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.

What are the next steps in myelofibrosis research?

That's obviously a large topic. I think we've made important understanding of the disease in the past decade. Unrevealing the biology of the disease, we know now about the main driver mutations such as JAK2, calreticulin (CALR), or MPL mutations. We know about the impact of other mutations on the outcome, mutations in genes called ASXL1 or SRSF2 with worse outcome, certain mutations like IDH1 or IDH2 are predictive of disease progression to leukemia.

If we are in better shape understanding the biology of the disease, the next steps in research obviously still continue to explore treatment for patients, although ruxolitinib had been a major improvement for patients, it works for a few years and then stops working. So there is definitely unmet need for patients after ruxolitinib failure. Our group and our colleagues from MD Anderson had published data on ruxolitinib failure that, unfortunately, the average survival is 14 month after ruxolitinib failure with lack of really good options of treatment. Fedratinib hopefully now will become one of those options available for the patients immediately. There are a couple of other JAK2 inhibitors in development: pacritinib, which could be particularly useful for patients with low blood counts, especially severe thrombocytopenia; and momelotinib, which could be helpful for patients with anemia.

And there are many clinical trials ongoing exploring agents, either as we call as “add back strategy,” so continuing the ruxolitinib or the fedratinib and adding those medications or using them after ruxolitinib failure; a drug called imetelstat had been tested recently in a phase 2 with two different doses, on the higher dose the 9.4 mg/kg. Although the responses were not high, there was a signal of improved survival for patients where the median overall survival on the study was approaching almost 30 months compared to the historical control that I just mentioned of 14 months. So that drug is further tested. There are several other drugs tested. One of the interesting drugs are called BET inhibitors. There were some initial reports presented again recently at the European Hematology meeting, and we will have more data presented at the American Society of Hematology.

And again, there are different classes of drugs - MDM2 inhibitors, as I mentioned telomerase inhibitors, BET inhibitors. Sometimes we do combinations of treatments, so there are studies looking at ruxolitinib plus thalidomide to alleviate some of the cytopenias. As I mentioned,

luspatercept is a drug that's going to be approved for MDS and is being tested in myelofibrosis for patients with anemia, so there are several ongoing studies.

One thing to mention obviously also, interferon had been used for all patients with myeloproliferative diseases. There are newer formats of interferon, PEGASYS (peginterferon alfa-2a) that we use and another one called ropeginterferon that had been approved in Europe for patients with polycythemia vera (PV) and essential thrombocytopenia (ET) that also would probably be tested in patients with myelofibrosis. I think with our understanding of the underlying biology, I'm excited about all those clinical trials going on and hopefully we'll be able to improve patient outcome and get many of those medications in the near future for our patients.