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

I'm Dr. Rami Komrokji from Moffitt Cancer Center answering the following question related to myeloproliferative neoplasms.

Where do Janus kinase inhibitors (JAK inhibitors) fit in the treatment of myelofibrosis, for whom and when?

Ruxolitinib, or Jakafi®, has been approved for several years for patients with myelofibrosis. And fortunately, recently we had the approval of the second drug, fedratinib, for treatment of myelofibrosis.

JAK2 inhibitors in general are used for patients with intermediate-risk and high-risk myelofibrosis who are symptomatic, namely with spleen enlargement or spleen-related symptoms or constitutional symptoms including fatigue, weight loss, night sweats, bone pains, and so forth. Ruxolitinib had been shown to be better than best available therapy or hydrea in terms of spleen reduction and symptom control, and there had been indirect suggestions that obviously it improves the survival for patients because they feel better. They do better. So usually the JAK2 inhibitors are reserved for patients that are symptomatic with spleen or constitutional symptoms. And we do observe improvement in the patients' quality of life, potentially driving survival advantage of those treatments.

Again, until now we only had ruxolitinib approved as a first line. Recently fedratinib was approved. This can be used in patients upfront or after ruxolitinib failure. The use for fedratinib in second-line had been based on a phase 2 study that looked at patients after ruxolitinib failure, and there were responses observed. Following certain stringent criteria similar to the recent criteria used in clinical studies defining ruxolitinib failure, which is basically either a primary failure of response or loss of response later on with the spleen and symptoms coming back or being intolerant, having low blood counts and cytopenias that are persistent, fedratinib had almost 30% responses in those patients after ruxolitinib failure.