ASH 2017: Dr. Choi Discusses the Potential of Non-Chemotherapy Regimens for the Treatment of CLL - Transcript

Dr. Brian Koffman – Hi. I'm Dr. Brian Koffman. I'm a family doctor and a CLL patient, and I'm here as the founder and medical director of the CLL Society, on the second day of the American Society of Hematology meeting in Atlanta, Georgia.

Dr. Michael Choi – And I'm Michael Choi. I'm a hematology-oncology specialist at UCSD Moores Cancer Center. I'm part of the CLL program there.

BK – Dr. Choi, one of the areas that UCSD has pioneered is non-chemotherapy approaches to CLL. And one of the first approaches that's been used and keeps getting modified and improved is high-dose methylprednisolone (HDMP) with an antibody. Can you tell us a little bit about what high-dose methylprednisolone is for a patient and why the combination with an antibody might make sense, why you're looking at this?

MC – Sure, yeah, definitely. I certainly credit doctors Kipps and Castro for, even 10, 15 years ago knowing that there were other ways to treat patients with CLL, besides chemotherapy agents. I think it's been known for some time that steroids have activity against CLL cells, and leukemia cells, and lymphoma cells. And so, it is incorporated in regimens like CHOP. We decided to look at very high doses of about 1,000 milligrams per meter squared, so people are getting on average to 1,000 milligrams of methylprednisolone.

BK – And that's a massive dose, like if you had an asthma attack you might get 60.

MC – 60. Yeah. Yeah. So, it's a much larger dose than typically used just to treat inflammation or allergies. But at those doses we could definitely see sometimes rapid killing of tumor cells. We even feel that we need to monitor for tumor lysis syndrome at those doses. We give it over pulses, so just over three days at a time, or sometimes up to five days at a time with other regimens… but stop it at that point so that we don't have to have a long taper or that we don't feel that we risk side effects of chronic steroid use, like osteoporosis, or muscle wasting. We still do have precautions to use antibiotics, and antifungal agents, and antiviral agents, because steroids, in addition to killing CLL cells, still also have a fairly significant effect on the immune system. But with those doses, especially in combination with anti-CD20 antibodies, we have consistently seen high response rates, and often, durable responses, remissions lasting several years, even in cases of 17p deletion, because, unlike chemotherapy, the high dose steroids have a mechanism of action that isn't dependent on p53. So, it still works in all subgroups of patients.

BK – And you have a paper here that you and Dr. Castro and others did, with a more modern antibody, obinutuzumab. Can you tell us a little bit about that?

MC – Yeah. So, Dr. Castro and Dr. Kipps, they led a study that used high-dose methylprednisolone with obinutuzumab, not only to build off of previous work, but looked at the combination of ofatumumab, and a study with rituximab, or a few studies with rituximab. The

study enrolled about 40 patients, total. It looked both at the effectiveness and safety in the relapsed setting, as well as in the frontline setting. In the frontline setting we also thought we would use as an historical control, or compare the results to the results of the CLL11 study, which used the same anti-CD20 antibody, obinutuzumab, with chlorambucil. So, this was a chance, maybe not directly in the same study, but across studies, to compare the same antibody with chemotherapy versus with the high dose steroids. We found that the combination was very active. Really, every patient responded.

BK – Wow, that's impressive.

MC – Yeah, yeah.

BK – And some of those are 17p and relapsed/refractory patients.

MC – Yep. Half were relapsed/refractory. I think about 10% had 17p deletion, so not the majority, but we did have a fair number of patients with that high-risk characteristic. I think about a quarter of responses were complete responses, a little bit more in the frontline setting. So, the response rate was comparable to the Gazyva/chlorambucil CLL11 results. The progression free survival was also excellent… about 30 months, 31 months in the frontline setting, so a little bit longer even than the patients that were on the Gazyva/chlorambucil combination, albeit in a different study. So, we were certainly pleased that our patients were able to have a meaningful remission off-treatment without receiving chemotherapy as part of their treatment. The tolerability was good. With the incorporation of the antibiotics there were not a high number of infections, and there were not infections we would consider opportunistic, or things that occurred only due to the steroid use. We did not encounter, or I guess we were able to manage, any infusion-related toxicity from the Gazyva. Probably the high doses of steroids helped in that regard. And we didn't encounter significant tumor lysis syndrome either, although we certainly were able to kill a lot of tumor cells with this.

BK – In the past there's been some severe infections with high-dose methylprednisolone, and I think in the past it was a five-day regime, and then it was cut back down to three, and there were even deaths related to this.

MC – Yeah.

BK – Do you think you've got that down now where patients are, you know, life doesn't come with guarantees, but it's a much safer regimen than it was a few years ago?

MC – Yes. I do think so. That's a good point. I think our group has been very... what's the right word? We really make sure that everyone is taking prophylaxis against fungal infections, so we have everyone take fluconazole, 400 milligrams twice a day. We have everyone on Septra, double-strength, twice daily, twice a week, and acyclovir, as well. Things still come up, we have patients with pneumonias, and coughs, and colds. And I think one patient even had diverticulitis, not quite an infection, but certainly something significant. But I think with that

combination we didn't encounter things like aspergillus pneumonia, or meningitis, or things that could've been more significant.

BK – Any final thoughts you want to share with the patient community about this, and the role that it might play in CLL down the line?

MC – Yeah, that's a great question. Fortunately, we have so many really promising and active drugs that are along the same lines, that we want something that can be effective, durable, and perhaps not involving drugs that can risk the side effects we commonly associate with chemotherapy. So, I think this is one of those. Where it fits… I think it's an alternative. It's an option. There are times when we have trouble getting access to ibrutinib or venetoclax right now, and hopefully, hopefully we can get those drugs for every patient. But I think when there are times where we can't, either due to side effects, or comorbid conditions, or sometimes even just the logistical reasons. I think this is an option that we often kind of keep in our back pocket ready to use. I've used it to kind of stabilize disease before, while we're trying to figure out other treatment options. So, I think it remains a very active combination. I think one of the advantages is that it's not as costly as other treatments. So maybe it's something that we can incorporate into treatment regimens. I think, where it falls, I'm not sure. I think it probably is one option that we can discuss kind of on a case-by-case basis, depending on the individual patient.

BK – Dr. Choi, thanks so much for what you're doing for the CLL community.

MC – Oh, thanks.