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Novel drug regimen can improve stem cell transplantation outcomes

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Adding bortezomib (Velcade) to standard preventive therapy for graft-versus-host-disease (GVHD) results in improved outcomes for patients receiving stem-cell transplants from mismatched and unrelated donors, according to researchers from Dana-Farber Cancer Institute.

In a new phase 2 trial, patients treated with bortezomib had lower rates of severe acute GVHD and treatment-related mortality, and experienced better one-year overall survival than has been seen historically with such patients receiving standard preventive therapy, the investigators reported at the American Society of Hematology annual meeting.

"This regimen appears to improve not just GVHD prevention but more importantly, overall and relapse-free survival for myeloablative transplant recipients lacking matched sibling donors," said John Koreth, MBBS, DPhil, of Dana-Farber, the lead author and study PI. The senior author is Edwin P. Alyea, III, MD, also of Dana-Farber.

Stem cell transplantation following myeloablation (high-dose chemotherapy to wipe out the patient's bone marrow and immune system) is a curative therapy in advanced or aggressive hematologic malignancies, Koreth said. However, recipients who lack preferred matched sibling donors have worse outcomes, with higher treatment-related mortality and severe GVHD, and poorer survival.

Bortezomib, a proteasome inhibitor drug, is a mainstay of treatment for multiple myeloma. In addition to killing cancer cells, bortezomib

dampens some immune responses, suggesting it may have a role in mitigating GVHD, the result of donor immune cells attacking the transplant recipient's normal tissues.

The prospective, single-arm phase 2 trial of a bortezomib-based regimen enrolled 34 patients with hematologic malignancies who received myeloablative stem cell transplants. In addition to standard GVHD prophylaxis medications – tacrolimus and methotrexate - the patients received three doses of bortezomib (on the first, fourth and seventh day after transplant). The treatment was well-tolerated with no patients missing doses because of toxicity.

Historically, recipients of unrelated and mismatched donor transplants have severe acute GVHD rates of 28 percent and 37 percent, respectively, with one-year treatment-related mortality of 36 percent and 45 percent, respectively, and one-year overall survival of 52 percent and 43 percent, respectively.

In patients treated with bortezomib in the new study, the rate of severe acute GVHD at 180 days after transplant was only 12 percent. By two years, only 8.8 percent of patients had died from treatment-related mortality, and 5.9 percent had died from disease relapse. Overall survival at two years was high at 84 percent.

Koreth said that a randomized trial of bortezomib for GVHD prevention is ongoing at Dana-Farber.

Provided by Dana-Farber Cancer Institute