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Experimental graft-vs.-host disease treatment equivalent to standard care in Phase 3 trial

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An experimental drug combination for preventing graft-versus-host disease (GVHD) was not significantly better than the standard regimen on key endpoints, according to a report of a phase 3 trial at the American Society of Hematology annual meeting.

The combination of two immunosuppressive compounds—tacrolimus plus sirolimus—did not provide a statistically significant, GVHD-free survival benefit over the long-used standard of care, tacrolimus plus methotrexate, said researchers from Dana-Farber Cancer Institute who led the multi-center trial.

However, there were some "upsides" of the tacrolimus/sirolimus treatment that could prove advantageous for certain patients, said Corey Cutler, MD, MPH, first author of the report. Among them: patients engrafted slightly more rapidly and suffered much less from mucositis, a common and painful side-effect that causes sores in the mouth and throat.

But there were also "downsides," Cutler said – an increased incidence of veno-occlusive disease (blood clots in the liver) and a slight increase in the rate of late-onset GVHD.

"We were a little disappointed in the results, but excited to offer an alternative to the standard of care for the past 25 years," said Cutler,

who, along with Joseph Antin, MD, of Dana-Farber, senior author of the report, had led clinical studies of sirolimus beginning in 2000 in hopes that it would promote better survival from GVHD than the standard treatment.

The phase 3 randomized controlled trial was carried out by the Bone and Marrow Clinical Trials Network (BMT CTN) at 26 centers. It enrolled over 300 patients, the majority of whom had acute leukemia in remission. The patients had received stem cell transplants from a matched sibling donor.

The primary endpoint of 114-day acute GVHD-free survival was 67 percent in the tacrolimus/sirolimus group and 62 percent in the tacrolimus/methotrexate group – a difference that was not statistically significant. At two years after transplantation, there was no difference in disease-free survival and overall survival.

"This study establishes this regimen as an alternative to the standard of care – it could be preferable in certain scenarios," Cutler said. "It will continue to be the standard of care at Dana-Farber"

Provided by Dana-Farber Cancer Institute