Combined Treatment with Lenalidomide and Epoetin Alfa Leads to Durable Responses in Patients with Epo-Refractory, Lower Risk Non-Deletion 5q [Del(5q)] MDS: Final Results of the E2905 Intergroup Phase III Study - an ECOG-ACRIN Cancer Research Group Study

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Welcome to *Managing MDS.* My name is Dr. Alan List and I am live at the 61st Annual ASH Conference in Orlando, Florida. Today I'll be reviewing the findings presented during an oral session, which looked at combined treatment with lenalidomide and epoetin alpha and the durable responses in patients with EPO-refractory lower-risk non-del(5q) MDS. This presentation included the final results of the E2905 Intergroup phase 3 study. As a bit of background for this study, when patients fail recombinant erythropoietin or what we consider ESAs, we had no firm second-line therapy. Things that are considered are treatments with the hypomethylating agents or lenalidomide. In that situation, lenalidomide alone will improve transfusion dependence and eliminate need for transfusions in roughly 25% of patients. What we do know is lenalidomide acts very differently in non-del(5q) bone marrows than it does in patients with deletion(5q) MDS. In the ladder, it will kill that population of cells by virtue of synthetic lethality. However, in non-del(5q) MDS, it inhibits a specific enzyme called ubiquitin kinase that will enhance erythropoietin receptor signaling, and that was the rationale for combining this with epoetin alpha in people who had failed prior treatment with ESAs.

In this study, patients who received the combination had a superior response rate, what we considered a major erythroid response that was defined by elimination of the need for transfusions and having a 2-gram or greater rise in hemoglobin, and overall 28% in the combination achieved that major erythroid response compared to 11.5% of patients that were treated with lenalidomide. Patients who've had a what we call minor erythroid response or those who had a 1-gram to 2-gram rise in hemoglobin or a 4-unit reduction in transfusions and overall, the response rate, major and minor, was over 50% in patients in the combination and just 40% in patients receiving lenalidomide. What was so impactful about this study was the durability of these responses. Those major erythroid responses that we saw in the combination lasted for a median of two years, whereas with lenalidomide, that response duration was only 13 months. So, the final results of the study are the fact that we have a good alternative for the treatment of patients with lower-risk MDS once they have failed treatment with an ESA. The combination, by adding lenalidomide to the ESA, gives approximately a 50% response rate that can last for a median of two years or longer.

Reference: List AF, et al. Combined Treatment with Lenalidomide and Epoetin Alfa Leads to Durable Responses in Patients with Epo-Refractory, Lower Risk Non-Deletion 5q [Del(5q)] MDS: Final Results of the E2905 Intergroup Phase III Study - an ECOG-ACRIN Cancer Research Group Study, Grant CA180820, and the National Cancer Institute of the National Institutes of Health. Abstract 842. ASH 2019.
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