Managing Myeloma

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What is deep sequencing PCR?

Hello, my name is Ray Comenzo. I am a hematologist and professor of medicine and pathology at Tufts University School of Medicine. I am here today to answer some frequently asked questions. In my practice, I am often asked by patients and physicians “What is deep sequencing PCR?” Now, this is a complicated area, but I think the best way to present it is to begin with an area that everyone understands, sampling. If you wanted to know how many left-handed redheaded men of the age of 50 were in New York City, you would take a sample. You might take a sample of 200 or 300 men and then make an estimate. That is standard PCR, where we take a sample of cells and we look for a specific marker. Deep sequencing PCR essentially takes the entire population of New York City. It takes all of the genes, both in the template, the DNA form of the gene, and the expressed or RNA form of the gene, and it identifies each of those genes of interest. It can also tell us, for example, where every left-handed redheaded 50 year-old man lives and who his neighbors are because we are sequencing the genes, so it is a very effective and highly powerful tool. Now, we have to distinguish between the categories of tests that we have and the significance of the tests. We have tests as many of you know to measure proteins in the blood and those proteins are often called M-proteins or monoclonal proteins or free light chains, and we specifically identify them, for example, as IgG kappa, IgG lambda, and so forth. We can measure those proteins in the blood, and taking a sample of blood is actually very effective because blood circulates throughout the body. It is a large organ, and the actual measurement that we get correlates fairly well with the burden of myeloma cells in the patient. So that is a category of test that has a high reliability and significance because as the myeloma population is decreased, the monoclonal protein decreases as well. Deep sequencing PCR is a very, very powerful tool to measure the genes that make the monoclonal protein and also to measure the frequency of the mutated genes that cause myeloma, either in the blood cells or in the bone marrow cells. We do not really know the significance of these findings yet. Therefore, deep sequencing PCR remains an investigational tool and not a tool that is used in clinical practice. There are companies that have developed techniques to do deep sequencing PCR for so-called minimal residual disease, but we do not know the significance of the results that we get. And because we do not yet have a marker for cure in myeloma, we are still struggling with these various ways to estimate minimal residual disease and the multiple clones that we know are associated with multiple myeloma. Thank you for your attention.