As a clinician, what should guide my decision on which second-line therapy to choose for my patients?

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We have more and more therapies available for our patients, we already have three approved drugs, ruxolitinib, fedratinib, and pacritinib. Momelotinib is believed to be close to approval. Most of us at least think so based on the MOMENTUM data and the previous SIMPLIFY studies. Obviously, the space is getting crowded. A question that comes up is, “How do we decide what to do second-line or when do we think we need a second line agent after ruxolitinib?”

I think the way I look at this is that starting with fedratinib, since that was the first one approved, it has really nice data for spleen and symptoms in the second-line setting. As far as I know, probably as good as anything else that is out there in the second-line setting for spleen and symptoms. For a more proliferative patient, and again, that is not easy to define in exact numbers for platelets, hemoglobin, et cetera. For someone with robust counts, I think fedratinib should be the way to go in the second line setting based on the data that we have from JAKARTA-2 even after the re-analysis.

However, we do often encounter cytopenias in the second-line setting. I actually think that's probably more common than splenic progression or symptom progression with preserved counts. I think the cytopenias are a bigger problem. Then of course, we have pacritinib already approved. We have momelotinib likely coming. I think we again have good data based on PERSIST-2, for example, where the platelet count could be up to 100. Now as a quick reminder the label for pacritinib is less than 50 but PERSIST-2 to did include patients all the way up to 100. We have some good second-line data there.

I think the thrust here is on being able to use the full dose of a drug in the face of cytopenias where we know we have to reduce the dose of ruxolitinib with drugs like pacritinib, momelotinib and actually also fedratinib in that 50 to 100 space, we're able to give the full dose. I think those are some of the considerations that are going to apply based on the blood count and based on what kind of progression we're talking about.

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