Changing CLL Treatment Landscape: Updates From an Expert

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Andrew Schorr:
With us is Dr. Nicole Lamanna from Columbia University. She is a CLL specialist and researcher. Dr. Lamanna, patients who are watching want to know what the leading edge of CLL is. Where is it going now?

Dr. Lamanna:
There’s a lot of exciting data that’s coming forth at some of the meetings recently—ASCO, EHOC, and we have of course the iwCLL coming up in September and of course ASH due later this year—and as the field moves forward and as many of the patients are reading about some of these new oral medications some of them are not so new anymore, like ibrutinib (Imbruvica) and venetoclax (Venclexta). Venetoclax recently got approved in the upfront setting, meaning for patients who had never treatment along with a monoclonal antibody, obinutuzimab (Gazyva), and now that’s been approved upfront as well.

There are many options of therapy for CLL patients, which is fantastic, but one of the areas we’re all trying to figure out of course is how do we use these drugs to the best of our ability based on what we know. We’re all trying to figure that out. We’re running many new clinical trials that are looking at combination therapies. Can we halt, or are we able to discontinue some of these oral therapies once somebody gets a deep remission? If you get a good response can you not be on the oral agents indefinitely? Venetoclax has been the go-to drug for that where we have sort of a finite period of times where we may only use it for 12 months or 24 months.

I think there are many clinical trials looking at that much closer, so you’ll be seeing that there will be a lot of new combination studies to get a better idea of how to use these agents thoughtfully. I think also the question is how do we sequence one drug from another drug is coming. What’s the best agent to start first and then what do you do after that if you need treatment again at some point in the future? Can you restart the same oral medicine?

There’s a whole bunch of stuff going on. We need a little time. I’m always happy to have these new agents and there are newer drugs being looked at as well; some early Phase I and Phase II studies looking at some new therapies for patients even who might develop resistance to Ibrutinib or a BTK inhibitor, so stay tuned for that. There will be some newer clinical trials trying to address what if you develop resistance to some of these new medications, so there’s a lot going on.

Andrew Schorr:
What about management of side effects? These are powerful medicines but they can have side effects, so what about the ability to have people take the right medicine but limit the side effects?
Dr. Lamanna:
I think that’s an important issue because obviously when any new, exciting therapy comes along we always are extremely excited because obviously it benefits patients. Just like when ibrutinib got approved everybody was really, really excited because it really did change how we treat CLL compared to some of the more traditional intravenous chemotherapy regimens we were using, but to be fair even with these oral medications it doesn’t mean that they come without any side effects either. You have patients who tolerate them well, and I’m sure a lot of them read online in some of the patient blogs about them and they do really well and there are other patients who can have every side effect in the world from some of these new oral medications.

We’re still tweaking and I think that’s a really important part of the discussion about these oral medications. It’s how to manage patients through the side effects, whether or not somebody needs to discontinue or dose reduce or what other ancillary medicines we can give patients depending upon the side effect that they’re going through. I still think that’s a really important part. It’s not that you start somebody on oral and that’s it. I think that these are medications with side effects, and so we have to teach and navigate them along with any other—even if we gave intravenous chemotherapy. I think it’s similar even with the orals, but as we’re seeing that there are side effects that people come off of and so that’s an important aspect of these newer medications as well. There’s a lot of education and a lot of teaching.

Andrew Schorr:
You may have another medicine you could switch someone to with a different side effect profile.

Dr. Lamanna:
Correct. That wasn’t necessarily the case several years ago obviously when ibrutinib first got approved. We tolerated a lot of the side effects if somebody had atrial fibrillation or had one of these potential side effects, because they might not had other options at that point depending on what they had gotten previously to Ibrutinib. Now, there are other medications. Even with the same class of drug there are other medications they can be switched to if they develop a side effect.

I mean not that we want to do that haphazardly either. I mean this is again one of those I think it’s important to discuss with your physician, because I think certain side effects people can be treated through if it’s important enough and if you can get through that. There are ways to finesse that and again, maybe you can consider part of that the art of medicine a little bit. The more that somebody has used some of these medications I think the physicians become very astute about how to manage them versus just frank discontinuation. There are some side effects that absolutely patients should be discontinued and given a break or have dose reduction.

Thankfully, now there are many more potential oral medications that patients with CLL can be changed to, and so now that’s not a deal-breaker anymore. I think there are many more options that we have available now for our CLL patients, which is great.

Andrew Schorr:
Many CLL patients are older and they have what you would call co-morbidities, other conditions, and it used to be that there were some powerful medicines you just couldn’t give them. Do you have a range of medicines now so that somebody even with other conditions in an advanced stage has real hope for living with CLL?

Dr. Lamanna:
Absolutely. Remember, the median age of CLL is in the early 70s. This is a disease typically of older individuals and yes, frankly many of the more aggressive chemo-immunotherapy programs that were chemotherapy based for example—if they were not fit we would not be giving those types of aggressive chemo-immunotherapy programs to an older individual. Now, with these oral medications you can’t use age anymore as a barrier because there are ways to finesse all of this now. Even good therapies, these oral medicines are good therapies period and not just for age but even patients with what we call more aggressive features to their disease.

Now, there’s no reason to say, “Oh, I have CLL. I can’t be treated.” I mean that’s a personal choice, but there are many good options of therapies and absolutely people should have hope. Age shouldn’t be a barrier to treatment necessarily anymore.
Andrew Schorr:
In looking to the future and what you have in the lab, do you feel there’s a pretty good, steady stream of new medicines coming that show promise so that if some of these other medicines no longer work for someone that there might well be something else that’s in development now?

Dr. Lamanna:
Absolutely. Not only that, not only are we always looking for newer medications obviously to eventually find a cure for this disease, but the fact is because there are so many opportunities for some of these different oral medications the thought is everybody is always thinking about what treatment am I getting now? I always like to turn it back on people and say; well, you’re thinking about what I’m starting you on now, but I’m always thinking about well, what’s the next treatment and the next treatment and the next treatment?

The goal is to have people with CLL—until we find this a curative disease and we have something that’s going to cure everyone—the goal is to be able to have a good quality of life, minimize side effects, try to obviously do great with reducing the disease when we’re treating it and fixing the problems that there are but being able to go from one therapy potentially to another if needed in the future and sort of string those out until we can do better with newer medicines. Even some of these oral medicines sometimes we can do some combinations with antibodies and other things that may improve upon what we’re doing even at this time or for the next go-around with another medication.

We’re always looking for new drugs in the lab. Definitely, there are some early phase studies on some newer drugs that look promising that we’re doing now.

Andrew Schorr:
Lastly, do you want to say anything about the research that’s going on in chimeric antigen receptor, T-Cell therapy?

Dr. Lamanna:
Yeah, sure. Obviously I know this has gotten a lot of attention of late, and for sure through the years as CAR therapy, as Andrew is referring to, has sort of tweaked an evolution the side effect profile of using this type of technology is improving. We’re hoping as time goes on and with more finessing that not only is it more palatable—in other words, we are able to offer this more to individuals with CLL and obviously reducing the potential side effects of the therapy—will go a long way to its use because obviously we know that it has a lot of efficacy. Some people really do extremely well with CAR therapy and go into remission for a very long time.

Right now, in CLL it’s approved for acute ALL or acute lymphoblastic leukemia in young individuals and it’s approved for multiply relapsed, non-Hodgkin lymphoma. It is not quite yet approved for CLL. There are clinical trials that are ongoing now even in combinations, so not only CAR T-cell therapy by itself but also in combination with some other agents as well. So, stay tuned but certainly we’re tweaking this modality. Think of it as a slightly different modality of trying to use your own T cells to fight your leukemia. This is ongoing and I suspect that as well that as we improve upon this it will not only for CLL but for all of oncology and other diseases, as we improve the side effect profile, this modality will be used more frequently.

Andrew Schorr:
Dr. Nicole Lamanna from Columbia University, thank you so much.