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Dual stem-cell transplant improves outlook for children with high-risk neuroblastoma

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Children with high-risk neuroblastoma whose treatment included two autologous stem-cell transplants were more likely to be free of cancer three years later than patients who underwent a single transplant, a Phase 3 clinical trial has found. The results of the Children's Oncology Group trial, led by investigators at Dana-Farber/Boston Children's Cancer and Blood Disorders Center and Seattle Children's Hospital, were presented today at a plenary session at the annual meeting of the American Society of Clinical Oncology. (Abstract LBA3).

The tandem transplant technique, initially developed by researchers at Dana-Farber/Children's in the 1990s, produced even better results when followed by treatment with immunotherapy agents, investigators found.

Three years after completing treatment, 61.8 percent of the participating patients who received two autologous transplants—transplants using their own stem cells rather than a donor's—were alive and cancer-free, compared to 48.8 percent of those who underwent a single transplant.

"Our ability to treat children with neuroblastoma has improved significantly over the past 25 years, particularly with the introduction of high-intensity chemotherapy regimens and stem-cell transplantation," says Lisa Diller, MD, chief medical officer of Dana-Farber/Boston Children's and senior author of the study. "The findings of this study define a new standard for the treatment of this disease."

Julie R. Park, MD, of Seattle Children's Hospital, is the study's lead

author.

Neuroblastoma is a tumor that begins in nerve cells outside the brain and usually occurs in children under 6 years old. Though rare - with about 700 new cases annually in the United States - it is the second most common pediatric solid tumor and the most common cancer in infancy.

The trial enrolled 652 patients newly diagnosed with high-risk neuroblastoma, the vast majority of whom had Stage 4 (metastatic) disease. The median age of the participants was 3.1 years.

All patients were initially treated with surgery and six cycles of high-dose chemotherapy with multiple drug agents. Blood-forming stem cells were collected after the first two cycles for use in transplantation.

After the last chemotherapy cycle, 355 patients deemed good candidates for transplantation were randomly assigned to receive a single autologous stem-cell transplant with three chemotherapy drugs or a double transplant with a different chemotherapy combination. For patients receiving two transplants, the second was begun about six weeks after completion of the first. Patients received radiation therapy at the site of the initial tumor and, in some cases, the sites of metastases as well.

A subset of patients received immunotherapy after transplant, as participants in a separate clinical trial of dinutuximab, an agent that the federal Food and Drug Administration ultimately approved for use in neuroblastoma in 2015. In those patients, double transplant was also associated with an improved outcome: Among patients who received immunotherapy, 73.7 percent of the double-transplant patients were alive and cancer-free at the three-year mark, compared with 55.5 percent of single-transplant patients.

The investigators found that both event-free survival - survival without

recurrence of disease or development of a second cancer—and overall survival were higher in the two-transplant group, although the increase in overall survival was not statistically significant. The rates of severe acute side effects were similar in both treatment groups.

"As encouraging as these results are, the fact remains that we are treating some of our youngest patients with the most toxic therapies in our arsenal," Diller says. "While we continue to improve survival, we must also seek ways to reduce the toxicity of our treatments and the late effects many of these children will suffer."

Provided by Dana-Farber Cancer Institute