ASH 2017: Dr. Jennifer Brown Discusses the Association Between Idelalisib and Liver Inflammation in CLL - Transcript

Dr. Brian Koffman – Hi, Dr. Brian Koffman here on the last day of ASH 2017 in Atlanta, Georgia.

Dr. Jennifer Brown – And I'm Jennifer Brown, Director of the CLL Center at Dana-Farber Cancer Institute and Associate Professor of Medicine at Harvard Medical School.

BK – Idelalisib is a very active, potent drug in CLL, but you've done some research on some of the problems with it, including liver inflammation, and you updated that at ASH. Can you tell us what you found, being able to look more deeply into some of the data and looking at it more long term?

JB – Well, this study really arose out of our prior study, which was a small study of about 25 patients who received idelalisib as their first therapy, in whom we saw that about half had quite significant liver inflammation, and this was due to an immune system reaction. And we noted that this was more common in the younger patients, as well as those with the lower-risk IgVH type, the mutated IgVH type of CLL. And so, I was very interested in trying to confirm this in a larger data set and was able to access the registration trial database, in collaboration with Gilead. And so, we looked across six different trials from their experience, both frontline and relapsed, and it was very, very clear that the risk of the liver inflammation was much greater in the patients who were receiving it in first-line therapy than in a later-line therapy setting. That validated very well. And then the age-dependence was also quite remarkable, both separately analyzed in the frontline and in the relapsed patients, that the younger you were, the more inflammation you had… almost by decade. So, patients less than 50 had the most, 50 to 60 were next, 60 to 70 was next, and patients over 70, the least.

BK – Wow. So, can I jump in? Are one of the things you're thinking is that the more intact your immune system is, if you haven't been beaten up by chemotherapy or by having the disease for a long time, that you might do worse if it's immune-modulated? Is that what your postulate is?

JB – That's exactly what our hypothesis is. And we are actually testing that in the lab, as well. We're looking at the T-Cells, the immune system cells, that seem to mediate the liver inflammation, prior to idelalisib, across the broad swatch of patients… and then what happens in patients who do and do not get the toxicity.

BK – So, it's such a powerful drug and it's so helpful to have an alternative. So, how do you picture this being used and how do you fit that in when you have a patient where you think idelalisib would be a good choice for them? How do you approach this issue, knowing the liver toxicity and other auto-immune toxicities that come with it?

JB – Right. So, I view idelalisib as a good choice, particularity in older patients. Many of them have significant cardiac issues that will make ibrutinib potentially problematic, and/or they've tried ibrutinib and had problems with it. And so, I've have actually quite good luck with it in older patients with cardiac issues. And my general approach is just to check the liver tests weekly, which is a little bit more frequently than is generally recommended on the label but has always been my approach since I've been working with the drug. And you only have to do it for about the first two months or so. After that, you can taper way back on it.

BK – So, this is an early problem, unlike the colitis and stuff which can come on months later?

JB – Right. And that you just have to have a high awareness that, if it starts, it could be from the drug and need to jump on it early. I often will try to jump on it early with the just the oral non-resorbable budesonide drug, so that people don't have to go on prednisone or stop the drug. And that usually works. And so then, that keeps people seamlessly on the drug and knocks it back and then we taper that off, slowly over time.

BK – And while we're talking about this, pneumonitis, which seemed to be an issue, are you seeing that, and having any advice on how that should be handled?

JB – Right. So, I have certainly seen that. It also happens relatively late, but can happen month 3, 4 or later. The main issue is that since there's also a risk of infection, we have to evaluate carefully for infection. The drug-related pneumonitis often has a certain characteristic pattern on scans. And if you haven't found an infection within a day or two, then I often consider giving steroids at that point. And it's very important to hold the drug, whenever someone gets admitted for any type of respiratory complaint with idelalisib or ibrutinib, for that matter. I hold the drug immediately just in case it is a drug-related problem… that it won't continue to worsen. Spend a little while establishing that they don't have a very serious infection and then consider the steroid option.

BK – Any final thoughts for patients on idelalisib, and the benefits versus the toxicities that you want to share?

JB – Right. So, I was involved with idelalisib from the very beginning and it was truly remarkable, just like ibrutinib. We had people who had had many, many lines of therapy and huge amounts of disease, who just, it just melted away. And they did phenomenally well. And so, it can be a very, very good drug. I think the key is just trying to select the best patients for it, who again, may be older, may have had more prior therapy and that might include cytotoxic therapy in the past, may also...

BK – Chemotherapy.

JB – Chemotherapy. Right… which may deplete the immune system. And then, just having a good awareness of what the side-effects are and trying to jump on them early. But I've had people go years with none of these side-effects… if you select the right people.

BK – Dr. Brown, thanks so much for what you're doing. Thank you.