Scleroderma Lung Study II:

Mycophenolate vs. Oral Cyclophosphamide in Scleroderma Interstitial Lung Disease

INCLUSION AND EXCLUSION CRITERIA

INCLUSION CRITERIA

A staged approach to screening will be employed in which subjects are first evaluated for age, disease, symptoms and pulmonary function criteria and, if meeting these criteria, undergo screening thoracic HRCT. All inclusion criteria must be met in order for subjects to be eligible for randomization.

Inclusion criteria at screening prior to HRCT

1. Age ≥ 18 and < 75 years.
2. The presence of either limited (cutaneous thickening distal but not proximal to elbows and knees, with or without facial involvement) or diffuse (cutaneous thickening proximal to elbows and knees, often involving the chest or abdomen) SSc as determined by ACR criteria.
3. Dyspnea on exertion (grade ≥2 on the Magnitude of Task component of the Mahler Modified Dyspnea Index).
4. FVC <80% of predicted
5. Onset of the first non-Raynaud manifestation of SSc within the prior 5 years.

Additional inclusion criteria after completing HRCT

6. Presence of any ground glass opacification (any GGO) on thoracic HRCT
7. Repeat FVC at the baseline visit (Visit #2) within 10% of the FVC measured at screening. If this criterion is not met, a repeat FVC may be obtained within 7 days and the subject may qualify for randomization if the repeat FVC agrees within 10% of the FVC obtained at screening.

EXCLUSION CRITERIA Subjects will be excluded from participation if any of the following findings are documented:

1. FVC <45% of predicted
2. D_LCO (Hemoglobin [Hbg]-corrected) <40% of predicted
3. FEV_1/FVC ratio <65%
4. Clinically significant abnormalities on HRCT not attributable to SSc
5. Diagnosis of clinically significant resting pulmonary hypertension requiring treatment as ascertained prior to study evaluation or as part of a standard of care clinical assessment performed outside of the study protocol.
6. Persistent unexplained hematuria (>10 red blood cells [RBC]/hpf)
7. History of persistent leukopenia (white blood cells [WBC] <4000) or thrombo-cytopenia (platelet count <150,000)
8. Clinically significant anemia (<10g/dl)
9. Baseline liver function test (LFTs) or bilirubin >1.5 x upper normal limit, other than that due to Gilbert's disease.
10. Concomitant and present use of captopril
11. Serum creatinine >2.0mg/dl
12. Uncontrolled congestive heart failure
13. Pregnancy (documented by urine pregnancy test) and/or breast feeding
14. Prior use of oral CYC or MMF for more than 8 weeks or the receipt of more than two intravenous doses of CYC in the past.
15. Use of CYC and/or MMF in the 30 days prior to random-ization.
16. Active infection (lung or elsewhere) whose management would be compromised by CYC or MMF.
17. Other serious concomitant medical illness (e.g., cancer), chronic debilitating illness (other than SSc), unreliability or drug abuse that might compromise the patient's participation in the trial
18. Current use, or use within the 30 days prior to randomization, of prednisone (or equivalent) in doses >10 mg/day.
19. If of child bearing potential (a female participant < 55 years of age who has not been postmenopausal for > 5 years and who has not had a hysterectomy and/or oophorectomy), failure to employ two reliable means of contraception which may include surgical sterilization, barrier methods, spermicidals, intrauterine devices, and/or hormonal contraception.
20. Use of contraindicated medications (see Appendix A or section 4.5 for interactions of MMF and CYC with other drugs).
21. Smoking of cigars, pipes, or cigarettes during the past 6 months.
22. Use of medications with putative disease-modifying properties within the past month (e.g., D-penicillamine, azathioprine, methotrexate, Potaba).