Transcript Details

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https://reachmd.com/programs/cme/mezigdomide-cc-92480-a-potent-novel-cereblon-e3-ligase-modulator-combined-with-dexamethasone-in-patients-with-relapsedrefractory-multiple-myeloma-preliminary-results-from-the-dose-expansion-phase-of-the-cc-92480-mm-001-trial/14335/

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Mezigdomide (CC-92480), a Potent, Novel Cereblon E3 Ligase Modulator, Combined With Dexamethasone in Patients With Relapsed/Refractory Multiple Myeloma: Preliminary Results From the Dose-Expansion Phase of the CC-92480-MM-001 Trial

Announcer:
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Dr. Mateos:
Hello, my name is Maria Victoria Mateos from the University Hospital of Salamanca in Spain. And I would like to share with you the most recent information coming from mezigdomide in combination with dexamethasone in relapse and in refractory myeloma patients in a dose-expansion cohort of patients treated with this combination.

You know, mezigdomide is a novel, potent oral cereblon E3 ligase modulator with enhanced tumoricidal and immuno-stimulatory effects in comparison with the conventional IMiDs and preclinically, mezigdomide has demonstrated the synergistic effect with the dexamethasone, proteasome inhibitors, as well as anti-CD38 monoclonal antibodies. And mezigdomide was designed for maximal degradation of target proteins including Ikaros and Aiolos, leading to increased apoptosis in myeloma cells as well as immune stimulation.

In this study, in this dose-expansion cohort, 101 relapsing and refractory myeloma patients after at least three prior lines of therapy, all of them exposed to proteasome inhibitor, IMiDs, and anti-CD38, and refractory to the last line of therapy were included and treated with mezigdomide at a dose of one milligrams on days one to 21, followed by a week rest period with dexamethasone, 40 milligrams once per week. From the baseline characteristics point of view I would like to remark the median age is 67, but important to note that almost 40% of the patients presented plasmacytomas either extramedullary soft tissue only or soft tissue bone-related plasmacytomas.

And 36% of the patients presented with any high risk cytogenetical normality. The population was heavily pretreated and the median number of prior lines was six. All patients were triple-class exposed, and triple-class refractory. But I would like to remark that approximately 30% of the patients had been previously treated with BCMA-targeted therapy, including antibody-drug conjugate, CAR T, or T-cell engager. When we evaluated the patient disposition and the treatment exposure, it is important to see how approximately 10% of the patients do continue receiving treatment. And the main reason for discontinuation in the patients who had to discontinue the study has been a progressive disease and there were few patients who discontinued or died because of adverse events.

From the hematological point of view neutropenia is the most frequent hematological adverse event reported in this study. And from the non-hematological point of view, infections including pneumonia and some patients with COVID-19 was the most frequent adverse event. However, when we focus on other non-hematological adverse events like gastrointestinal toxicity, asthenia, fatigue, decreased appetite, or insomnia, they had been reported only in few patients with this combination.

The primary endpoint of this study has been overall response rate and in the all patient population the overall response rate was 40.6%

with some patients even achieving complete response and a stringent complete response.

But it's important to see how in the patients with plasmacytoma, remember 30% of the patients presented with any type of plasmacytoma, the efficacy was maintained with an overall response rate of 30% and the same is applicable to the 30% of the patients who had been previously exposed to BCMA-targeted therapy and the overall response rate was 50%, again with some patients achieving complete response or a stringent complete response and this is extremely important because the population exposed to PI, IMiDs, and CD38 and in addition the BCMA-targeted therapies, the new unmet medical need and mezigdomide and dexamethasone covered this unmet medical population with an overall response rate of 50%.

In terms of a progression-free survival, the medium PFS has been a 4.4 months. What it's good medium PFS for the heavily per treated population. And in terms of durability of the response, we focus on the 40% of the patients who responded, the median durability was almost eight months, and if we focus on those patients who achieve at least VGPR rate, the durability of the response was 9.2 months. From the pharmacodynamic point of view, it has been also observed how the treatment with mezigdomide plus dexamethasone resulted into an increase in the NK cells as well as the T-cell proliferation, as well as a decrease in the Aiolos, Ikaros that they are the targets for mezigdomide in this case the potency in combination with dexamethasone.

So in summary I think mezigdomide plus dexamethasone showed encouraging efficacy and safety results in heavily pretreated relapse and refractory myeloma patients including patients with extramedullary disease and including patients already exposed to the BCMA-targeted therapy and mezigdomide is currently ongoing, being evaluated in combination with standard therapies in myeloma and there are phase three clinical trials ongoing, evaluating mezigdomide in combination with bortezomib and carfilzomib and are currently enrolling patients. Thank you very much for your attention.

Announcer:
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