ASH 2017: Dr. Ian Flinn on duvelisib treatment of CLL - Transcription

Dr. Brian Koffman – Hi. Dr. Brian Koffman, a family doctor and a CLL patient, and the Founder and Medical Director of the CLL Society. I'm here in Atlanta, Georgia, on the last day of ASH 2017.

Dr. Ian Flinn – I'm Dr. Ian Flinn. I'm the Director of the blood cancer research program at the Sarah Cannon Research Institute in Nashville, Tennessee.

BK – Dr. Flinn, you've done a lot of research, but one of the things that I wanted to ask you about, you were one of the investigators, the principal investigator, on this trial was the drug duvelisib. Could you tell us what duvelisib is, and what you were able to find, what you presented here at ASH today on that drug?

IF – Sure, duvelisib is a PI3-kinase inhibitor. There are a variety of different types of PI3-kinase inhibitors, and this one's what's called a dual inhibitor of two different parts of the PI3-kinase complex, the delta and the gamma components.

BK – So, and the PI3-kinase is part of the B-cell receptor pathway, like ibrutinib and other drugs.

IF – Absolutely. Absolutely. It has those similarities. It also is downstream of some other survival signals that help keep CLL cells alive, but it's also part of the B-cell receptor complex.

BK – And, people might know idelalisib, which is the approved PI3-kinase inhibitor in CLL.

IF – Right. Like idelalisib, duvelisib inhibits the delta isoform. Duvelisib also inhibits the gamma isoform. And we're not sure whether that makes a difference or not. There's a hypothesis. The hypothesis is that by inhibiting this other isoform, we're not only targeting the malignant cells, the CLL cells, but we're targeting the microenvironment, the soil that the CLL cells grow on. And so, by stopping those interactions between the cells and the microenvironment, maybe that will also improve the efficacy of the drug.

BK – And what were you able to present today? What did your data show when you presented it at ASH?

IF – This is a randomized trial comparing the anti-C20 antibody ofatumumab to duvelisib. And duvelisib was given as a single agent as well, orally, twice a day. And what we saw was that there was a tremendous improvement in progression-free survival, so greater than 12 months, almost 13 months, of progression-free survival with duvelisib, with a little bit more than 9 months with ofatumumab. So, this was not unexpected. We had certainly gone into the whole trial with a notion based on the Phase I study that we had previously done, that this was going to improve progression-free survival. I think the other things that we saw in this study, was that the toxicity profile was manageable. Right? I mean, we know that with the PI3-kinase inhibitor, there's a set of side effects, such as diarrhea, colitis, and infections. But we found in this protocol that we could manage that pretty well. And that rarely did the drug cause patients to

have to come off the therapy. We were able to restart patients on the drug after holding for a brief period of time, then getting them back on treatment.

BK – So, we've become more sophisticated at handling these, and are more aware, and can intervene more quickly. Were there prophylactics being used for infection with these patients?

IF – I think both things are true. I mean, certainly there's been a learning curve since idelalisib was first studied in Phase I studies, and subsequently, Phase II and Phase III. We've learned about these handful of side effects, and we're much better about being aware, perhaps stopping earlier, while allowing people to recover, and restarting patients on it. And from an infectious standpoint, you're right. All patients on this study received prophylaxis for pneumocystis. There were people who did develop pneumocystis pneumonia, you know this type of pneumonia that occurs in very… what's called an opportunistic infection. It occurs--

BK – In people that are immunosuppressed.

IF – Right… patients that are immunosuppressed. There were two people that developed the pneumonia on this trial, but they weren't taking the required prophylaxis. And so, I assume that they were actually taking the medicine that was required for the protocol, but they wouldn't have gotten that either.

BK – Any final thoughts you wanted to share with patients about duvelisib and its potential role in treating CLL?

IF – I think we're going to have a new therapy for the treatment of CLL. This drug, I have every reason to believe, that will ultimately be FDA-approved. I think it's important to have more and more options for patients. As some of the new novel agents are making their way earlier into the course of therapy, we need things for patients when some of the frontline therapies stop working. I think this is a really good option for patients.

BK – Dr. Flinn, thanks so much for the research you're doing, and what you're doing for the CLL community. Thank you.

IF – My pleasure. My pleasure.