Should Novel Agents Always Be Used in the CLL Frontline Setting?

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Andrew Schorr:
Here's a question we got in from Jeff. He says, for young and fit patients with relapsed disease what are the best combos and follows now and coming. And I suspect maybe Jeff had received FCR, so if he relapses after FCR, what about that?

Dr. Furman:
So my belief is that these novel agents should always be used up front, or if you've gotten chemotherapy up front they should be used immediately at relapse. A lot of patients and physicians have the idea that there's a benefit to holding back until you really need something, but I believe putting our best foot forward first is always the best approach. So I always recommend going forward first with BTK inhibitor therapy, followed by venetoclax (Venclexta) or venetoclax followed by BTK inhibitor therapy. And I think so in a patient who has relapsed after FCR it will be ibrutinib or acalabrutinib (Calquence). In a patient who has relapsed after acalabrutinib and ibrutinib would then move on to venetoclax.

Now, what I'm really very excited about is the possibility of the combination of either BTK inhibitor therapy plus venetoclax or PI3 kinase inhibitor therapy with venetoclax.

You know, both of these combinations really take advantage of the synergy that happens when you take a BCR antagonist like ibrutinib, acalabrutinib or idelalisib (Zydelig) and duvelisib (Copiktra) and combine it with a Bcl?2 inhibitor. And it really sort of enables us to get very, very deep remissions with actually as short as just 12 months of treatment. And so those are what we're currently testing in patients right now and what I hope will be the frontline treatment for patients in the not?too?distant future.

Andrew Schorr:
Now, one of the things people wonder about is if you take these big guns and put them together could you, like you've been able to do with FCR, stop treatment or take a break from treatment at some time.

Dr. Furman:
So I'm a big believer in that if something's working and you're tolerating it well that we shouldn't mess with it,

But we are currently studying two different processes with relationship to the ibrutinib plus venetoclax combination. So we're taking patients who become MRD negative on the combination after 12 months and randomizing them to either just get ibrutinib or to get placebo. And so that's going to give us information as to whether or not it's safe to stop patients on the combination and treat them with nothing long term. We'll see, one, how many patients relapse, and hopefully none, and, two, if they do relapse whether or not we can then restart ibrutinib and control their disease. So this will provide us that important question as to whether or not we're giving up something by discontinuing the therapy.

We'll have as our comparative those patients who got ibrutinib plus venetoclax for 12 months and then just remained on the ibrutinib.

And so that will sort of be the patients who will continue on with their therapy, and then the other half will be patients who have discontinued all their therapy.

My belief for going to venetoclax is that you're going to get almost all of the bang for your buck out of the first 12 to 24 months, so continuing it is unlikely to yield an additional benefit, so I think stopping it is safe. But, once again, these are the studies that will provide us with those data.