatest use in North America would be the APOLLO study, which took pomalidomide and dexamethasone, and now added daratumumab to it, versus pomalidomide and dexamethasone alone. And so in the APOLLO study in which patients were mostly had had at least one - all had had at least one prior line, although the majority had had two prior lines of therapy, we saw again that the triplet was superior to the doublet in progression-free survival by adding about 5 months to it with pomalidomide/dex being at 6.9 months, and the dara/pon/dex being a little over a year at 12.4 months. This was then followed up with the follow-up data at ASH in 2021 with a very similar outcome, where again, we saw this roughly 5-month benefit of adding the daratumumab to the pomalidomide and dexamethasone.

We also have a smaller MM014 study using daratumumab/pomalidomide/dex in the non-randomized fashion here in Cohort B, as you see, where these patients who had fewer lines, the majority were one or two prior lines. And in that situation, we saw a median PFS of actually up to 31 months. So we know that we can use pomalidomide in LEN-refractory patients, even in those who again were most recently LEN-refractory.

One of the largest phase 3 studies was adding a different CD38 antibody with isatuximab in the form of the ICARIA trial. So the ICARIA trial was a large phase 3 trial comparing isatuximab/pomalidomide/dex, versus pomalidomide/dex. Now, these patients had all had two prior lines of therapy, so they're a little bit further along than what we had just looked at. But again, we see this roughly 5- to 6-month benefit here of 6.5 months with pomalidomide and dexamethasone, to 11.5 months to the isatuximab plus pomalidomide and dexamethasone. And so we again see this recurring theme that we can use pomalidomide. And when we add a CD38 antibody to it, we see a benefit. Interestingly, in the ICARIA study, we actually now also see an overall survival analysis that was recently presented that demonstrates a benefit there from 17 months with pom/dex to about 24.5 months with isatuximab, pomalidomide, and dexamethasone.

And then, as we move to the ELOQUENT study, which is now adding elotuzumab to pomalidomide and dex, which we use more in this

context because we're using elotuzumab less with lenalidomide by virtue of how many patients are LEN-refractory, we also saw in this ELOQUENT-3 study, a benefit of adding the elotuzumab to the pom/dex, as opposed to pom/dex alone, as you can see here, with a hazard ratio of 0.54, and this actually also had an overall survival analysis that demonstrated the benefit of Epd, or elotuzumab/pom/dex, over pom/dex alone.

So trying to put this all together and we know in relapse disease, that ongoing therapy is better for patients. We know that we can use triplets to overcome what we would be able to achieve only with doublets, and we still can divide patients basically into those who are lenalidomide-refractory and those who are not lenalidomide-refractory.

In those LEN-sensitive patients that I didn't discuss today, we have several options like DRd, KRd, and even IRd as we use the LEN-sensitive - use lenalidomide in those patients. Or now we can see in LEN-refractory patients, we have options like PVd, DVd, DPd, as well as the isatuximab/pom/dex, daratumumab/carfilzomib/dex, and isatuximab/carfilzomib/dex, which we will discuss in another episode. And just as a last comment, as we manage these patients with pomalidomide, we know it has a very similar side effect profile to lenalidomide and we manage them in a similar way.

Announcer:
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