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

Using a patient-centered approach, how do you determine the best treatment options for each patient?

So we are talking mostly myelofibrosis, that there are a couple of important steps in management. The first thing is really assuring the diagnosis because not every fibrosis which is a description of scarring is myelofibrosis. We can see that with other blood diseases such as CML, which is highly treatable and potentially curable with treatment like imatinib or tyrosine kinase inhibitors. We can see fibrosis with myelodysplastic syndrome. We can see the reactive fibrosis in patients with connective tissue disease or from medications. So we really spend some time making sure that the diagnosis is the correct diagnosis for patients.

The next step is really gauging the risk of the disease because the only curative option we have for patients with myelofibrosis is allogeneic stem cell transplant, which cures around half of the patients, but the procedure itself has around 20% transplant-related mortality. We are always weighing the benefits and the risk of the procedure. I always say, you have to have a bad disease to justify a bad or intense procedure. So we gauge the risk of the disease to try to decide whether we are going to proceed to transplant or not. We do that by looking at several variables, clinical variables, if patients are symptomatic, their blood counts, the blast percentage, and also some more in-depth analysis of the chromosome makeup of the cells. Nowadays we do something called somatic gene mutation testing where we look at molecular mutations. There are several models used for myelofibrosis, clinical things called IPSS, International Prognostic Scoring System, or DIPSS, DIPSS Plus, and there are some of them that are also enriched by molecular data such as genetically inspired model or MIPSS.

So we input all that information and we put the patient in a risk group. Those that will come at an intermediate- to high-risk if they have no major comorbidities and if they are functional, we are going to be thinking of transplant. If patients with myelofibrosis are lower risk and they are totally asymptomatic, then observation is acceptable because we have no evidence that we can alter the natural history intervening so early, with maybe one exception - in younger patients if they are in good shape, sometimes we try interferon therapies because that could reverse the natural history. For the rest of the patients, if they are not going to transplant or if they are symptomatic, the treatment is really symptom-based. For those with splenomegaly constitutional symptoms, JAK2 inhibitors had become the standard. A certain number of patients, the main problem when

they present to us is really low blood counts, and for those patients if they have anemias or cytopenias we try different things, including erythropoietin stimulating agents injections like Procrit. We try sometimes steroids, anabolic steroids like danazol, thalidomide, or lenalidomide are used in that setting, and there are clinical trials going on with the drug called luspatercept for treatment of anemia in myelofibrosis. Now even patients going to transplant sometimes, unfortunately with the nature of the disease are sick. They have a lot of constitutional symptoms. They've lost weight. Their spleen is big. So we start patients on ruxolitinib because that improves their performance status, and we use that as a bridge to take patients to the transplant if they are eligible to go to transplant.