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Combination immunotherapy shows high activity against recurrent Hodgkin lymphoma

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A new combination of three drugs that harness the body's immune system is safe and effective, destroying most cancer cells in 95 percent of patients with recurrent Hodgkin lymphoma, according to the results of an early-phase study.

Presented Dec. 3 at the annual meeting of the American Society of Hematology in San Diego, the study in 19 men and women found that injections of ipilimumab (marketed as Yervoy), nivolumab (Opdivo), and brentuximab vedotin (Adcentris) safely decreased tumor size or spread to some degree in 18 patients after at least six months of treatment, with 16 patients showing complete disappearance (remission) of tumors. After nine months of treatment, 15 remained in complete remission with no sign of their cancer's return (relapse).

Researchers say the triple therapy was "generally well tolerated" with relatively mild effects, such as rash, diarrhea, and nausea—issues that mostly went away when treatment stopped.

The multicenter clinical trial, led by Catherine Diefenbach, MD, at NYU School of Medicine and its Perlmutter Cancer Center, was conducted in patients for whom initial standard chemotherapy or stem cell transplantations failed to stop cancer cell growth. The research team says its latest results extend work reported at the same meeting in 2015 and 2016, which found that double combinations with brentuximab vedotin and nivolumab, or brentuximab vedotin and ipilimumab, were also safe and highly active against relapsed lymphoma.

The success of these efforts spurred Diefenbach and her colleagues to investigate how well other immunotherapy drug combinations performed in such hard-to-treat cases, including the current Phase I safety study.

Diefenbach, a Perlmutter hematologist-oncologist, says treatment options are "extremely limited" for the three in 10 Hodgkin lymphoma patients who fail to respond to initial therapy. The disease, she notes, affects mostly those under age 40, leading to some 1,300 deaths per year. However, most cases of Hodgkin lymphoma are considered curable if diagnosed and treated early.

"Our study results are promising and demonstrate the potential for combination immunotherapy to dramatically improve if not change the standard of care in how we treat patients whose Hodgkin lymphoma returns after initial treatment," says Diefenbach, an assistant professor at NYU Langone and clinical director of lymphoma program services at Perlmutter.

Diefenbach says a larger, Phase II, clinical trial is already underway in which patients are randomly assigned to receive the triple or double combinations, allowing the scientists to demonstrate if either strategy is better than the other.

According to Diefenbach, brentuximab vedotin works by homing in on CD30, a protein on the surface of some Hodgkin lymphoma cells, and then delivering an attached dose of chemotherapy to destroy the cell. Nivolumab turns off an inhibitory switch, or "checkpoint," called PD1on T cell surfaces, undoing the immune system's inability to identify and attack tumor cells. Ipilimumab works very similarly to nivolumab, she says, but targets a different checkpoint, called CTLA4.

More information: This presentation, Abstract #679, is titled A Phase I Study with an Expansion Cohort of the Combination of Ipilimumab,

Nivolumab, and Brentuximab Vedotin in Patients with Relapsed/Refractory Hodgkin Lymphoma: a Trial of the ECOG-ACRIN Cancer Research Group (R4412 Arms G to I). The study will be presented in Room 6F at the San Diego Convention Center in California.

Provided by NYU Langone Health