



## Transcription: ASH 2016: Dr. Anthony Mato Presents Real-World Data on Ibrutinib in CLL

**Dr. Brian Koffman** - Hi, Dr. Brian Koffman. I'm a family doctor, turned CLL patient. I'm the founder and volunteer medical director of the CLL Society, and also of my blog. And I'm here at ASH 2016 in San Diego on day two. Do you want to introduce yourself?

**Dr. Anthony Mato** - Hi, Anthony Mato from the Center for CLL at the University of Pennsylvania. I'm the director of the center, and joining Dr. Koffman here at ASH 2016.

**BK** - And Anthony, you've done some very interesting, real-world research on what's happening with patients taking ibrutinib: How good they are about staying on their meds, why do they go off their meds. This was a large number of patients with a lot of help from other people in terms of that. Can you tell us a little bit about that research and how it applies to patients?

**AM** - Sure. Last year we presented at the ASH meeting a series of 178 patients who had discontinued their kinase inhibitor, either ibrutinib, or idelalisib. This year we wanted to expand that experience and we are presenting over 600 patients who were treated with ibrutinib both on the front line and relapsed/refractory settings in commercial use of drug, as well as in clinical trials.

**BK** - So it would've been a whole bunch of different places, not just at university settings.

**AM** - There were two major collaborators. There were nine academic medical centers that participated, and then data were also provided by the Celgene Connect CLL Registry, which comprised 199 mostly community centers across the country. So a real mix of academic and community practice, and then to try to give us a flavor of how the drug is being used in practice at this point in time.

**BK** - And what were some of the interesting findings?

**AM** - Sure, so we really were interested to see whether the results from clinical trials have translated into practice. And I think that one of the biggest messages from the particular trial is that ibrutinib is a very well-tolerated, active drug for the majority of patients with CLL. And the responses to the drug appear to be very durable in multiple settings: Front-line, relapsed/refractory, high-risk. But we started to really focus in on reasons for discontinuation, and in the small number of patients who discontinued this drug. In front-line and relapsed/refractory setting we're still learning that side effects were a major issue for patients to have to deal with. Side effects or intolerance were the most common reasons for discontinuation of ibrutinib in our series, with a distant second being progression of CLL, and then very few other reasons for patients discontinuing the drug, for example, Richter's transformation. So even though it's a very active drug, it's well-tolerated, in general there are a subset of patients who just can't tolerate the drug. We view this as is an opportunity number one, for education, so it helps the physicians and the nurses taking care of patients to



recognize that you need to have a dedicated team in order to manage patients with CLL. With expertise, not only in how to administer the drugs, but also with expertise in how to manage the particular side effects. For example, ibrutinib has some side effects like atrial fibrillation, or bleeding, arthralgias, or rash. Idelalisib has issues with colitis, pneumonitis, and liver dysfunction. And there's certainly a learning curve for the physicians and the nurses for how to use these drugs. And so, this provides an opportunity to say hey, across the country patients are still coming off of these drugs because of side effects for the most common reason, and are there strategies that we can use either with potentially considering changes in dosing, or administration, or thinking about next generation drugs? Some of whom will be presented here at the ASH meeting.

**BK** - And I think at your center, you even have a team of cardiologists and other specialists to help you keep patients on their medications.

**AM** - So at our center at University of Pennsylvania, we have the Center for CLL. It's a relatively large staff that are focused in management of patients with CLL. So, we have an assistant who is in charge of our schedule. We have a program nurse who focuses specifically on managing our patients' side effects, specialty pharmacy issues, pathways, and adherence. We have a research nurse. We have a research nurse practitioner. We have two data coordinators. And then from an inter-departmental perspective, we have a cardio-oncology department headed by Dr. Carver, who focuses on managing all of the cardiac-related toxicities associated with cancers and cancer medications. And we also work closely with our infectious disease colleagues to help minimize the risk of infection, which is a common issue for patients with CLL. We also have a collaboration with dermatology, where all of our patients are screened for skin-related cancers, which is also a common issue for patients with CLL.

**BK** - Do you have any sense or any data on whether that makes a difference having that kind of input to keep people on?

**AM** - Not yet. So, we haven't done comparisons with our center and other academic centers. But certainly, I think that the old paradigm of giving a patient six months of chemotherapy and then stopping, where the side effects are largely focused in the first few months, and then patients get better, and they go on to resume their lifestyle, is changing. And with these drugs, the newer drugs, although they're active, they're practice-changing, they are life-saving. Certainly the side effects that you see aren't in the first month or two, but there are patterns of side effects that you need to have a staff available and ready to address, whether they're at month one or at month 10. And so it's a different approach to managing patients. I do believe that we are very successful with adherence, and that's because of our program nurse, and also because of the fact that we have tight collaborations with our specialty pharmacy for administration of these meds.

**BK** - Any final message you'd want to give to patients in terms of the importance of staying on these meds and working with your doc if you have a side effect, rather than just stopping them cold.



**AM** - Right. I think that if you have a side effect, it may require you to stop the drug. But I think it's very important to have an open discussion with a physician about their comfort level in using these medications: Discuss the side effect, what are the long-term data available, and the consequences of continuing or re-challenging with that medication. Certainly, B cell receptor antagonists are by far the most important, innovative medications in CLL right now, and we're very hesitant because of a toxicity to abandon the drug. So, it's important to have a team that has expertise and specialty in utilizing these medications most effectively.

**BK** - Dr. Mato, thanks so much.

**AM** - Thank you so much, Dr. Koffman.