Rami S. Komrokji, MD
Professor of Medicine and Oncologic Sciences
University of South Florida College of Medicine
Vice Chair, Malignant Hematology Department
Moffitt Cancer Center
Tampa, Florida

What is the clinical significance of SF3B1 in MDS and what are the key points I need to be aware of to determine treatment and outcome of these patients?

Hi, I'm Dr. Rami Komrokji, and I'm frequently asked, what is the clinical significance of SF3B1 somatic mutation in MDS, and what are the key points I need to be aware of to determine treatment and outcome for those patients? I think that's a very good question. Obviously, we know that splicing mutations are enriched in MDS patients. We know that SF3B1 has a genotype/phenotype association with patients with MDS ring sideroblasts. Now the International Working Group is moving, probably, in the near future to have a unique entity of SF3B1 mutated MDS patients. We know that the SF3B1 mutation is a driver mutation in MDS. It's probably a disease initiating mutation that happens early on, often observed unknown. It can help us establishing the diagnosis. When we see SF3B1 nowadays by the WHO criteria if the ring sideroblasts are more than 5%, one could call diagnosis of MDS with ring sideroblasts. SF3B1 has a prognostic significance. It's the only somatic mutation in MDS associated with favorable outcome when we don't have excess blasts and in absence of complex or karyotype or chromosome 5 or 7 or 3 abnormalities, so it can help with the diagnosis. It's part of the WHO criteria now to classify patients with ring sideroblasts. It also has a very important prognostic influence, and also nowadays, it's used to tailor therapy for those patients. As you know, luspatercept is the first drug approved by the FDA for patients with MDS in the last decade, particularly for patients with ring sideroblasts where we happen to see 80% to 90% of the patients having SF3B1 mutation. Also, some promising treatments like imetelstat is showing promising activity in patients with SF3B1 mutation. From small series, we know for example, that patients with SF3B1 mutation don't do well with immunosuppressive therapy. Nowadays, we know that SF3B1 is important in diagnosis and establishing or predicting outcome for those patients. Maybe now we have options for treatment of patients with SF3B1 mutation particularly, namely luspatercept and hopefully in the near future imetelstat if the phase 3 trial is positive in that population.