ASH 2017: Anthony Mato on Kinase Inhibitor Intolerance in CLL - Transcription

Dr. Brian Koffman – Hi. Dr. Brian Koffman here at ASH 2017.

Dr. Anthony Mato – Anthony Mato from University of Pennsylvania, Center for CLL.

BK – So, intolerance to good therapies is a big problem. You've done some research on that. Can you share that with us?

AM – Sure. We've done some outcomes research looking at the most common reasons for discontinuation of a kinase inhibitor, largely ibrutinib-treated patients, and in all lines of therapy, front-line and relapsed/refractory. We're finding, in practice, that intolerance is a major reason for discontinuation, probably the most common reason. One of the questions that we've asked previously is whether or not those patients could be rescued with another kinase inhibitor. The original work was ibrutinib to idelalisib, for example, and whether those toxicity profiles overlapped. Based on those findings, which suggested you could maintain that response, we initiated a prospective clinical trial with TGR-1202, or umbralisib, looking at whether or not patients who are intolerant to ibrutinib or idelalisib could be rescued with that drug, not have the same toxicities, but maintain that response. And this is particularly important before thinking about switching to other classes of drugs, like a BCL-2 inhibitor, for example. Today at the ASH meeting we're reporting results on 35 patients treated with umbralisib, all of whom were intolerant to ibrutinib or idelalisib. The take-home from that particular presentation is that, number one, the drug seems to be very active, but I think more importantly, well-tolerated. We report the reason for discontinuation for ibrutinib or idelalisib, and then compare that AE (Adverse Event) table to the events associated with umbralisib. No patient has come off of umbralisib at this point in time due to a toxicity event that mirrored the one that led to the discontinuation of the first kinase inhibitor, and we've seen a relatively well tolerated AE profile for that drug in this high risk for toxicity…

BK – An adverse event.

AM – …adverse event profile… in this high risk for toxicity patient population. So, it's an ongoing study. This was born from our real-world evidence efforts, opened

up at 15 centers, and now we are accruing patients. Hopefully the study will be fully accrued in the next month or two.

BK – Well, as a patient, I am always excited to have other options because I think some of your earlier data suggested that adverse events (side effects) were one of the … or often, the most common reason that patients stop taking drugs that were working for them.

AM – Right. And so, I think the major push here is to not give up on classes of agents and if we can still target the B-cell receptor pathway, we should continue to do that in the setting of intolerance.

BK – The more options you can have as a patient, the better. So, the sooner these drugs get to market and patients can get them, the better.

AM – I completely agree.

BK – Dr. Mato, thanks so much for what you are doing.

AM – Thanks so much.