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Iberdomide in Combination With Dexamethasone in Relapsed/Refractory Multiple Myeloma: Results From the Anti-BCMA-Exposed Cohort of the CC-220-MM-001 Trial

Announcer:
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Dr. Lonial:
Hello, I'm Dr. Sagar Lonial from the Emory University School of Medicine in Atlanta, Georgia and I'm going to spend the next few moments, talking about the presentation at ASH, evaluating iberdomide and dexamethasone in patients with relapsed and refractory myeloma, particularly focusing on the anti-BCMA-exposed cohort of patients in the CC-220-MM-001 clinical trial. As an introduction, iberdomide is a novel and potent oral CELMoD with greater tumoricidal and immune stimulatory effects, compared with the IMiDs, thalidomide, lenalidomide and pomalidomide. And the objective of this presentation, was to demonstrate the efficacy and safety of iberdomide and dexamethasone in an anti-BCMA-exposed expansion cohort, also known as Cohort I from the CC-220-MM-001 initial phase one study.

In terms of eligibility, what you'll see here, were that a total of 41 patients were enrolled with iberdomide given at 1.6 milligrams, days one through 21 on a 28-day cycle in combination with weekly dexamethasone. We also did pretty intensive PD and immunophenotyping during the treatment course of this cohort. You can see again the eligibility criteria, listed on the left with the primary endpoints being overall response rate and secondary endpoints being safety and additional efficacy endpoints. In terms of baseline characteristics, what you'll see is that the median age was in the sixties and that certainly a large number of these patients were exposed to a number of different stages.

I think it is important to recognize that about a third of these patients had high-risk genetics and about 20% of these patients had extramedullary disease at the time of study entry. If you look at prior therapies, what again I think you'll see, is a very heavily pretreated group of patients with a median of seven prior lines of therapy prior to entry into the study. They've been exposed to both LEN and POM at over 97%. And again if you look at what the anti-BCMA treatments were, about 40% had had prior CAR T-cell, about 30% had had a ADC and about 22% had had prior T-cell engagers.

So, a very balanced group of exposure across prior BCMA exposure. More importantly, if you begin to look at their resistance, you can see that 97% were refractory to IMiD agents, either lenalidomide or pomalidomide, 97% were refractory to PIs and about 85% were refractory to anti-CD38 with about 80% being triple-class refractory in aggregate. If you look at treatment-emergent adverse events, what I think you'll see, is consistent with other iberdmide clinical trials where you get mostly grade one, grade two, non-hematologic toxicities, we did see a little bit higher incidence of infections. And we know with a median of seven prior lines of therapy, infections certainly can be an issue or a concern.

But certainly fatigue, diarrhea, constipation or other IMiD-associated side effects were not noted at either grade three, grade four with any significant frequency. And there was some hematologic toxicity, but this is expected from this and is an on-target effect of this class

of agents and so not terribly a big surprise overall. When we look at response in cohort I, what you'll see is an overall response rate of 34.1% and when you look at the swimmer-lane plot, you'll see some patients certainly achieved deep responses with patients achieving complete remission, VGPR and that in many of these cases, they lasted beyond six to 12 months with a median DOR of 7.5 months and a median PFS of about 2.3 months in aggregate for this cohort.

If you look at the pharmacodynamics summary, what I think you'll see is that many patients did come in with an exhausted phenotype of T-cells and that the use of iberdomide and dexamethasone was able to reverse this. And this really has pretty significant implications for combinations, particularly with T-cell engagers or post-CAR T as a way to enhance efficacy of these agents and certainly does speak to the ability of iberdomide, not only to target myeloma cells, but also to target innate immunity and potentially reverse many of the markers that lead to drug resistance in this context.

In summary, we see that iberdomide and dexamethasone was well tolerated and induced meaningful clinical activity with an overall response rate of about 34.1%. These responses occurred in patients that have been exposed to BCMA-directed CAR T-cells, T-cell engagers and antibody drug conjugates, suggesting that the activity is retained, even after patients develop potential resistance to a BCMA-directed therapy. And more importantly, PD data suggests that iberdomide and dexamethasone, does remain immunostimulatory, even with a median of seven prior lines of therapy. This really does support additional phase three studies and combinations with other immune agents in the future. Thank you very much for your attention.

Announcer:
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