



Transcript: ASH 2016: Dr. Mark Wildgust on the Efficacy of Ibrutinib in CLL

Dr. Brian Koffman - Hi. Dr. Brian Koffman. I'm a family doctor and a CLL patient, and I'm the founder and the Volunteer Medical Director of the CLL Society. I'm here on the third day of ASH. There's been some incredible information here and I'm happy to share. You want to introduce yourself?

Mark Wildgust - Hi. Hello. My name is Mark Wildgust. I'm the Global Medical Affairs head at Janssen for Oncology.

BK - And Mark, there's been a ton of exciting information about ibrutinib, some really strong, I just talked with Dr. George Follows about the long-term follow up on ibrutinib and we all know ibrutinib is a BTK inhibitor, but that might not be the whole story. Can you kind of walk us through, in terms of what we're beginning to understand about how ibrutinib might work, and what other activities it might have besides just the B-cell receptor blocking?

MW - So, it's interesting because we've all become so familiar with ibrutinib as a BTK inhibitor, but at the end of the day when we see the data Susan O'Brien presented here at ASH, or the data that Dr. Paul Barr presented, with this remarkable progression-free survival. What you see in those patients is ibrutinib being used, but it's ibrutinib. It's not necessarily just a BTK inhibitor. And ibrutinib does hit 10 other kinases in a covalent manner. Those data have been reported. One of those kinases is ITK. And there's been a lot of data that's being published on ITK and it would suggest that people like John Byrd have talked about this where we see this TH1 to TH2 shift... Adrian Wiestner, as well...

BK - So, I'm going to stop you there. TH1 to TH2, can you explain that a little bit, what that means?

MW - Yes. We're seeing a change in the immune system, really a change in the immune system where the immune system is really shifting to a state where it's able to perhaps work more functionally, but we also see the data from Adrian Wiestner at NIH which suggests that ibrutinib is having an ability to perhaps restore the immune system, to allow those T-cells that help us fight infections perhaps recover as well. And, now whether that's BTK or ITK, what we know is that these effects that we're seeing are because of ibrutinib. Now it's hard to tease out what's BTK and ITK, but the clinical benefit we see today with ibrutinib is because of ibrutinib, and I think that, I know there are a lot of other companies also looking at other BTK inhibitors and changing things, but at the end of the day, the clinical benefit we see that patients are receiving is because of what ibrutinib is. And as a company at Janssen, we're continuing to explore that, but I think that other companies that look to start to explore perhaps more, or different molecules, I think the burden is going to be on them to demonstrate that there are differences, meaningful differences. I think on the Janssen side, we're going to continue to explore really the clinical efficacy and safety of this compound, a look how we can really try to advance care for patients with CLL.



BK - I'm going to pull you back to kind of the molecular level here and some of our understanding. Some of the information that I've heard is that the effects that ibrutinib has may be more on the micro-environment and not just on the B-cell, the cancer cell itself. Is there any insights you can share with us on the effects of the micro-environment and how that might contribute to efficacy?

MW - I think again, Adrian Wiestner at NIH has done a tremendous job here and he and his researchers have shown, and they're showing here at ASH, that we're seeing that restoration, that perhaps of that immune system and recovery of the immune system, perhaps going back to more of a normal immune system, and that's because of ibrutinib. It's hard to understand what that then delivers, what that means, but I think that we're learning that, we see direct cell-killing with ibrutinib, but we also see these important changes in the micro-environment. I think we're increasingly becoming important that those micro-environmental changes, too, are really incredibly important. T-cell recovery, reversal of T-cell exhaustion, those are all very important things, and it's hard to know, you know, again, what kinase specifically is bringing the benefit, but for example, here in the late-breaker session tomorrow, we're seeing data on using ibrutinib to treat chronic graft versus host disease, where potentially the mechanism of action there is a dual BTK and ITK effect and that's a key, perhaps, signal that there's more perhaps to the efficacy of ibrutinib than just BTK. And so I think that we have to remember that the efficacy and safety that we see with ibrutinib is because of ibrutinib and that's all of the pieces of ibrutinib. And I think that's the benefit that we see for these patients.

BK - Any final words you'd want to share with patients who have CLL and are looking for a treatment options?

MW - Janssen is really very much committed to trying to advance care for patients. We've been working with our partner, Pharmacyclics, for many years now to try to advance care. We're really excited to be able to present updated data, five-year data with ibrutinib. Susan O'Brien presented long-term data from the Resonate-2 trial, but we're not stopping there. Then we have another seven Phase Three studies, just in CLL alone to read out. We're really looking to try to drive towards cure. Janssen has been working on that for many, many years. We've got a strong commitment with that, working both as a company ourselves. We just started a new trial with ibrutinib and Venetoclax and treatment naïve patients, looking at using those two drugs together to hope to drive patients to MRD and the benefit of perhaps continuing or stopping at MRD. We have collaborations with the German CLL Study Group, cooperative groups in the United States, but also in the United Kingdom, looking also at novel combinations driving to cure. And I think that we've made tremendous progress, but I think what we want to do at Janssen is go beyond where we are today and look to see if we can strive for cure.

BK - I'm with you on that. Mark, thanks a lot.

MW - Thanks so much.