Differentiation syndrome associated with enasidenib, a selective inhibitor mutant of isocitrate dehydrogenase 2

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I want to discuss is an abstract entitled, "**Differentiation syndrome associated with enasidenib, a selective inhibitor of mutant isocitrate dehydrogenase 2**." My name again is Eytan Stein, and this is an interesting abstract for the following reason. We have noted that in patients treated with enasidenib, which is the IDH2 inhibitor, there is a subset of patients who as the leukemia cells that are mutant and frozen in an undifferentiated state, start to differentiate. There is a group of patients who will weight gain, shortness of breath, overall fluid accumulation, sometimes purulent pericardial effusions which is very, very reminiscent of what we see in acute promyelocytic leukemia in patients treated with all-trans-retinoic acid or ATRA where we call that a differentiation syndrome. As these cells are being unfrozen from their immature state and starting to differentiate, those cells, probably through cytokine release, lead to a noncardiogenic pulmonary and pulmonary edema and a capillary leak syndrome where patients have the symptoms I described previously. We were interested because we saw that occur in a few patients treated with enasidenib. We were interested in getting a better idea of how many patients this occurred in. A Differentiation Syndrome Review Committee was established that really went over two things in the patients treated on the larger enasidenib relapsed/refractory clinical trial. They went over all of the cases where the local investigator reported signs and symptoms experienced by the patients in differentiation syndrome. They also went over cases that came from the clinical database where there were symptoms that could have been attributed to differentiation syndrome but maybe were not by the study investigator. For example, this Differentiation Syndrome Review Committee looked at all patients who might have had pleural effusions or pulmonary infiltrates, really to adjudicate whether the committee thought that this was a sign and symptom of a differentiation syndrome which had not been picked up by the local study investigator. DSRC (Differentiation Syndrome Review Committee) did a lot of work and ultimately what came out of this work was that approximately 10% of patients who were treated with enasidenib had a differentiation syndrome. There were no good predictors of who was likely to develop differentiation syndrome and who was not. We are looking at that a little bit more closely now to try to tease out whether we can predict who is going to develop differentiation syndrome. Then perhaps most importantly when this differentiation syndrome was identified early, the treatment of it, which is 10 mg of the steroid dexamethasone twice a day, was extremely effective in reversing this differentiation syndrome. The take-home from this abstract is that the patients who get treated with enasidenib, their physicians need to look out for this differentiation syndrome and at the first sign that they might have this differentiation syndrome treat them as they would for a patient with acute promyelocytic leukemia with dexamethasone 10 mg twice a day.