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How and When to Manage Ruxolitinib Failure

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Mascarenhas:
This is CME on ReachMD, and I'm Dr. John Mascarenhas. Today, I'm reviewing how to recognize and manage ruxolitinib failure when treating patients with myelofibrosis.

So reasons for stopping ruxolitinib, which happens at about a median of 3 years, are varied, but one of the leading causes is anemia and worsening anemia and the need for transfusion dependence, but also includes disease progression and suboptimal response in some patients and frank transformation to AML [acute myeloid leukemia] in about 1/4 of patients.

We know that through multiple trials that have been done prospectively, but also from retrospective real-world data, that between 2 and 3 years, half the patients have discontinued treatment. And the treatment and the outcomes of those patients when they discontinue is, unfortunately, quite dismal. We know from the COMFORT studies that dose matters. So the dose of ruxolitinib can be tied into the depth of spleen reduction, not so much symptom, improvement, which usually maxes out at 10 mg twice daily. But the greater the dose, the greater the spleen reduction. And there is some data that would suggest the greater the spleen reduction, the better the overall outcome in terms of survival. So that's something to consider when treating patients and maximizing their dosing.

As I mentioned, when patients do discontinue ruxolitinib for any one of those reasons, but particularly for worsening cytopenias, the median survival is, unfortunately, pretty poor and ranges between 12 and 14 months over multiple, studies. It's even worse in patients who start with low platelets, end with low platelets, or have clonal evolution, which the survival can be less than a year.

There are prognostic tools that can be used, like the RR6 model, to prognosticate on outcomes such like survival in the first 6 months of ruxolitinib use. And this includes the need for red cell transfusions at baseline, 3 months, and 6 months, spleen reduction of less than 30% after 3 months and 6 months, or rux doses less than 20 mg twice daily at start, 3, and 6 months, which I would say is the majority of patients that are treated with ruxolitinib. One can use the RR6 model online at www.rr6.edu and it gives you a sense, generally speaking, within the first 6 months where your patient with ruxolitinib is expected to fall from a survival perspective. This could help make a determination of optimal timing for transitioning to transplant, for example, or even considering second line or salvage clinical trial options. So one must be aware of the fact that ruxolitinib, although great at improving spleen symptoms, does not usually address anemia. That can be a leading cause for discontinuation, and discontinuation in half the patients occurs around 3 years. And when patients discontinue, their outcomes tend to be poor, and therefore one needs a plan in place, and that's where a model like RR6 may be helpful to determine the next therapeutic changes, whether it's sequencing to another JAK inhibitor, add-on strategies, clinical trial options, or even transplant.

So in summary, anemia is one of the leading causes for discontinuation of ruxolitinib. The median time to discontinuation of ruxolitinib is

about 2 to 3 years. Dose matters for ruxolitinib, so higher doses afford better spleen reduction, which is associated with better outcome. And when patients discontinue ruxolitinib, unfortunately, their outcome is poor. So one wants to maximize JAK inhibition

with ruxolitinib by optimizing the dose. And the RR6 model, which was based off the RUXOREL study, can be used within the first 6 months of treatment, using red cell transfusion dependence, spleen reduction, and dose of rux to predict for survival for those patients treated with ruxolitinib.

Our time is up. I hope this information will be useful for you in your clinical practice. Thanks for listening.

Announcer:
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