The Challenge of p53 Mutations in Treating AML

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I wanted to talk a little bit about the results that I'm most excited about at this year's ASH Annual Meeting. I think one of the trials that we're really very eager to hear about is the results of a trial combining a drug called APR-246 with the hypomethylating agent azacitidine. The reason this is exciting is because, as all oncologists know, having a p53 mutation, whether you've got acute myeloid leukemia or whether you've got ovarian cancer or breast cancer or any other kind of cancer, it portends a poor prognosis. APR-246 is a small molecule drug that is said to reactivate mutant p53. So, you take p53 that's mutant, you give patients this drug, APR-246, and through a variety of mechanisms, some of which have been worked out, some of which I think more study needs to be done, is said to sort of cause that mutant p53 protein to become normal again. And when that mutant p53 protein becomes normal again, it can exert its influence to kill malignant cells. In this study that's being presented at this year's ASH Annual Meeting, the combination of APR-246 with azacitidine has led to an overall response rate in the mid-80% range, that's really very, very high, and very, very exciting. One thing that we're a little concerned about with APR-246 is that one of the side effects that patients have is neuropathy, and that's something that can obviously be problematic for patients. The thing that's really going to get us excited are when the results of a randomized phase 3 trial that are randomizing MDS patients to APR-246 with azacitidine or to azacitidine alone are reported, and hopefully that's going to be reported within the next couple of years.