

Stem cell transplant for severe scleroderma improves survival, quality of life

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New clinical trial findings show that a therapeutic regimen involving transplantation of a person's own blood-forming stem cells can improve survival and quality of life for people with severe scleroderma, a life-threatening autoimmune disease. The regimen, known as myeloablative autologous hematopoietic stem cell transplant (HSCT), includes chemotherapy and total body radiation to destroy the bone marrow followed by transplantation of the person's own blood-forming stem cells to reconstitute the marrow and immune system. The study, funded by the National Institutes of Health, found myeloablative HSCT to be superior to treatment with the immune-suppressing drug cyclophosphamide.

The findings appear in the Jan. 4 issue of the *New England Journal of Medicine*.

Scleroderma is characterized by hardening of the skin and connective tissues. Diffuse systemic sclerosis is a severe, often fatal form of the disease that also involves the internal organs. Treatment options are limited. People with the disease may take antirheumatic drugs and immune-suppressing drugs like [cyclophosphamide](#) to help manage symptoms, but none of these medications has been proven to provide long-term benefit.

The clinical trial, called Scleroderma: Cyclophosphamide or Transplantation (SCOT), compared the safety and potential benefits of the two [treatment](#) regimens among 75 people with diffuse systemic sclerosis who had lung or kidney involvement.

Compared with cyclophosphamide, transplantation offered significantly greater long-term benefits, but also carried known short-term risks, such as infections and low blood cell counts.

"We need effective therapies for scleroderma and other severe autoimmune diseases, which can be not only debilitating to the patient but also difficult to treat," said Anthony S. Fauci, M.D., director of NIH's National Institute of Allergy and Infectious Diseases (NIAID), which sponsored the study. "These results add to the growing evidence that stem cell transplants should be considered as a potential treatment option for people with poor-prognosis scleroderma."

Two previous clinical trials suggested HSCT benefited people with severe scleroderma. Participants in these earlier trials received non-myeloablative HSCT, a less intensive procedure using lower doses of chemotherapy that does not completely destroy the [bone marrow](#). However, neither trial changed clinical practice in the United States, in part because of concerns about the durability of responses to treatment and the safety of these [transplant](#) regimens. The SCOT trial assessed a myeloablative transplant regimen, which researchers thought might offer better long-term outcomes. Investigators followed the [participants](#) for up to six years to assess safety and durability of remission.

Participants in the SCOT trial, conducted at 26 clinical research sites in the United States and Canada, were randomly assigned to receive either myeloablative autologous HSCT or one year of treatment with monthly doses of [intravenous cyclophosphamide](#). Of the 36 participants assigned to the transplant arm, 33 received a transplant. The procedure began with doctors collecting a participant's [blood-forming stem cells](#), after which the participant received chemotherapy and radiation to eliminate the bone marrow. Finally, doctors infused the participant's own blood stem cells to rebuild the bone marrow and a normally functioning immune system. Of the 39 participants assigned to the cyclophosphamide arm, 34

received at least nine of the 12 prescribed monthly doses.

The study investigators used an analytic approach based on a hierarchy of clinical outcomes specific for severe systemic sclerosis to compare every participant in the study with every other participant. These outcomes included death, survival without scleroderma-related organ damage, progression of lung and skin disease, and quality of life. At four and a half years of follow up, participants who received a transplant experienced significantly better outcomes overall than those who received cyclophosphamide. In addition, 44 percent of participants who received cyclophosphamide had begun taking antirheumatic drugs for progression of their scleroderma, compared to only 9 percent of those who received a transplant.

During the study, seven participants in the transplant arm died, compared to 14 in the cyclophosphamide arm. Of these deaths, three in each arm were among participants who did not complete their assigned treatment by either receiving the transplant or an adequate regimen of cyclophosphamide. Participants who received transplants were much less likely to die from progression of their scleroderma compared to those who received cyclophosphamide. Only two participants who received a transplant died due to disease progression, while 11 such deaths occurred among those who received an adequate regimen of cyclophosphamide. The two other deaths in the transplant arm were attributed to the treatment, which is a lower rate of transplant-related death than previously reported for HSCT. No deaths were attributed to cyclophosphamide.

Participants in both study arms experienced treatment side effects, such as infections. Most serious adverse events among transplant recipients occurred during the first 26 months after transplant. Overall infection rates in the two study arms were similar, although more [transplant recipients](#) developed infections with varicella zoster, the virus that causes

chickenpox and shingles.

"Our findings indicate that undergoing stem cell transplantation for severe scleroderma poses more short-term risks but offers greater long-term gains than cyclophosphamide treatment," said Keith M. Sullivan, M.D., of Duke University, Durham, North Carolina, who served as a principal investigator of the SCOT study. "While treatment decisions should always be made on an individual basis, we hope that our work will help define a new standard of care for this severe, life-threatening autoimmune disease."

The investigators are continuing to follow many of the SCOT participants to further assess their long-term health outcomes.

More information: KM Sullivan et al. Myeloablative autologous stem cell transplantation for severe scleroderma. *New England Journal of Medicine*, DOI: [10.1056/NEJMoa1703327](https://doi.org/10.1056/NEJMoa1703327)

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