The Role of Venetoclax in Treating CLL

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Jeff Folloder:
We have a question from online. I find this one fascinating, because it's involving how we figure out what drug to give what person. The question is, I could not take ibrutinib (Imbruvica), because I was on an anti-coagulant. Fair enough. He's now getting a combination of venetoclax (Venclexta) and rituximab (Rituxan). And, he seems to be responding rather well. Where does venetoclax fit in with all these therapies that we've been discussing today?

Dr. Keating:
My impression is that venetoclax is probably the best drug that we have for CLL. I think that it gets to the root of the matter, better than anything else.

It's more likely to be part of a regimen that gets to the point where you actually clean out the disease from the blood and the marrow completely. That doesn't mean it's not gonna come back, but it seems to be much more likely to occur. And, it will occur much more quickly than with ibrutinib. So that, instead of having to take it forever, you may have combinations together with an antibody, or these days, here and other places are doing a lead-in for a few months with ibrutinib, to decrease the amount of disease in the first three months, and then they add venetoclax, and at the end of 12 months of treatment, if it's frontline, almost all of the patients, you can't find any CLL. So, venetoclax is going to be a terrific drug.

When—it's already the best drug I think we have for the 7 A&P group of patients. The other part of it though, is that we know ibrutinib can cause in 5 to 7 to 10 percent of patients atrial fibrillation, and they get on anti-coagulants. And, that's the most common situation, but that doesn't mean, if they're on anti-coagulants, you can't give them ibrutinib. Because they already have the atrial fibrillation, so there's no evidence that it's making it worse. So, just—there's a misconception in the mind of a lot of doctors, as to why they shouldn't have it. One reason that you perhaps shouldn't have it is that if you're on anti-coagulants, and ibrutinib weakens platelets, two elements of a defense system against bleeding are inhibited.

So, we might have a somewhat higher incidence of—so, you'd have to watch it very closely initially, to get it, but there's no absolute contraindication to having that. We haven't spoken at all about the new drugs that are coming along, that are lookalikes for ibrutinib. One of them, acalabrutinib (Calquence), and the other is I can't, it starts with a P, pano…

Dr. Ferrajoli:
…BCG3.

Dr. Keating:
BGB3111, BCB3111, and that comes from China, and there's almost no CLL in China, or very low incidence, but there are so many Chinese that there are still a lot of CLL. So, anyway, they have very different aspects, and neither of them seem to cause the atrial fibrillation.

So, that again, it's getting to the point that it's a bit like antibiotics, different people will have different sites, they'll have different things that are causing infection, so use a different antibody, because it has different characteristics, and, but if you go back to the '70s, before fludarabine (Fludara) came along, we were basically using chlorambucil (Leukeran) plus or minus steroids. Just like going to a fancy restaurant, and the entire menu is a hamburger or a cheeseburger.