ASH 2017: Dr. Mato on Real World use of Venetoclax for CLL - Transcription

Dr. Brian Koffman – Dr. Brian Koffman of the CLL Society, here at ASH 2017.

Dr. Anthony Mato – Anthony Mato, Director for the Center for CLL, here at ASH 2017.

BK – Venetoclax has revolutionized the way CLL is treated. You've looked at the real-world data of how it's being used, not just in clinical trials, but by the community of hematologists. Can you tell us what your findings were?

AM – Sure. Well, I think one of the most important things that we can do is try to make sure that the results reported from clinical trials are generalizable to patients who would not necessarily be the best candidates for those clinical trials, or didn't participate in those clinical trials. Venetoclax is a new drug. It's incredibly active. I think there's a learning curve in terms of how to use it. And what we wanted to do was to gather the experiences from centers across the country, and really, around the world, because there's an international component here to see how the practitioners are using venetoclax, what those outcomes are, and see whether or not they're comparable to the results from clinical trials. So, we have 19 or 20 centers participating in this effort from as far away as Australia and we're gathering the data on 204 patients who were treated with venetoclax-based therapy. What we're learning is that venetoclax is well-tolerated, and actually, the outcomes that we're finding are very comparable to the results from clinical trials. Here, the major reason for discontinuation, and it's a very small number of patients, is actually progression of disease, not intolerance. Venetoclax seems to be well tolerated. The toxicity profile is very predictable. We're able to manage the toxicities of that quite well because they're similar in some ways to the results that we've seen from chemotherapy combinations. We did a detailed look into the supportive care utilized for managing patients on venetoclax. We looked into how the ramp-up period is undertaken. So, if you don't know, for patients, venetoclax is a drug where we start at low dose and escalate to a high dose. Over five weeks we go from 20 milligrams to 400 milligrams, and during that time there are some nuances in terms of supportive care, potential need for hospitalizations, and maybe a risk of something called

tumor lysis syndrome, where if cells are killed fast enough it can interfere with the electrolyte metabolism and the renal function.

BK – And there were some early deaths when we didn't know how potent it was…

AM – Exactly.

BK – … and we just started at a higher dose.

AM – So, we wanted to verify whether or not venetoclax was safe from a community perspective and those are the results that we're reporting. It turns out that patients… that there were very few events associated with tumor lysis in these patients, and that although the ramp-up is steep in terms of learning how to use the drug, that in this large series of patients, including some community practitioners, the drug has been delivered safely to the vast majority of patients.

BK – That's wonderful news.

AM – The other question that we're asking… we have very limited data… but I think it's important… is that I think we have a clear understanding of, if a patient fails chemotherapy we can rescue them with ibrutinib. If a patient fails ibrutinib, we can rescue them with venetoclax. There's not really a picture of what practice patterns are emerging when venetoclax stops working. And so, in this series we do have several patients who've discontinued venetoclax and we've looked at next agents that are being used. One of the most important findings is that there's a small component of patients who've had venetoclax without having ibrutinib, and then have gone on to receive ibrutinib, and we're reporting the activity for Ibrutinib in that small subset of patients. And it turns out ibrutinib seems to be able to rescue venetoclax in patients who haven't received ibrutinib in the past. The other analysis that we did is that we looked at risk factors for venetoclax failure, and it seems that some of those older prognostic factors, like the presence of a deletion 17, for example, do seem to still stratify patients for differences in outcome. So again, another important piece of data to support the use of… to support the participation in clinical trials for patients who have high risk features of their disease.

BK – Dr. Mato, you're really pushing things forward. We're very excited. Thanks so much.

AM – Thanks, thanks Brian.