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Will I Be Able To Use CELMoDs® in IMiD-refractory Patients?

Announcer:
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Dr. Lonial:
Hello, my name is Sagar Lonial, and I'm from the Emory University School of Medicine in Atlanta, Georgia. And I will be talking about the topic, Will I be able to use CELMoDs in IMiD-refractory patients? So, I think it's important to look at clinical data, not just opinion, when we're thinking about how the CELMoDs may be active in the context of patients who've been exposed to or resistant to prior IMiD agents. And when we do this with Iberdomide for instance, in the expansion cohorts of Iberdomide plus dexamethasone, there were two Cohorts of patients that were evaluated. The first was Cohort D, where patients had to be refractory to an IMiD agent, a PI, a glucocorticoid, and an anti-CD38 monoclonal antibody, and then a second cohort, which is Cohort I, where basically they had to be resistant to a BCMA targeted therapy, in addition to having had three prior lines of therapy.

When we look at who these patients were in the CC-220-MM-001: Cohort D and I, what I think you'll see is that the prior lines of therapy is six and seven, which is reflective of a very highly active and refractory patient population in general. If you look at the percentage of patients that were triple class refractory, it was 97% in Cohort D, and 80% in Cohort I, and then specifically, if you look at IMiD-refractory 100% were IMiD-refractory in both Cohorts, with about 85 to 90% being resistant to either POM or LEN in both of these two Cohorts of patients.

When we begin to look at response rates in this, what you'll see in Cohort D is an overall response rate of about 26.2%, and in Cohort I, an overall response rate of about 25%. And this is for the use of iber plus dexamethasone. And what I think this clearly demonstrates is that even in patients who are refractory to prior IMiD, whether it's LEN or POM, or both, there clearly are subsets of patients that can respond to an oral CELLMoD in combination with dexamethasone, a pretty easy treatment to take in general.

Now let's switch gears to 92480, or mezigdomide, which is the other CELLMoD class of agents. And if you look at the 480-MM-001 clinical trial, you'll see again prior number of of therapies was six. If you look at prior LEN it was 97%, prior POM, it was 92%. If you look at IMiD-refractory, it was 89%. And LEN and POM refractory were in the seventies, high seventies, in terms of percentage of patients that were resistant.

If you then look at efficacy in the MM-001-480 trial, what you'll see for all patients is an overall response rate of about 21%. If you look at patients at the MTD, you'll see an overall response rate of about 40%. And then if you look at the recommended phase two Cohort, what you'll also see is an overall response rate of about 54%. And this further confirms the idea that the CELLMoD class of agents can in fact overcome prior resistance to the image class of agents specifically lenalidomide and pomelidomide.

So I think in terms of summary data, it's clear that the CELMods can be effective in the context of IMiD-refractory Patients. And cell line data clearly set this up from preclinical models where both iberdomide and mezigdomide are clearly active in LEN and POM resistant cell lines. This has been validated in clinical trials where patients whose whose myeloma was resistant to LEN and POM, clearly

responded to both mezigzomide or to either mezigdomide or CC-220. And this activity was confirmed in clinical trials. The real question is if a patient has immune function separate from the direct anti myeloma activity, can that also be overcome with these new drugs. And my suspicion based on very solid preclinical data, is that the answer to that is yes, but I think we need additional translational data from the early phase trials to really feel more confident in that data. But the take home message is that these can be active even in IMiD refractory patients. Thank you again for your attention.

Announcer:
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