**Abstract 1886**

# Four-Year Follow-up of the Phase 3 POLLUX Study of Daratumumab Plus Lenalidomide, and Dexamethasone Versus Lenalidomide and Dexamethasone Alone in Relapsed or Refractory Multiple Myeloma

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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 study titled "Four-Year Follow-up of the Phase 3 POLLUX Study of Daratumumab Plus Lenalidomide, and Dexamethasone Versus Lenalidomide and Dexamethasone Alone in Relapsed or Refractory Multiple Myeloma."

So, as we begin to think about this study, it's important to realize the role of daratumumab in the treatment of myeloma. We've seen studies that had started in the five or more prior lines of therapy, the SIRIUS trial that was published several years ago. We then saw the CASTOR and the POLLUX trials with early presentation demonstrating significant benefit for the addition of daratumumab to standard treatment. And at this meeting, we are announcing a number of trials using daratumumab as part of initial induction therapy.

Remember, the rationale for combining these drugs together was that daratumumab clearly has an immune mechanism of action, lenalidomide, in addition to directly killing myeloma cells, also enhances immune activation, making it a nice synergistic partner with daratumumab. And what we've known for a couple of years now, was that the addition of Dara to Len/Dex versus Len/Dex significantly improved progression-free survival, overall response rate, and MRD negativity. What's being reported on at this meeting is an update of this trial. Again, 1 to 3 prior lines of therapy, triplet versus double-based therapy with a reasonable patient population that's been reported on previously.

So, what's being reported now was, again, a total of 569 patients were randomized to either Dara/Len/Dex or Len/Dex with a median follow up now of 51.3 months, and what we can see is that we finally hit the median progression-free survival for the Dara/Len/Dex group around 43 to 45 months, and the Len/Dex arm has not changed appreciably with a median PFS of about 17 months. Now, this high number for the Dara/Len/Dex arm in terms of PFS is actually one of the longest progression-free survivals we've ever seen in a relapsed myeloma trial, and in some situations is longer than the PFS that we see in the setting of newly diagnosed myeloma. So, certainly very exciting long-term follow-up data.

When we look at subgroups that may or may not have gotten benefit as measured by hazard ratio, patients that had one prior line of therapy versus more than one line of prior therapy, high-risk or standard-risk genetics all appear to benefit relatively similar, and this actually is

somewhat different, particularly in the high-risk group, than some of the induction trials that we've seen, where the high-risk group the hazard ratio seems to be not quite as good, as we've seen in the standard risks. So, this is really an interesting difference for many of those studies and a significant improvement in progression-free survival for patients who had also received prior lenalidomide or patients that were resistant to bortezomib.

So again, when we start to look at some of these numbers in terms of PFS benefit for the triplet combination, 38 versus 18 months for prior Len, refractory to bortezomib was 34 versus 11 months, and again, higher overall response rate of 93 versus 76%, CR rate of 57 versus 24%. So, in pretty much every category across the board, a significant improvement in progression-free survival, overall response rate, and depth of response rate. The follow up for overall survival is currently pending.

When we look at safety, deaths between the two arms were relatively similar, with a slightly higher incidence in the Len/Dex arm. Duration of treatment on average was about 34 months in the Dara/Len/Dex arm versus only 16 in the lenalidomide and Dex arm. The incidence of heme and non-heme toxicities, slightly higher in the Dara group, but that's not unexpected. And I think certainly a slightly higher incidence of infections we see is common for many of the daratumumab-based approaches and is the reason why we're usually very careful with antibiotic prophylaxis or treatment to try and address this overall.

So, I think what this actually gives us in terms of overall findings is that we now see the median progression-free survival has been reached. It's a really, really long progression-free survival that in many trials rivals the duration of response in induction trials at 44 months. This really significant improvement in PFS, I think speaks to why, at least at our center, the salvage regimen of choice is an immunomodulatory agent plus daratumumab; that's our go-to in first salvage. Patients who have not had lenalidomide or not refractory to lenalidomide, this POLLUX data is sort of our go-to regimen. And again, it's relatively well-tolerated, easy to give, and results in very long progression-free survival.

So, thank you again for your attention.