iwCLL 2017: Dr. Mato Discusses Atrial Fibrillation in CLL - Transcription

Dr. Brian Koffman – Hi, Dr. Brian Koffman. I'm a family doctor and CLL patient. I'm here at IWCLL. Want to introduce yourself?

Dr. Anthony Mato – Hi, Dr. Anthony Mato from the University of Pennsylvania, a CLL Specialist and Director of the program in University of Penn.

BK – Dr. Mato, you'll be talking today on one of the complications in CLL, a cardiac complication. Can you explain that in a patient-friendly way?

AM – Sure. Today we're going to be presenting data on trying to predict the complication of atrial fibrillation which is an arrhythmia which is commonly seen in older patients and seems to be exacerbated by ibrutinib. Ibrutinib by administration may increase the risk of developing atrial fibrillation. It does have some long and short-term potential complications. We're trying to identify which of our patients were treated with ibrutinib may have the highest risk of developing AFib.

BK – One the problems with atrial fibrillation is, depending on the patient's risk factor (something called CHAD2 Analysis of the patient), they may need to be on significant blood thinners which can be dangerous in combination with ibrutinib. Tell us how you address that challenge.

AM – Sure. What we did as part of our analysis was number one, look at about 150 patients treated at our center, tried to estimate the rate of the development of new AFib, then also looked at some management strategies, including the use of aspirin therapy or anticoagulation therapy. We did look at complications associated with both the AFib and also the medications used for managing the AFib. Fortunately, it doesn't appear that there are many short-term toxicities associated with management in terms of the use of rate-control medications or medications associated with anticoagulation. Clinically, at least at this point, we didn't have any patient treated with ibrutinib who developed AFib who needed to come off of ibrutinib because of that complication.

BK – One of the other things that I guess is in the mix and you're looking at statistically is, it's an older population that has CLL. It's an older population that gets atrial fib. I'm sure that that's something that you're looking at teasing out.

AM – It is true, although I think that it is really fortunate that we have at least three randomized trials that were ibrutinib-based studies where it's clear that the cases and the controls are well-balanced for everything like age, and hypertension, cardiac risk factors, for example. And yet, there does seem to be an AFib signal. So, I don't think that it's necessarily just age-dependent patients, or necessarily age-dependent regarding the risk of AFib. I think ibrutinib clearly is causing a certain number of events for patients. We did identify in our data, though, that if we studied the patient's EKG or ECG before they start ibrutinib, there are some

electrophysiological characteristics. There are some markers on the EKG which can help us to decide which patient is likely to have that AFib event over time.

BK – Well, that's pretty exciting! Is that going to be stuff that you'll be publishing and that will be out in the community?

AM – Yeah. So that will be presented at the meeting. The abstract will be published as of this meeting. The plan is to present that in manuscript format. The EKG is actually a very simple test. It can be done at any doctor's office. It's relatively easily read for a left atrial abnormality. We found that that was probably the most important clinical predictor we could identify for a long-term risk of developing atrial fibrillation.

BK – Last question: Is there anything we know, about ibrutinib in particular, about why... Do we have any mechanistic understanding about why it precipitates this irregular heartbeat?

AM – Ibrutinib is a kinase inhibitor that inhibits the activity of many enzymes. There's a family of kinases called TEC kinases. There is some thought that there may be TEC interaction with ibrutinib in the heart, but that's really contested. I think at this point, we know clinically that it occurs. There's not a clear mechanism of action that's been proposed, and then validated, at this time.

BK – Dr. Mato, thanks so much for the research you're doing. Thanks.

AM – Thank you, Brian.

BK – Thanks.