Do Genetic Mutations in MPNs Affect Treatment Choices?

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Andrew Schorr:
Dr. Komrokji, so there are subsets that you're identifying of people with these conditions based on genetic markers that you're learning about. We've heard about JAK2. Some people have heard about calreticulin.

There are a few others now you're identifying. And that seems to continue. So when we break these down to people who have maybe a different course that you can identify and, ultimately, different treatments, even within a myelofibrosis group or an ET group or a PV group.

Dr. Komrokji:
Right. So I think, first, the point also is that those tests also make us be able to make a more firm diagnosis, because each of those diseases could mimic other things. And I think I always say the first step is really to step back and to think about the diagnosis, because we've seen all cases that were diagnosed as myelofibrosis or essential thrombocythemia, and they were not. So those tests definitely help us now in diagnosis. They, in a way, exclude sometimes reactive process.

So if somebody has a JAK2 mutation, it's unlikely to be a reactive process that the platelets are high. So they have definitely important diagnostic value.

And they, obviously, could be in the future a way to tailor treatment according to those mutations. But, for example, at this point, patients, even if they don't have the JAK2 mutation, they could respond to some of the treatments, because it's a little bit more complicated than that.

It's not just a mutation or the abnormality in the receptor or the antenna. It's really the whole pathway is overactivated. So it could be from a mutation. It could be just from so [many] signals coming to that.

Andrew Schorr:
And that's why some people, you have one approved drug, ruxolitinib (Jakafi) for myelofibrosis right now and maybe others coming. So it's not only whether you're JAK2 positive.

Sometimes, those medicines work even if you're not, right?

Dr. Komrokji:

Right. Again, because you could think of it—when we talk about those things, we are talking about like the JAK2 or the mutations. I always tell the patients to think of them like a switch that usually somebody would have to go and turn the switch on for the light to go on and the signals to go. And the switch is turned on all the time. But it could be turned on, because also there are so many people coming and turning that switch on. It's not just always that the switch is not working normally. So they could work. Now, down the road, we could find different things. So we could find a subset of patients that respond to one of those JAK2 inhibitors better than the other.

We could have certain abnormalities, if we figure them all out, that we can go after them with newer targeted therapy.

In terms of those abnormalities or mutations predicting the course of the disease, they also could have some value. So we are learning that if somebody has a certain mutation like calreticulin, those patients probably could do it a bit better. If patients don't have any mutation, those could have a little bit more difficult course. There are some data that suggests like, even in polycythemia vera, if patients have the two switches of the JAK2 hit, those patients could be attributed to higher risk to go to myelofibrosis down the road. So we are learning about this.