Drug regimen enough to control immune disease after some bone marrow transplants

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Johns Hopkins and other cancer researchers report that a very short course of a chemotherapy drug, called cyclophosphamide, not only can prevent a life-threatening immune response in some bone marrow transplant recipients, but also can eliminate such patients' need for the usual six months of immune suppression medicines commonly prescribed to prevent severe forms of this immune response. Patients receive cyclophosphamide for two days after their bone marrow transplant, in addition to two other chemotherapy drugs given before the transplant.

Johns Hopkins Kimmel Cancer Center scientists first used cyclophosphamide to prevent severe graft-versus-host disease (GVHD) after bone marrow transplant involving haploidentical or "half-matched" transplants, a treatment first used in 2000 at the Cancer Center to treat leukemias and other blood cancers. The scientists began to use post-transplant cyclophosphamide in clinical trials of fully matched bone marrow transplants in 2004.

Now, the new multi-center study confirms that the post-transplant cyclophosphamide is safe and effective for people who have received fully-matched bone marrow transplants.

The shortened regimen, described online Sept. 29 in the *Journal of Clinical Oncology*, begins with intravenous busulfan and fludarabine, two chemotherapeutic drugs that wipe out a patient's immune system and prepare his or her body to receive donated marrow. After the transplant, patients receive two days of cyclophosphamide to prevent GVHD and rejection of the new bone marrow. Conventionally, most transplant patients get six months of immunosuppressive treatment for that purpose.

The bookended pre- and post-transplant treatments, which have been tested separately in other studies, already had promising track records in controlling cancer and preventing severe GVHD. Those successes led researchers from three hospitals, including Johns Hopkins, to combine the two therapies, says Leo Luznik, M.D., an associate professor of oncology at the Johns Hopkins University School of Medicine and leader of the study.

The new study enrolled 92 patients with high-risk blood cancers. Forty-five of the 92 patients received matched transplants from relatives, while 47 received matched transplants from unrelated donors.

After their transplants, 51 percent of the patients experienced grades II to IV acute GVHD, the milder form, and 15 percent of the patients experienced the severe forms of acute GVHD (grades III to IV). Only 14 percent of the patients developed chronic GVHD. A leading cause of post-bone marrow transplant deaths, chronic GVHD affects approximately one-half of patients who receive conventional treatments.

Two years after their transplants, 67 percent of patients were living, and 62 percent of all patients were cancer-free.

Luznik says he was encouraged by the low rate of chronic GVHD seen with the regimen, noting that the percentages of acute GVHD cases are similar to those seen with the standard six-month regimen of immunosuppressive drugs. Reducing the post-transplantation treatment to two days with cyclophosphamide, he explains, "also allows for the earlier integration of other treatments."

For example, immunotherapies used to eradicate any remaining cancer could be started much sooner under this regimen, says Christopher Kanakry, M.D, a Kimmel Cancer Center researcher and co-first author of the study. "If you give patients immune cells to eradicate any remaining cancer cells that might be present," he says, "those immune cells would not be prevented from doing

their job by ongoing immune suppression drugs that are being used in patients treated with conventional transplant approaches."

Luznik says that the researchers' next step will be to test the short course therapy in a phase III randomized clinical trial that would directly compare results in patients who receive the cyclophosphamide treatment with those who receive either a separate, experimental approach to prevent GVHD or the more traditional six-month immunosuppressive therapy.

More information: Read the study in the *Journal of Clinical Oncology*.
jco.ascopubs.org/content/early …
4.0625.full.pdf+html

Listen to a podcast discussing the study, produced by the *Journal of Clinical Oncology*.
jco.ascopubs.org/content/early …
13.54.0625/suppl/DC2

Provided by Johns Hopkins University School of Medicine

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