



## Why Is Venetoclax Approved for Only a Subset of Patients?

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**Andrew Schorr:**

So venetoclax, or Venclexta, recently approved, was approved for people with the 17p deletion who've been previously treated.

**Dr. Thompson:**

Correct, yeah.

**Andrew Schorr:**

Right? Okay. So one would say, all right, well, why not just go broad. And I know here there's a lot of concern about doing it right and safety.

**Dr. Thompson:**

Yeah, safety concerns were the biggest things with venetoclax. This is a drug that kind of suffered from being too potent.

Actually, I remember the first patient that was treated was treated in a hospital I worked at back in Australia. And this patient had a wide, so kind of a 100,000—they'd failed a few therapies previously. And they got a dose of venetoclax; I think it was 200 milligrams. And eight hours later, we measured the blood counts, and the white count was one. So it had gone from 100,000 to one in eight hours. And in association with that, all of the substances within those CLL cells were released into the bloodstream, and that can cause problems with the kidneys, and heart rhythm disturbances. So as a result, we have to start the drug at a very small dose, 1/20 of the eventual dose, and then we have to increase it on a weekly basis. And we have to monitor the blood tests very carefully to make sure that this tumor lysis syndrome is not developing.

And I guess the concern is that academic centers like ours, we're used to doing this. We have a lot of infrastructure that helps us do this safely. But once it gets out into the community with people who are less experienced in its use, can this be done safely? And I think that's why the FDA has initially restricted it to such a narrow group of high-risk patients.

**Andrew Schorr:**

Okay. So it's showing respect for the drug.

**Dr. Thompson:**  
Right.

**Andrew Schorr:**

And having physicians around the U.S., and maybe ultimately around the world, Nicole, get experience with it. And patients and the doctors monitoring for certain things so that it's used powerfully but safely. Did I get it right?

**Dr. Lamanna:**

Yeah, absolutely. I mean, venetoclax is an extremely active therapy. And it would be a shame for the therapy to fail because patients aren't monitored appropriately. Because we've seen this before. We've seen this with lenalidomide (Revlimid).

This was another very active agent in CLL that the doctors just need to know how to use it thoughtfully. And it's also an oral therapy. And so unfortunately, because of some of the side effects with lenalidomide, it just wound up not getting used and never got approved for CLL. Doesn't mean you can't get it for CLL, but it's not officially approved for CLL. So the point is, now we've been getting smarter with some of the newer therapies that are evolving, and we're trying to make steps—and I actually have to applaud—to be fair, they stepped back and went, okay, we have to go back to the drawing board. And we're gonna, even though this may be very difficult for the physicians and patients running the clinical trials, we're gonna admit patients every week to watch their electrolytes and make sure that they're safe until they go through the dose escalation of this drug. So it was very labor-intensive, but it's a very active therapy—and in the right hands, can be used very, very well.

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