ASH 2017: Dr. Matthew Davids on Umbralisib (TGR-1202) for CLL - Transcript

Dr. Brian Koffman – Hi. Dr. Brian Koffman, a family doctor and CLL patient myself, and I'm the Medical Director of the non-profit CLL Society here at ASH 2017 in snowy Atlanta.

Dr. Matthew Davids – I'm Dr. Matthew Davids from Dana-Farber Cancer Institute and Harvard Medical School in Boston, and I'm a CLL specialist there.

BK – So, it's always a challenge to pronounce the names of new medications, but "umbralisib"? Did I get that right?

MD – Exactly right.

BK – You've done some research on how that drug works and the pharmacokinetics. Could you share that with us, from a patient's perspective and how it might be helpful?

MD – Sure. So, patients may be familiar with idelalisib. This is an approved PI 3-kinase delta inhibitor for patients with CLL. It's a very effective drug, but it also has significant toxicities that tend to be immune-mediated. So, umbralisib is a next-generation PI 3-kinase delta inhibitor, and we think it has a differentiated safety profile compared to idelalisib. So, the point of our analysis was to try to show that with a substantial amount of data. We were able to look across the umbralisib early-phase development program and pool together 350 patients…

BK – Wow!

MD – … treated with umbralisib, and we found just what we expected, which is that the rates of colitis and transaminitis (liver inflammation) are much lower than what we've seen with idelalisib. And we have pretty good follow-up now, with many patients out one to two years on umbralisib, and that's a period where we'd expect to see toxicity if there were going to be some.

BK – And do we have any idea why this is different than the experience with idelalisib?

MD – So, this is an active area of investigation. The drug does hit PI 3-kinase delta. We have KINOMEscans that suggest that it's very selective for that target, but interestingly, it hits another protein called CK1 epsilon, which we think may have effects on regulatory T cells. So, there's interesting animal data to suggest that that might actually be one reason why it mitigates the toxicity of the drug is through this regulatory T-cell effect, but this needs to be confirmed in humans.

BK – Well, I'm excited about us having another option because the PI 3-kinase pathway is clearly an active and important pathway in CLL. Any final thoughts you have that you wanted to share?

MD – The other thing I would say is that, as we put together combination regimens of novel agents, we want to use the agents that have the best toxicity profiles, so we're currently

running a study of umbralisib with ibrutinib, and I think that's a promising study given the toxicity profile of these drugs.

BK – Dr. Davids, as always, thanks so much for the research you're doing. Thank you.

MD – My pleasure. Thanks.

BK – Thanks.