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Fixed-Duration vs Continuous-Dosing Approaches in CLL: Impact on QoL and Toxicity Risk

Announcer:
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Dr. Wierda:
Hi, I'm Bill Wierda from the MD Anderson Cancer Center in Houston, Texas, and this is CME on ReachMD. And I'm going to be reviewing, briefly, fixed-duration treatment and strategies for frontline treatment for patients with CLL, focusing on quality of life and risks of toxicity.

Now, there's a lot of data that supports both strategies of treatment for patients with CLL in the frontline setting, and both of those treatments include maintenance-based treatment with a BCL-2 for the BTK inhibitor and fixed-duration treatment with a BCL-2 inhibitor. The BTK inhibitor-based therapy is continuous treatment until progression. We now know that the median progression-free survival with ibrutinib, for example, in the frontline setting, is 10 years. So if you commit a patient to maintenance therapy with a BTK-based treatment, you're really essentially committing them to lifelong treatment. Lifelong treatment means taking medications every day, and that also comes with a risk for side effects and toxicities.

Now, we know generally some of the concerning toxicities associated with BTK inhibitors at a lower frequency would be very concerning issues like cardiac events, atrial fibrillation, etc. Those are rare and the second-generation BTK inhibitors tend to have a lower incidence of those cardiac, more concerning, toxicities. Bleeding and bruising events occur with the BTK inhibitors, and those are somewhat cosmetic and can be managed and, in general, tolerated by patients. Some patients can have rash; some patients can have arthralgias and myalgias; some patients have GI toxicity associated with the BTK inhibitors. But again, that strategy of treatment is continuous and indefinite until patients progress, and that's for many years. And once they progress, typically they will go on to another maintenance-type strategy. So you're, again, committing them to lifelong therapy, whether it’s in the frontline setting or if they progress and develop resistance, also including in the relapsed setting.

That's in contrast to fixed-duration treatment. Currently fixed-duration targeted therapy includes venetoclax-based treatment. There are challenges with venetoclax-based treatment that are different than maintenance strategies that I just mentioned, particularly those are the inconvenience of the ramp-up. The initiation of venetoclax requires patients to come in weekly and be monitored for tumor lysis syndrome, electrolyte abnormalities, and hydration status. And that process is a 4- to 5-week process and can be an inconvenience for patients, particularly if they have limitations in terms of access to the clinic. But once you get a patient up to the target dose of venetoclax, it's a relatively well-tolerated treatment. We do have some challenges with neutropenia occasionally. That can be exacerbated with the addition of the CD20 antibody. But by and large it's a relatively well-tolerated drug, venetoclax. And other drugs within that category that are not yet approved but are in development.

And venetoclax is given for fixed-duration or finite-duration treatment. It's in the frontline setting, typically used and administered for a year, and that's currently as a standard given with CD20 antibody and particularly obinutuzumab. That also requires patients to come in

for monthly infusions and can be an inconvenience for patients. And also, it is somewhat immunosuppressive. The CD20 antibody can increase their risk for infection. But again, that is a finite-duration treatment. Patients get a year of treatment total, 6 months with venetoclax plus obinutuzumab and then an additional 6 months of venetoclax monotherapy. But once patients have finished treatment, they're done and they're in remission, and they're off treatment, and they're living their life relatively normally in that situation and are monitored with observation. If they progress – and the median progression-free survival with venetoclax/obinutuzumab in the frontline setting is 6 years – if they progress they're reassessed and typically they can receive re-treatment with fixed-duration venetoclax-based therapy. If they progress while on venetoclax, that would be a situation where we're changing treatment and moving to a BTK inhibitor-based therapy. But that period in remission off treatment, after patients have completed their finite-duration treatment, is an opportunity for them to live a relatively normal life in remission, and they don't have the same concerns with side effects and toxicities and, in my experience, have had a very good quality of life.

Well, that's a lot of information in a brief period of time. I hope that it was helpful and gives you something to think about. And again, thank you for your time and attention.

Announcer:
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