Preliminary Results from the Phase 2 Study of the IDH2 Inhibitor, Enasidenib in Patients with High-Risk IDH2 Myelodysplastic Syndromes

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Welcome to *Managing Myelodysplastic Syndrome*. I'm Dr. Eytan Stein, and I'm live at the 61st ASH conference in Orlando, Florida. Today I will be reviewing Abstract 678, which is the data recently reported on the Preliminary Results from the Phase 2 Study of the IDH2 Inhibitor, Enasidenib in Patients with High-Risk IDH2 Myelodysplastic Syndromes. I think it's important for the audience to know that IDH2 mutations, although they are more common in patients who have acute myeloid leukemia, they do occur in approximately 5% of patients who have myelodysplastic syndromes, and because of that it is important at the time of diagnosis of MDS to test for mutations that might be targetable with specific inhibitors such as enasidenib, the inhibitor of mutant IDH2. There was a very small study that was done as part of the initial approval study for enasidenib where about 17 patients with mutations in IDH2 and myelodysplastic syndrome were given the IDH2 inhibitor enasidenib, and the results in that very, very small sort of subset of the original phase 1/2 trial was relatively positive with about 50% of patients having a complete remission or hematologic improvement. This clinical trial builds on that data and this is an early analysis of a new trial where enasidenib is being given, both as a single agent in patients with IDH2 mutations and in combination with azacitidine in patients with IDH2 mutations. What this trial has found to date is that the combination and the drug as a single agent has been very, very safe. It seems to be very effective, with an overall response rate in the combined data set of 67% in the published abstract. There have not been any new adverse events that have been observed giving enasidenib to patients with myelodysplastic syndromes. One concern that I think we always have with drugs like enasidenib, that are what's called differentiation agents, is that these drugs, especially in patients with high blast percentages (with MDS, they're going to have blast percentages up to 20%), that as those cells are differentiating, a patient might develop a differentiation syndrome. In this trial, that has not been a particularly big issue; however, it is possible that patients can develop a differentiation syndrome, and because of that, it is important to be cognizant that if a patient comes in and says that they're short of breath, they've got a little bit of leg swelling, they've got fevers, that will be something that might tip you off that they might have differentiation syndrome and you should do an evaluation to be sure that they do not. I think the key points for practitioners in the community are that enasidenib is not yet approved for patients with myelodysplastic syndrome; however, these clinical trials, especially this clinical trial that is ongoing, will hopefully provide the data so that if a physician has a patient with myelodysplastic

syndrome, that ultimately will be able to give this drug to patients with myelodysplastic syndromes that have an IDH2 mutation. Thank you very much for your attention.

Reference: Richard-Carpentier G, et al. Preliminary Results from the Phase II Study of the IDH2-Inhibitor Enasidenib in Patients with High-Risk IDH2-Mutated Myelodysplastic Syndromes (MDS). Abstract 678. ASH 2019.
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