Medical Xpress

Study rejects biologic age as limiting factor for stem cell transplants

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More than 40 percent of older patients with acute myeloid leukemia (AML) can remain in long-term cancer remission through a modified, less aggressive approach to donor stem cell transplantation, according to the results of a phase 2 study led by oncologists at The Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC—James).

AML is an aggressive blood cancer that is life threatening and is typically diagnosed in patients older than 60. The data represents new hope in a disease where the five-year survival rate is often below 10 percent, despite achieving initial remission.

Previous observational studies have suggested that allogeneic hematopoietic stem cell transplantation—which involves infusing a patient with healthy stem cells from a donor—can reduce cancer recurrence and, therefore, improve overall survival for AML patients. Patients over 60, however, traditionally have been considered poor candidates and excluded from stem cell transplants due to other prohibitive health conditions or concerns about their ability to tolerate the intensive chemotherapy treatments necessary to eradicate leukemia cells before infusing the body with donor stem cells to rebuild healthy bone marrow.

Study Methods and Findings

Under the direction of OSUCCC—James Director of Blood and Marrow Transplantation Steven Devine, MD, the current study sought to determine whether a modified conditioning regimen for stem cell transplantation could improve long-term cancer remission rates for patients with AML between the ages of 59 and 75.

The phase 2 cooperative group trial enrolled 114 patients with a median age of 65 at 21 U.S. hospitals between Nov. 2004 and Nov. 2011. The trial was conducted with grant support through the National Cancer Institute's cooperative group trials network (Alliance for Clinical Trials In Oncology, formerly the Cancer And Leukemia Group B).

Treatment with bone marrow transplant involves collecting stem cells—which are produced in the bone marrow—either from the cancer patient (autologous) or a donor (allogeneic). Traditionally, these stem cells are then infused back into the patient after high-dose chemotherapy cancer treatment is completed to help restore bone marrow's ability to produce red and white blood cells that fight infection.

For this study, all patients received reduced-intensity chemotherapy (fludarabine followed by busulfan) prior to transplant—which essentially cut treatment strength by half compared to the traditional high-dose chemotherapy regimens used in younger patients. Patients were also given medications (tacrolimus and methotrexate) to help prevent graft-versus-host disease, a condition that can occur when the newly transplanted donor cells try to reject the patient's normal cells.

Researchers found that 42 percent of patients enrolled onto the study remained cancer free two years after stem cell transplantation. Previously published data suggested that not more than 20 percent of similar patients who underwent conventional chemotherapy regimens would remain cancer free after two years.

Devine and his colleagues reported their results in the *Journal of Clinical Oncology* online ahead of print Monday, Nov. 2, 2015. This is the first prospective study of this less-intense approach (known medically as 'reduced-intensity conditioning').

"This new data offers strong support against using biological age as a limiting factor for stem cell transplantation in AML patients who are otherwise well positioned to tolerate and achieve long-term remission with this approach," says Devine, corresponding author of the JCO study and principal investigator of national clinical trial. "Close to half of the patients treated in this study achieved long-term cancer-free survival after two years. These outcomes are similar to what we would expect to see in younger patients and appear to be better results than those that can be achieved with conventional chemotherapy-based approaches typically used in AML patients over 60."

Adult acute myeloid leukemia is a type of cancer in which bone marrow makes abnormal myeloblasts (a type of immature white blood cell), red blood cells or platelets. Nearly 21,000 cases of AML are diagnosed annually, the majority of them in adults.

Provided by Ohio State University Medical Center