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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Relapsed/Refractory CLL Care: Tailoring Treatment and Addressing Adverse Events

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Lilly. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss strategies for individualizing treatment plans for patients with relapsed/refractory chronic lymphocytic leukemia, or CLL for short, is Dr. Adam Kittai. He's an Assistant Professor in the Division of Hematology at the Ohio State University Comprehensive Cancer Center. Dr. Kittai, thanks for being here today.

Dr. Kittai:
Thanks for having me. Looking forward to this talk.

Dr. Turck:
So why don't we start, Dr. Kittai, by reviewing the treatment landscape for relapsed/refractory CLL. What options are currently available?

Dr. Kittai:
Yeah, so we've come a really long way in CLL. And actually, the treatment landscape for patients who have relapsed/refractory disease is actually very similar to those patients who have treatment-naïve disease. And so when we think about treating patients with CLL for their entire lives, we usually start with one mechanism of treatment and then we switch to the other mechanism of treatment. So the two main mechanisms of treatments are targeting the BTK protein, and the other mechanism is targeting a molecule called BCL-2. And we can target BTK using the BTK inhibitors, and that's going to be ibrutinib, acalabrutinib, zanubrutinib, and the new pirtobrutinib, which I'll mention in a second. And we can target BCL-2 by using venetoclax. And that's always paired with a monoclonal antibody, either rituximab or obinutuzumab.

So in general, and this has its caveats, whatever someone is treated with in the frontline will get the other in the second line, and vice versa. So if you start with a BTK inhibitor in the frontline, typically you're going to get a BCL-2 inhibitor and venetoclax in the second line. And typically, if you start with venetoclax in the frontline, you're typically going to get a BTK inhibitor in the second line. That being said, that treatment paradigm is rapidly changing in that we're using more time-limited therapies in the frontline; specifically, venetoclax is a time-limited therapy. And so if you do relapse after receiving venetoclax, you can actually get retreated with venetoclax.

Another addition to the patients who have relapsed/refractory disease is that drug called pirtobrutinib, which was just approved by the FDA. It's a new type of BTK inhibitor that binds slightly differently than ibrutinib, acalabrutinib, and zanubrutinib to BTK. And it is currently approved for patients who've already been treated with a BTK inhibitor—the three I just mentioned—and venetoclax. And so this is actually a third-line agent.

And so I think that the treatment for patients with relapsed/refractory disease is constantly evolving and getting better. And in general, the sequencing goes BTKi to BCL-2i, and vice versa. And now we have the pirtobrutinib, which can be used after patients have received both a BTK inhibitor and a BCL-2 inhibitor.

Dr. Turck:
Now when it comes to selecting a therapeutic approach, what communication tactics help you learn about a patient's priorities and preferences?

Dr. Kittai:
So this is what I really love about CLL is because I get to really meet my patients longitudinally, meaning that I have a lot of time with them. So for a patient that I treated in the treatment-naïve setting, most likely I've already known them for years before they start to relapse. And so I get to really know them, I get to really meet their family, I usually know what they do for work, and I get to know how many kids, grandkids, or even great grandkids they have. And I really get to know how they did with the previous therapy. So I think about that when I think about communicating with my patients. And what's great about my patients with CLL is that I really get this longitudinal experience where I get to know them over time.

Now if I'm first meeting somebody who is coming to see me with relapsed/refractory disease, I think what is really important is getting to know what their preference is in terms of wanting an oral therapy versus a time-limited therapy. Can they take the time off work to come and get the ramp-up that's required for venetoclax plus an anti-CD20 monoclonal antibody? And how I get to those questions is I really try to make a relationship with my patients, getting to know them, getting to know what they would like, getting to know what their life looks like, and hopefully finding a treatment regimen that clearly fits in with what they would want. Really allowing for good communication and making sure that I understand where they're coming from and where they want to go.

Dr. Turck:
And once you find that out, how do you craft a personalized plan that prioritizes treatment efficacy and a patient's goals and quality of life?

Dr. Kittai:
Overall, given that we have these two major classes of drugs that work really well, I do try to use my patients' preferences to really figure out what drug is best for them. But unfortunately, in the relapsed setting, since we've already gone through one prior line of therapy, I'm trying not to use that prior line that they already got. Sometimes we're kind of stuck with getting an oral regimen versus an oral regimen plus an infusion. And so usually, by the time I see my patients and they're requiring the second line, they know what's coming, and we've had a long conversation of what that might look like. This is really for those patients who received our new therapies, the BTK inhibitors and the BCL-2 inhibitors.

If they've received prior chemotherapy and then are coming in relapsing, really the conversation is more like the treatment-naïve setting where I can really focus the treatment on whether somebody wants an oral therapy that is continuous or a venetoclax regimen that's time limited.

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Adam Kittai about individualizing treatment for patients with relapsed/refractory CLL.

So, Dr. Kittai, if we continue exploring strategies for creating personalized treatment plans, how can we incorporate proactive symptom management, beginning with a patient's diagnosis?

Dr. Kittai:
Yeah, so CLL causes a lot of symptoms. This was highlighted in a recent trial that compared ibrutinib to placebo in patients who otherwise would not have indications to treat their CLL, where the patients who received placebo just had a high rate of adverse events and toxicities that I would expect it. So what this tells me is that our patients with CLL are probably suffering more than we realize. And so even though we ask all our patients specifically about the B symptoms, and those are going to be fevers, chills, weight loss, night sweats, and fatigue, I really open up to my patients to let me know if they're having any symptoms that are bothering them. And I try to help them get through those symptoms or triage them to a specialist or primary care doctor who might be better else to help them.

So at baseline for my patients with CLL, I really spend a lot of time asking them how they're feeling and letting them know that if anything new comes up that they might be worried about that might be related to their CLL or really if anything new comes up that they want to get my opinion on, I'm happy to hear it and help them through it.

Now when it's time to start therapy, and even in the treatment-naïve and relapsed/refractory setting, this is pretty much the same; I go over the main toxicities with my patients. So for instance, with BTK inhibitors, I talk about hypertension. I talk about headache with acalabrutinib. I talk about joint pains, heart disease like atrial fibrillation, and easy bruising and bleeding. I also talk about hypertension with ibrutinib, and also neutropenia with zanubrutinib. So in my conversation, not only we'll talk about the class of drugs and what I expect to occur for my patients in that class, but also the specific details that might occur with a specific drug within that class that I'm treating. And so I really let them know that if they experience any of these things, I want to hear about it right away.

And with venetoclax, the things that I coach my patients about specifically are going to be the diarrhea, as well as monitoring them for their low cell counts because venetoclax can cause low cell counts. And so I make sure that my patients know that if they spike a fever

or if they get an infection, they should call me right away so we can talk about it and run by it. So we're really proactive in our clinic, letting our patients know that this is an open space to discuss whatever symptom they might have and also letting them know about the symptoms that we know patients experience at a high rate, whether it's due to the CLL or the treatment they're receiving.

Dr. Turck:
And are there any other supportive care strategies we can use throughout a patient's journey?

Dr. Kittai:
I think that one thing that we have to remember is that our patients with CLL tend to be from an older population. And so I think we should be making sure our patients are hooked in with a geriatrician if they need it. Think about polypharmacy because polypharmacy is a huge problem in our older group, and really thinking about how we can support these older patients with cancer. So CLL specifically, it is a disease of older patients, which comes with a whole set of other problems, and being proactive and being careful about these very sensitive folks who have a lot of comorbidities and thinking about how those comorbidities might interplay with the treatment they're receiving and their CLL is very important.

Dr. Turck:
Now given everything we've discussed today, Dr. Kittai, would you tell us why personalized approaches are so important in the long-term care of patients who have relapsed/refractory CLL?

Dr. Kittai:
Yeah, so our patients with CLL are living longer and longer. And so when we think about every single patient in front of us, we want to make sure that whatever we choose to treat them with, they are most successful with and can stay on therapy and not come off therapy for a toxicity. And so what that entails is being proactive and making sure that our treatments are meeting each of our patients needs and accounting for what they want out of treatment and also accounting for what might be their comorbidities to make sure that we pick the most effective and safe treatment to allow our patients to have the best opportunity for success with treatment as possible.

Dr. Turck:
That's a great comment for us to think on as we come to the end of today's program. And I want to thank my guest, Dr. Adam Kittai, for joining me to discuss strategies for individualizing treatment plans for patients with relapsed/refractory CLL. Dr. Kittai, it was great having you on the program.

Dr. Kittai:
Thanks for having me. This has been wonderful.

Announcer:
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