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How Effective Is CC-92480 Monotherapy or in Combination in RRMM?

Announcer:
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Dr. Patel:
Hello, my name is Krina Patel. I'm from UT MD Anderson Cancer Center in Houston, Texas. This presentation is on how effective is CC-92480 monotherapy or in combination in relapsed refractory multiple myeloma? So, just as a quick introduction. Again, CC-92480 has a unique and rapid degradation profile that stems from an enhanced efficiency to drive the formation of a protein-protein interaction between Ikaros and Aiolos and Cereblon. It is one of our CELMoDs.

So, here is the trial design for the phase one trial for CC-92480 with mezigdomide, which is the CC-92480 plus dexamethasone. So, basically these are patients who are relapsed refractory multiple myeloma and not really eligible for any other available therapies and had progression of disease within the 60 days or on last anti-myeloma therapy. And the primary endpoints, we're looking at PK and safety, as well as defining the RP2D dose. And secondary was assessing preliminary efficacy. So, there were a couple of different schedules they looked at. Continuous schedules were basically 10 out of 14 days oral regimen times two versus 21 out of 28 days. And then the more intensive schedules were three out of 14 days times two, versus seven out of 14 days times two. And then this was followed by part two, which was an expansion cohort.

So, in terms of the patient characteristics, the majority of these patients, about 76% had had prior transplant. The median lines of therapy was six, with a range of two to 13. And then in terms of patients who were refractory to lenalidomide was 73.7%. And then POM refractory was 78.9%. So, 89.5% of patients were IMiD agent refractory. And then you also had 69.7% that were CD38 refractory. And about 50% of patients were triple-class refractory. So on the next slide, you can see the efficacy results. So for patients, all evaluable patients, the response rate was 21.1%. For patients who got to the MTD, which was the 10 outta 14 days times two at one milligram daily, the overall response was 40%. Then for the patients who got to the RP2D dose, which was 11 patients, this was one milligram daily for 21 outta 28 days. The overall response rate was 54.5%. So, pretty impressive for a single agent or a doublet, I guess we can say.

In terms of treatment-related emergent AEs, neutropenia, grade three, four, about 64%. Febrile neutropenia, about 6, 7%. Anemia, 31.6%. And most of the other things were overall okay. Infections, again, 32, 34%. And neutropenia was managed with dose interruption and reduction as well as G-CSF. And dose reduction occurred in about 17 patients, but no patients actually discontinued due to treatment-related AE. So on the next slide, you can see the swimmer's plot for the responders by different dose levels. And you can see that even in the lower doses, there are patients who have responded and gone beyond cycle 12 with a deepening of response. So of course the deeper the response, it seems to have better long-term response, but again these are small numbers, so hopefully we'll have an update in the near future.

So, this is actually looking at a combination. So, we know that we have single agent activity. Usually it's going to be better when you put it with something else that we know has anti-myeloma activity, and that other drug usually ends up being bortezomib initially. So, this

was a phase 1/2 trial looking at mezigdomide and bortezomib plus DEX. So here again, study design shows relapsed refractory myeloma, but these were patients who had two to four prior regimens. They had to have had prior treatment with LEN and they had to have PD during or after the last anti-myeloma therapy. And primary endpoint again was getting the RP2D as well as preliminary efficacy. So, the phase one was dose escalation with different cohorts. So, cohort A was CC-92480 plus bortezomib-DEX. Cohort B, DARA-DEX. Cohort C, carfilzomib-DEX. Cohort H, ELO-DEX. And cohort I, ISA-DEX. So really, they were just looking at the phase one dose escalation of bortezomib-DEX in this discussion. So, the treatment schedule for the mezigdomide, really the dose escalation was from 0.3 to 0.6 to one. And bortezomib was at 1.3 milligrams per meter squared on days one, four, eight, and 11 for cycles one through eight, and then day one and eight for cycles nine and more. And oral DEX was given at 20 milligrams per day and 10 milligrams per day if greater than 75 on days one, two, four, five, eight, nine, 11, and 12 for cycles one through eight. And then for cycles nine and beyond, it was days one, two, eight, and nine.

These were refractory patients, higher lines of therapy. Here was a little bit less at three. 100% of patients had an IMiD. About 47% had POM. And looking at refractoriness, 78.9% of patients were refractory to LEN, 42% to POM, and triple-class refractory was 21% of patients. So again, looking at the swimmer's plot, here the overall response rate was 73.7%. And then the swimmer's plot on the right shows responses even at the lower dose, 0.3, and then you can see the 0.6 and one milligram. And median time to response was about 1.17 months, and median duration was 10.4 months.

So, take home point here. Mezigdomide in a doublet and triplet combinations is safe and has efficacy, even in IMiD refractory patients. So, something we are all looking forward to to be able to give our relapsed refractory multiple myeloma patients. Thank you for your attention.

Announcer:
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