What Are CLL Prognostic Factors?

Recorded on February 1, 2014

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Jeff Folloder:
We've received an email from a member of the CLL community who wants to know what are the prognostic factors of CLL?

Dr. Wierda:
So you hit on a key area of my interest and something that I've been working on for many years, and that's these prognostic factors. And over the years, a number of newer prognostic factors have been identified.

One of the questions when I first became involved in the evaluation of these factors is which are the more important ones, and if you have a patient who has multiple features or multiple prognostic factor results and they don't all point in the same direction. So for example, they're not all good, you have maybe several good and one bad, which are the heavier weighted prognostic factors that really correlate with what's going to happen with the patient.

So we've gone through an exercise with our database of evaluating all of—many of these prognostic factors including the newer prognostic factors. Since about 2004, we've been evaluating routinely the newer prognostic factors and making correlations with those factors and outcomes. I think one of the important things to remember is that not all of the factors correlate with all of the outcomes. So I'll give you an example of a few of the outcomes. One outcome is time from diagnosis to first treatment. Another outcome is response to the first treatment. Another outcome is the remission duration for the first treatment. Another outcome might be the overall survival from the time of diagnosis to death.

So when you look at each of these parameters you may appreciate different factors involved or predicting for that—that end point, and so we've spent a lot of time and efforts in terms of evaluating these new prognostic factors and developing models and identifying which ones are important for each of those parameters.

If you look across those models, there are some that emerge as typically in the model or typically important. One of them is FISH, so chromosome abnormalities identified by FISH appear to be a very important parameter to look at when you're looking at outcomes.

Immunoglobulin heavy chain variable gene sequence analysis and mutation status is another feature that is typically in the models and appears to be an important parameter to evaluate.

In our models at MD Anderson, beta-2 microglobulin has been consistently important. Stage is important. And so there are some prognostic factors that relate to the disease itself and an individual's own leukemia characteristics, and those are different between individuals obviously, for example, FISH and IGVH mutation status.

And there I think are—there are also other parameters that are important. For example, whether or not a patient has been treated before, how many times a patient has been treated, the length of the last remission, those are all parameters that are prognostic features or prognostic factors for outcomes and are important to evaluate.

And if you have a patient who has been previously treated a lot of times, the number of prior treatments and whether or not they're resistant to standard treatments trumps all of those other prognostic factors. Those features become the dominating driving feature of their disease. The refractoriness to treatment and—is the strongest thing that correlates with outcomes. So it's a complicated system. We have a lot of new prognostic factors. There are some that are identified as important and are consistent, but I think it's important to realize that it changes depending on what end point you're looking at, and it also changes and based on the patient's experience, particularly their prior treatment, their exposure to, treatments etc.

I think another thing to remember and keep in mind is that for example, FISH, the chromosome analysis by FISH. Those features can change, so you can have a patient who doesn't have any chromosome abnormalities when they're first diagnosed but over time, and particularly it can be driven by treatment, patients can develop high-risk features in their FISH analysis, such as development of a 17p deletion or 11p deletion.

And that's in contrast to some of the other prognostic factors, for example, mutation status or ZAP-70, which are fixed and they don't change through the patient's disease course.

Jeff Folloder:
So if I'm hearing you correctly, this is kind of like a moving matrix where some prognostic factors for one patient are very, very important. But for someone with a different set of circumstances, they may not be quite as important. Would that be a fair statement?

Dr. Wierda:
That would be a fair statement. I think it's, again, it's important to remember where a patient is in their disease course, realizing that not every patient needs to be treated ultimately. Or you may have patients who have been treated and develop refractory disease. So an individual's disease status and where they're at in relation to their diagnosis and treatment is important to remember or keep in mind as well as some of these other features that I think people tend to focus on like FISH and mutation status and ZAP-70 and beta-2 microglobulin, which are very useful.

Some of them can change, and again after treatment some of those become less predictive for outcome. And the prior treatment and the resistance to treatment drives the outcomes for patients.