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Investigating the Impact of Momelotinib on Myelofibrosis Patients: A Poster from ASH

**Announcer:**
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by GSK. Here's your host, Dr. Charles Turck.

**Dr. Turck:**
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss a poster she co-authored and presented at the 2022 American Society of Hematology's Annual Meeting and Exposition that evaluated the patient-reported outcomes of momelotinib is Dr. Mary Frances McMullin. Dr. McMullin is a Professor of Hematology at Queens University Belfast. Dr. McMullin, thanks for joining us today.

**Dr. McMullin:**
Thank you very much for the invitation to discuss this exciting poster.

**Dr. Turck:**
So to start us off, Dr. McMullin, would you give us a brief overview of the Momentum study, including the overall objective?

**Dr. McMullin:**
Okay, so Momentum is a randomized, placebo-controlled trial comparing momelotinib to best available care for the management of anemia. Momelotinib is a JAK2 and an AVCR inhibitor and therefore is thought to be of benefit, not just in controlling spleen size and symptoms but also because of the AVCR mechanism that may help to improve the anemia. And this was a trial to try and document that this was better for the treatment of myelofibrosis. Now the primary outcome was to look to see if there was a greater than 50 percent improvement in symptoms, in particular using MFSAF—the symptom scoring index—and it was looking at that as the primary outcome.

**Dr. Turck:**
So with that purpose and primary outcome in mind, what else can you tell us about any key aspects of the design, the secondary endpoints, and the methods of the study?

**Dr. McMullin:**
So the design was a randomized, placebo-controlled trial with a 2:1 randomization between momelotinib and danazol, which was in the other arm. The placebo-controlled mechanism was interesting because it was momelotinib plus placebo or danazol plus placebo. So therefore, every patient was getting a placebo which mimicked the other treatment. That was 2:1 in favor of momelotinib versus danazol. There were 195 patients. It was planned for 180 patients with 195 recruited, and the initial follow-up was for 24 weeks. That is important because after that there was a possibility of crossover, so when we're looking at the outcomes, we're really looking at the first 24 weeks with that.

The other thing of importance in this trial was that there was a washout period before entering the trial, and this is important because many patients with this condition are on ruxolitinib. If they go straight into a trial, then you don't see if there are any symptom improvements. But in this trial, they had a 2-week washout before they started either momelotinib or danazol plus placebo. The primary endpoint was looking at better than 50 percent improvement in symptoms, and then the secondary endpoints included all the other things that we would expect people to look for, like transfusion independence and spleen response. And there was very extensive following of symptoms using not only MFSAF, but also the traditional AORTC and also PROMIS, which is a good way of looking at patient-reported outcomes. So that there was a lot of information on quality of life and on health status obtained from this trial.

**Dr. Turck:**
Another question. Why was danazol selected as a comparator?

**Dr. McMullin:**
Yes, an interesting choice. But really the question was to have a comparator that is used in the treatment of anemia. Now as I'm sure you are aware, the treatment of anemia in myelofibrosis is actually very difficult, but most of the American national guidelines recommend danazol, with danazol being an anabolic steroid that certainly shows some improvements in anemia in some patients with myelofibrosis. Anything else that might have been considered in guidelines will really not give you a clean result on anemia, and steroids sometimes help but you can't really have steroids in the broad spectrum. EPO was used in all sorts of cases, and these people are likely to have tried that already, so the only reasonable comparator for anemia is danazol.

**Dr. Turck:**
For those just tuning in, you're listening to *Project Oncology* at ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Mary Frances McMullin about patient-reported outcomes from the phase 3 Momentum study.

So if we turn our attention to the results, Dr. McMullin, what were the significant findings around health status and related quality of life?

**Dr. McMullin:**
Okay, so the first primary outcome was achieved in that there was a greater than 50 percent improvement in symptoms on momelotinib compared to danazol. There is a lot more information on this in the poster, and you can see looking at individual symptoms and comparing them that on most cases, the momelotinib does better than the danazol. In some cases, there's really very little improvement on the various symptoms on danazol. Also, the time to response was quick and better on momelotinib than on danazol. Responses were seen within 28 days. Responses, as well as being rapid, were progressive and durable, so overall momelotinib came out better than danazol. On secondary outcomes, there were also improvements in spleen response and good anemia responses, and of course the question is if you get a good anemia response, is that contributing to the symptom improvement?

**Dr. Turck:**
And did you get any information about patients' physical and social functioning?

**Dr. McMullin:**
Yes, I mean that fits in with the improvement in symptoms, and you can see that particularly on the PROMIS scoring system that their quality of life, their physical functioning, and their fatigue improved to some extent on momelotinib.

**Dr. Turck:**
And bringing us around full circle, how do the findings of the secondary endpoints again relate to the primary endpoint of the Momentum study?

**Dr. McMullin:**
Well, I think they're all linked. The primary endpoint in this case was symptom improvement, but the secondary endpoints—decreased in spleen size, improvements in anemia, and physical functioning—all are linked to that because one would expect symptom improvement across the board if we had the secondary responses.

**Dr. Turck:**
Now before we close, Dr. McMullin, what additional research can we look forward to coming out of the Momentum study?

**Dr. McMullin:**
So I think we will get a lot more information as time goes on from the long-term follow-up because these patients at 24 weeks had the ability to cross over to momelotinib, so you can already see in some of the information that the curves are coming together because as they cross over, they get the improvements on symptoms on momelotinib, and most patients have crossed to momelotinib. But they will continue on momelotinib so we will get long term follow-up on patients on momelotinib and see what the long-term outcomes are. We may even get more data on quality of life and how long they survive. I think there should be a lot more information, especially for those interested in translational research, as these patients will have been followed and their burdens will have been followed along with their mutation analysis and their bone marrows. And we will see long term whether there are any improvements in the molecular burden of disease and the bone marrows, again, with this long-term follow-up and how long the quality of life improvements continue for.

**Dr. Turck:**
Well, with those forward-looking thoughts in mind, I want to thank my guest, Dr. Mary Frances McMullin, for joining us to discuss the patient-reported quality of life and symptomatic outcomes from the phase 3 Momentum study. Dr. McMullin, it was great having you on the program.

**Dr. McMullin:**
Thank you.

**Announcer:**
This episode of *Project Oncology* was sponsored by GSK. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!