ASH 2017: Dr. Dearden on the Progress and Remaining Unmet Needs in CLL - Transcription

Dr. Brian Koffman – Hi. I'm Dr. Brian Koffman. I'm a family doctor and CLL patient. I'm the medical director of the CLL Society. I'm here on the first day of ASH 2017 in snowy Atlanta, Georgia.

Dr. Claire Dearden – Hi. I'm Claire Dearden. I'm a hematologist at the Royal Marsden Hospital in London in the UK.

BK – Dr. Dearden, we're very early at ASH so we haven't seen the latest data, but I'm wondering what things you are looking for and what you see are some of the unmet needs in the CLL community that the researchers are going to be presenting. What areas of abstracts and research are you particularly interested in looking at?

CD – I'm expecting that we're going to see some exciting data. It's data that's now emerging on how to use these new drugs in a way where we're combining them other therapies. If you remember when we spoke about five years ago, we had a lot of unmet needs in CLL: Older patients… those with comorbidities… those with high-risk genetics, and, wonderfully, over the last five years we've had access to drugs which have dealt with many of those issues that we were struggling with. But there were always unanswered questions: How long we had to give these drugs… what happened when patients failed those therapies, progressed on treatments… what happened if patients couldn't tolerate them? And I think we're beginning now, in the last couple of years, to answer many of those questions. We're understanding a little bit more about what we can expect to happen to patients who've been on these drugs, maybe now for three to five years, which is how long we've been using them. And how we can better optimize the use of these drugs to improve, say on things like preventing the emergence of resistance, being able to have a finite period of treatment rather than just an open-ended 'stay on the drug for life' approach? And some of the combinations are moving towards being able to identify a stopping point for patients where you've achieved such a good level of remission that we could anticipate them remaining in remission off treatment… so, this sort of treatment-free remission, which is something that the CLL doctors are now trying to explore and we need to be smart in CLL and not wait that long before we define that.

BK – And for these patients who might be able to stop therapy, and we know that's a wish for patients as well as for physicians and also for the community at large and society at large because these medications tend to be very expensive, to have a finite, durable period of treatment, are we looking for minimal residual disease negative? Is that what we're looking for? Could you tell us what that is and if that's an important piece of this in your opinion?

CD – Yes, I think we're coming back to that.

BK – Uh huh.

CD – Minimal residual disease negativity was defined very well on the trials where we were using chemoimmunotherapy, and it's been clear for a long time that whatever treatment a patient receives, if they achieve MRD negativity, that's a good thing… and it's a surrogate for a long remission and usually also for improved survival. When the new drugs were introduced, it seemed like we wouldn't be able to achieve that with some of the B-cell receptor inhibitors. For example, not many people actually achieve complete remissions, let alone MRD negativity, but now that these drugs have been combined with other drugs, particularly some of the novel treatments being used together, not with chemoimmunotherapy, but with other antibodies say, then we are seeing MRD negative remissions. So, I think one of the exciting abstracts that we're going to see at this meeting is the combinations with venetoclax and one of the late-breaking out abstracts is the trial where they compared conventional treatment, bendamustine plus rituximab, in first relapse, verses venetoclax plus rituximab. And the results, as the abstract presents at least, are outstandingly in favor of the venetoclax-rituximab combination, not only for improving progression-free survival, but also overall survival, even with relatively short follow-up, and importantly, a significant proportion of patients achieving MRD negative remissions. So, if you like, it's a bit the Holy Grail. If you can achieve that for a patient, then you know you have delivered a really good therapy, which hopefully will translate into a long period free from disease with a good quality of life.

BK – Well, as a patient I'm really excited about the possibility of non-chemo combinations, maybe novel agents, maybe with immunotherapy, that are getting me to where there's no detectable disease in my blood or bone marrow, and where I can stop the therapy and maybe have a long life, maybe not be cured, but maybe have a long-life period. For me, that's a very exciting prospect.

CD – Well, I couldn't agree more and it's what we want for our patients too. And I think we're moving towards that goal. And so, perhaps when we speak at the next ASH… or the next ASH… we won't be talking much about monotherapy any longer, we'll be talking about some of these combination strategies.

BK – Any final thoughts or anything you want to share with the CLL patient community?

CD – I think we know that one of the issues that we faced, one of the unmet needs, was for the high-risk cytogenetic group of patients. So, these are patients that have an abnormality of the TP53 gene. Either this gene is lost or it's mutated.

BK – That's the 17P deletion.

CD – That's the 17P, the gene is TP53. It lives on chromosome 17. So, that now we know that most of these new drugs, these B-cell receptor inhibitors, venetoclax, the next generation of these drugs, BCR inhibitors, do address that need. Patients can respond to these drugs when they didn't respond well to chemoimmunotherapy. That's crucial because, even at the first time that somebody needs treatment that will be a key test that needs to be done. Historically, we did the test. We'd know that this was a high-risk group of patients, but we didn't necessarily have a

better treatment to offer. Now, we have better treatments to offer. It's really important to identify patients early who have these abnormalities, so that they don't go through a treatment, such as FCR or BR, which isn't very effective… that they can go straight on to a treatment that will meet that need. And it's very important also to remember that this is a moving target; that this needs to be tested before each treatment that a patient receives, because they may have not had the abnormality at the first treatment but they may when they relapse.

BK – Yeah, “Test Before Treat” is one of our mantras. And we've both seen tragedies where one patient hasn't been tested in advance of treatment, or where they have been tested but the clinician wasn't aware of the therapeutic implications of that, and the patients have had therapies that have a very, very low chance of being effective.

CD – Yes, and these patients are going to suffer the toxicity of the treatment, without any benefit, and that's about the worst thing that you can do to anybody. So, I think that's probably one of the most important things that we need to be disseminating to the community of clinicians who treat patients with CLL, that we now have a really effective therapy for this group.

BK – Dr. Dearden, always great to see you. Thanks so much coming from a snowy London to snowy Atlanta, thank you.

CD – Yeah, thank you.