UKE Paper of the Month February 2016

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Antilymphocyte Globulin for Prevention of Chronic Graft-versus-Host Disease

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ABSTRACT:
BACKGROUND: Chronic graft-versus-host disease (GVHD) is the leading cause of later illness and death after allogeneic hematopoietic stem-cell transplantation. We hypothesized that the inclusion of antihuman T-lymphocyte immune globulin (ATG) in a myeloablative conditioning regimen for patients with acute leukemia would result in a significant reduction in chronic GVHD 2 years after allogeneic peripheral-blood stem-cell transplantation from an HLA-identical sibling.
METHODS: We conducted a prospective, multicenter, open-label, randomized phase 3 study of ATG as part of a conditioning regimen. A total of 168 patients were enrolled at 27 centers. Patients were randomly assigned in a 1:1 ratio to receive ATG or not receive ATG, with stratification according to center and risk of disease.
RESULTS: After a median follow-up of 24 months, the cumulative incidence of chronic GVHD was 32.2% (95% confidence interval [CI], 22.1 to 46.7) in the ATG group and 68.7% (95% CI, 58.4 to 80.7) in the non-ATG group (P<0.001). The rate of 2-year relapse-free survival was similar in the ATG group and the non-ATG group (59.4% [95% CI, 47.8 to 69.2] and 64.6% [95% CI, 50.9 to 75.3], respectively; P=0.21), as was the rate of overall survival (74.1% [95% CI, 62.7 to 82.5] and 77.9% [95% CI, 66.1 to 86.1], respectively; P=0.46). There were no significant between-group differences in the rates of re-lapse, infectious complications, acute GVHD, or adverse events. The rate of a composite end point of chronic GVHD–free and relapse-free survival at 2 years was significantly higher in the ATG group than in the non-ATG group (36.6% vs. 16.8%, P=0.005).
CONCLUSIONS: The inclusion of ATG resulted in a significantly lower rate of chronic GVHD after allogeneic transplantation than the rate without ATG. The survival rate was similar in the two groups, but the rate of a composite end point of chronic GVHD–free survival and relapse-free survival was higher with ATG. (Funded by the Neovii Biotech and the European Society for Blood and Marrow Transplantation; ClinicalTrials.gov number, NCT00678275.)

STATEMENT:
The results of this prospective, randomized multicenter study significantly improved the outcome of leukemia patients receiving an allogeneic stem cell transplantation from their HLA-identical sibling by reducing the risk of chronic graft-versus-host disease significantly without obvious risk of relapse, which improves the quality of life for patients after the transplant and will change daily practice.

BACKGROUND:
The work was performed as an investigator initiated trial (Sponsor according to AMG: UKE) from researchers of the Department of Stem Cell Transplantation and included 27 centers from 4 nations (Germany, Italy, Spain, and Israel). The Department of Stem Cell Transplantation at the UKE, headed by Nicolaus Kröger, is one of the largest transplant

centers in Germany and Europe, focusing on continuous improvement for mainly hematological malignancies by translating own laboratory research on stem cell biology, genetically modified cells, immunobiology, and molecular monitoring into clinic and by conducting large multicenter studies.