



The Medical & Scientific Advisory Board of the Scleroderma Foundation released the following statement on January 8, 2018.

The results of the National Institutes of Health (NIH) supported multi-center SCOT (Scleroderma: Cyclophosphamide or Transplantation) trial were published in the January 4, 2018 issue of the New England Journal of Medicine.

DESCRIPTION OF THE TRIAL:

The SCOT trial compared the safety and benefit of two different immunomodulatory treatments in patients with early and severe scleroderma. Patients recruited from 26 clinical research sites in North America were randomized to either high-dose chemotherapy followed by hematopoietic stem cell transplant (HSCT) or 12 monthly IV cyclophosphamide (Cytoxan) treatments. The stem cells came from the patients themselves, not from donors.

It is important to point out that the treatment procedure in the stem cell transplant group was composed of two parts: first the patients received high-dose chemotherapy with irradiation to effectively destroy the patient's abnormal immune system, and second, the stem cells (removed from the patients prior to chemotherapy) were infused to reconstitute the immune system with new or "naive" immune cells that would likely not contribute to scleroderma. Thus, the therapeutic benefit seen in the stem cell arm comes from the chemotherapy not from the stem cells themselves.

RESULTS OF THE TRIAL:

Seventy-five scleroderma patients were enrolled in the study. Each patient had severe skin disease along with lung or kidney involvement. 39 patients were randomized to treatment with monthly IV Cytoxan, and 36 patients were randomized to receive the high-dose chemotherapy, irradiation and stem cell transplant.

At an average of four and a half years of follow-up, patients who received the chemotherapy, irradiation and stem cell transplant had a lower death rate from scleroderma-related causes than patients who received the 12 months of IV Cytoxan. In the stem cell-treated group, only two patients died from progression of their scleroderma, compared to 11 patients treated with Cytoxan indicating that the stem cell group had a better treatment response than the Cytoxan group. However, this needs to be weighed against the fact that two patients died in the stem cell group due to transplant-related complications, whereas no patient in the Cytoxan group died from the treatment.

COMPLICATIONS OF THE TREATMENT:

There was a concern that infections might be more frequent in one group versus the other but this was not the case. Infections as complications of treatment were seen equally in both groups, but varicella zoster (shingles) infections were more common in the transplant group.

CONCLUSIONS:

These results are broadly consistent with favorable outcomes reported from two previous trials in Europe and the US, and provide support for the use of autologous stem cell transplant therapy for some severe scleroderma patients with kidney or lung involvement.

It is always important to weigh advantages versus disadvantages, that is, benefit versus risk, in any treatment decision particularly one with the potential for serious infections and (admittedly uncommon) treatment-related deaths.

The patients selected for the study had to have adequate kidney and lung function to be able to tolerate the procedure which would exclude many of our current patients.

This study is an extremely valuable contribution to the treatment of scleroderma. However, there are numerous unanswered questions, some of which are being addressed in follow-up studies, including how long the improvement lasts (is it in fact life-long or will the disease eventually relapse), which patients are the best candidates for this strenuous procedure, is there a better preparative regimen (combination of chemotherapy with/without radiation) that would provide the same results but with fewer side effects?

This treatment is clearly not recommended for all scleroderma patients. Many patients show a good response to current medical therapies, or show little progression of their disease over time. Therefore, it will be important to develop and validate guidelines for identifying those patients who are at high risk for disease progression or who have been shown to be non-responsive to current treatments. In addition, we recommend that patients for whom stem cell transplantation is considered a reasonable treatment option be referred for the procedure to expert centers where appropriate evaluative protocols, multi-speciality care - including scleroderma experts and physicians with substantial experience with the procedure and all of its complications - is available. The cost of stem cell transplant therapy, which can be as high as \$150,000, will likely be an impediment, but it is hoped that the results of the SCOT study will lead insurers/payors to cover such therapy in appropriate situations.

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