



Inhibitor Therapies: How Do They Treat CLL?

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Jeff Folloder:

Dr. Burke, how do the inhibitors work?

Dr. Burke:

I think if I had to summarize that, I would say first of all, we've learned a lot about the biology of CLL and what drives these cancer cells to grow and survive and do what they do. And not only is it advancing treatment for CLL and other cancers critically dependent on clinical trials, but also dependent on understanding this biology, because that's really what's leading to the next wave of effective clinical trials.

So, to your question, we know now that there are a series of interactions within cancer cells among proteins.

So these are proteins within cancer cells that are interacting in certain ways and then driving the cancer cells to grow and survive. So these inhibitor drugs that you're referring to, as a general rule, are binding to these proteins that are in this cascade and blocking those interactions. And, the effect of that has been shown to be that it can lead to the death of the cancer cell by probably a variety of mechanisms. But one way is when you start somebody on a drug like ibrutinib (Imbruvica), one of the things you see is that the lymphocytes move and migrate out of the lymph nodes and into the blood, and they're not allowed to move back.

So, what happens when you start someone on ibrutinib is that the lymph nodes shrink rather quickly, and the white blood cell count, the lymphocyte count in the blood, goes up at the same time probably because the cells are moving from the nodes out into the blood where, over time, with continued exposure to the drug, they gradually die off.

So that's sort of the mechanism of some of these targeted inter-cellular drugs. That differs from chemo where the chemotherapy drugs are damaging the DNA of the cells themselves leading to a rapid killing of a lot of these cancerous lymphocytes. So, in contrast, when we treat someone with chemo, especially in combination with a monoclonal antibody, you see a big drop in the lymphocytes pretty much right away.

So different mechanisms for the different drugs we're using.

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