**What key defining point should community providers be aware of when looking at patients considered to have failed ruxolitinib or have achieved only suboptimal response?**

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There are various definitions in clinical trials as it relates to eligibility for ruxolitinib failure and that could be a progression or loss of response or even patients who have suboptimal response in which there's add-on strategies to ruxolitinib. We've talked previously and this will continue to be a somewhat of a dilemma is, “How does that translate into the community setting and how should community practitioners be viewing their patients who are receiving ruxolitinib in order to determine whether it is in the best interest to continue the drug or maybe even increase the dose of ruxolitinib or make a decision to switch to an alternative therapy or a combination strategy?”

The reality is that right now, it's not a uniformed definition. Perhaps it doesn't need to be uniform. I think maybe, more importantly, is to impress upon the community practitioner to simply be aware of the fact that there are other alternative options for patients with myelofibrosis on ruxolitinib. If you see that a patient has not, or is no longer enjoying on the same degree of spleen benefit in terms of palpable spleen or symptom burden, or is developing progressive cytopenias, that really should be an indication to be more critical about the decision-making of continuing someone on ruxolitinib or considering switching over to commercial options like fedratinib, pacritinib, and perhaps momelotinib at some point or referral to a tertiary center for consideration for transplantation or one of these novel clinical trials that are either in phase one, two or three testing.

I think when the era of having only ruxolitinib which is an excellent drug, but only having that available, it was sort of a moot point. One would treat until you really couldn't get any benefit out of ruxolitinib. As we've seen that the outcomes are pretty poor at that point. I think now with so many different options available and emerging, it's really important for the practitioner in the community to simply be aware of that fact and to try to optimize the dose of ruxolitinib and be prepared to switch the therapy in a dynamic fashion when they see either a suboptimal response in spleen symptom or progressive spleen and symptom burden or cytopenias.

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