



Scleroderma: Cyclophosphamide Or Transplantation

SCOT is sponsored by the National Institutes of Health (NIH) through its Division of Allergy, Immunology and Transplantation (DAIT) in the National Institute of Allergy and Infectious Diseases (NIAID).

Have you seen this patient?

- Rapidly progressing systemic sclerosis (SSc)
- Extensive skin involvement (modified Rodnan skin score ≥ 16)
- Early internal-organ involvement

Refer to the back of this card for a more detailed list of the inclusion/exclusion criteria.

Study Design

A total of 226 patients with rapidly-progressing severe systemic sclerosis (SSc) will be enrolled.



Subjects will be randomly assigned in a 1:1 ratio to receive either:

High-dose immunosuppressive therapy (HDIT) with autologous stem cell transplantation

OR

Monthly pulse IV cyclophosphamide for 12 months



Subjects will be followed for 44 months.

Primary Study Objective

To evaluate the potential benefit of HDIT and autologous stem cell transplant as treatment for severe SSc by comparing event-free survival in subjects receiving HDIT followed by stem cell transplantation versus subjects treated with high-dose cyclophosphamide therapy alone.

Please refer **ALL** potential patients to:

1-866-909-SCOT

Inclusion criteria:

- 18 to 65 years of age
 - SSc as defined by the American College of Rheumatology criteria
 - Modified Rodnan skin score score of ≥ 16 verified on 2 separate occasions ≥ 1 day and < 28 days apart
 - Duration of SSc ≤ 4 years from the onset of first non-Raynaud's symptom
 - 1 of the following:
 - SSc-related pulmonary disease with forced vital capacity (FVC) or hemoglobin-adjusted DLCO $< 70\%$ and evidence of alveolitis by high-resolution CT scan or bronchoalveolar lavage
- OR
- History of SSc-related renal crisis or disease, not active at the time of screening

Exclusion criteria:

- Pulmonary, cardiac, hepatic, or renal impairment that would limit therapy and compromise survival. Includes, but is not restricted to any of the following:
 - Severe pulmonary dysfunction: hemoglobin-corrected DLCO $< 45\%$ or FVC $< 45\%$, **or** $pO_2 < 70$ mm Hg or $pCO_2 \geq 45$ mm Hg without supplemental O_2 , **or** O_2 sat $< 92\%$ at rest without supplemental O_2 as measured by forehead pulse oximeter
 - Significant pulmonary hypertension
 - Uncontrolled clinically significant arrhythmias
 - NYHA heart failure class III or IV
 - LVEF $< 50\%$ by echo or prior insertion of a pacemaker or cardioverter-defibrillator
 - Estimated CrCl < 40 mL/min **and** Cr > 2.0 mg/dL **or** active, untreated SSc renal crisis at time of enrollment
 - Active hepatitis (ALT, AST, or bilirubin $> 2x$ ULN) or periportal fibrosis by liver biopsy
- Active gastric antral vascular ectasia (GAVE, "watermelon stomach")
- Previous treatment with cyclophosphamide (Cytosan, CTX) as follows:
 - Prior IV CTX for > 6 months or total cumulative dose > 3 g/m²
 - Prior oral CTX for > 4 months regardless of dose, or
 - Prior combination of oral and IV doses for > 6 months regardless of dose
- Steroid therapy: > 10 mg/day prednisone or equivalent within 30 days prior to randomization or treatment for concurrent illnesses (e.g., asthma) with the equivalent of prednisone 1 mg/kg/day or its equivalent for > 5 days on > 2 occasions in the previous 12 months or > 1 occasion in prior 6 months
- Unwilling or unable to discontinue DMARDs for treatment of SSc
- History or presence of overlap syndrome
- Active uncontrolled infection that would be a contraindication for high-dose or pulse cyclophosphamide therapy
- Positive serology for hepatitis B or C, HIV
- ANC < 1500 cells/ μ L, platelets $< 120,000$ cells/ μ L, Hct $< 27\%$, or Hgb < 9.0 g/dL
- Malignancy within the previous 2 years, excluding treated skin cancer and carcinoma *in situ*
- Myelodysplasia
- Comorbid illnesses with an estimated median life expectancy < 5 years
- Uncontrolled hypertension
- History of hypersensitivity to murine or *E. coli* proteins
- Pregnancy or unwilling to use contraceptive methods for at least 15 months after starting treatment
- History of substance abuse within the last 5 years
- Demonstrated lack of compliance with prior medical care