Researchers find predictive tests and early treatment delay progression of blood cell cancer

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Mayo Clinic researchers say they have moved closer to their goal of providing personalized care for a common blood cell cancer. They have found that the use of predictive biomarkers along with two targeted treatments significantly delays the need for conventional chemotherapy in patients with early-stage, but high-risk, chronic lymphoid leukemia (CLL).

Their study, published Oct. 15 in the journal *Cancer*, found that in a small group of patients the use of the new tools delayed the need for standard chemotherapy treatment to about four years after cancer diagnosis. Typically, people with this kind of high-risk CLL require chemotherapy at about two years after diagnosis.

Because this was a small phase II study, the researchers cannot yet say that this strategy will improve the quality or duration of life for patients. However, they say that because of these promising findings, all CLL patients at Mayo Clinic now undergo the predictive tests, whose results can be used to risk-stratify therapy, including enrollment in ongoing experimental treatments if appropriate.

The two targeted therapies studied, alemtuzumab and rituximab, are widely used in advanced-stage CLL. Both are monoclonal antibodies that produce an immune response against the cancer cells.

"This is the first publication of a study on CLL in which patients were selected for early treatment of their disease based on molecular prognostic markers, and it is also the first one to test a combination of targeted therapies in a group of patients who would not ordinarily be treated yet," says the study's lead investigator, Mayo hematologist Clive Zent, M.D.

"The standard of care for these patients is to watch and wait until patients develop more advanced disease and then to treat them with chemotherapy and monoclonal antibodies," he says. "We believe this new approach is better for patients because it identifies those who will develop aggressive CLL sooner than later and helps delay need for more toxic treatments.

"While this is a novel concept in the field of CLL treatment, we think it moves us toward the day when we can treat all patients uniquely, based on the characteristics of their individual cancer."

CLL is the most common malignancy of lymphocytes. Annually, in the United States, it is diagnosed in more than 15,000 people and results in almost 5,000 deaths. CLL is a cancer of B-lymphocytes, infection-fighting white blood cells that originate in the bone marrow. The disease progresses as the number of lymphocytes increases in bone marrow and lymph nodes and can cause patients to become ill. The rate of progression varies among patients, according to Dr. Zent. "We know that roughly one-third of patients will need treatment within two years of diagnosis, one-third will need treatment at some point in the future, and the remaining one-third of patients will never need treatment and will not die of their disease," he says.

"Because, in the past, we could never predict which patients would have more aggressive disease, we have had to watch everyone, and that requires repeated blood tests and physical exams," he says. Once the disease progresses, treatment with chemotherapy and monoclonal antibodies such as rituximab and alemtuzumab can be prescribed, but these treatments do not cure the disease.

Researchers at Mayo Clinic and other centers have developed a number of different biomarker tests to

predict, with reasonable certainty, which patients are at high-, low- or moderate-risk for progression of their cancer. They have found that testing CLL cells for overproduction of CD38 and ZAP-70 proteins, and analyzing the altered state of several genes as well as chromosomal defects in the cells can significantly predict cancer that will grow faster.

In this study, Mayo investigators used the biomarkers to identify 30 early-stage CLL patients who had a 50 percent chance of needing treatment for progressive disease within two years of diagnosis and gave them a 31-day course of therapy using the two targeted treatments. They found that drug toxicities were manageable and that 90 percent of patients responded to the agent. Within this group, 11 patients had a complete response. Only nine patients required subsequent standard treatment for progressive disease at a median of 1.5 years. In contrast, time to treatment was a median of about two years in a comparison group of 117 patients who were at high risk but did not receive the targeted therapies.

"Using these tools and treatments, we hope to be able to substantially delay CLL progression in patients who are at risk," Dr. Zent says. "We don't know yet that this strategy will decrease mortality in patients, because that can only be proven in a phase III randomized clinical trial. But these good results now set the stage for such a study."

Source: Mayo Clinic