What Are the Goals of Myelofibrosis Treatment?

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Andrew Schorr:

I have a question just related to that. So, those of us with myelofibrosis, and all of you understand now there's scarring that's happened in the bone marrow, is that the goal of treatment to reduce the scarring? Or is it reduce JAK/STAT or you know?

Dr. Scott:

The goal of treatment should be based on patient-oriented outcomes. So, you know, I think, it's my opinion, that fibrosis is in essence a secondary end point or the poor surrogate marker. First of all, fibrosis is patchy. It's not confluent throughout your body. So, you can have differences in the degree of fibrosis depending where you do the bone marrow biopsy.

So I think you have to take with some level of caution the studies that have said, okay, this drug decreases fibrosis. I always think in the back of my mind how many biopsies did they have to do before they found one with a lower degree of fibrosis, I jokingly say to myself, but it is patchy.

So I think it's very difficult to design clinical trials with the primary end point of decreasing fibrosis. And, for me, I think it's important to have clinically oriented end points like survival, like improvement in quality of life, like reduction in spleen size.

To me, these are more important end points than degree of fibrosis, one, because it's hard to measure and, two, I'm not certain that there's a direct correlation between patient outcome and degree of fibrosis anyway.

If you look at all of our scoring systems, like the DIPSS scoring systems or the IPSS scoring system, none of those scoring systems that we use to measure survival is degree of fibrosis. And I think that has to do with the fact that it's patchy, and it's variable, and also between pathologists, there can be disagreement about degrees of fibrosis.

Andrew Schorr:

And correct me if I'm wrong, but at ASH, the American Society of Hematology meeting, in every December it's like the World Series for these guys. And they all are players there. And that's where all the big studies come out, early every December for our conditions, staked in what's going on.

There was the COMFORT-II data that said that with ruxolitinib (Jakafi), I believe there was an indication of increased survival. Am I right?

Dr. Scott:

Yeah. So, with both COMFORT-I and COMFORT-II, which are the two major trials that have been done with ruxolitinib, there was a benefit in survival. That was not the primary endpoint for either one of those studies. It was a secondary endpoint for both of those studies. But, there was a survival benefit for both COMFORT-I and COMFORT-II.

You could mention a lot about this because it's really complicated when you discuss it because both of these studies also allowed for crossover. And crossover basically means, okay, if you get randomized to the arm that didn't have ruxolitinib, at some later point you can crossover to get the ruxolitinib.

So when you start getting further and further out from these studies, you're essentially comparing early ruxolitinib to later ruxolitinib. And, so, what you would anticipate is that the survival curves would start to come together because essentially after crossover all patients are receiving the ruxolitinib.

Andrew Schorr:

Okay. It gets complicated which is why you need a specialist on your team.