

The Scleroderma Lung Study II (SLS II) Shows That Both Oral Cyclophosphamide (CYC) and Mycophenolate Mofetil (MMF) Are Efficacious in Treating Progressive Interstitial Lung Disease (ILD) in Patients with Systemic Sclerosis (SSc)

Philip J. Clements¹, Donald Tashkin¹, Michael Roth¹, Dinesh Khanna², Daniel E. Furst³, Chi-hong Tseng¹, Elizabeth R. Volkman¹ and Robert Elashoff⁴, ¹Medicine, University of California Los Angeles, David Geffen School of Medicine, Los Angeles, CA, ²Medicine, University of Michigan, Ann Arbor, MI, ³Medicine, University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, ⁴Biomath, University of California Los Angeles, David Geffen School Of Medicine, Los Angeles, CA

Meeting: 2015 ACR/ARHP Annual Meeting

Date of first publication: September 29, 2015

Keywords: cyclophosphamide, interstitial lung disease, mycophenolate mofetil, randomized trials and systemic sclerosis

SESSION INFORMATION

Date: Sunday, November 8, 2015

Session Title: Systemic Sclerosis, Fibrosing Syndromes, and Raynaud's - Clinical Aspects and Therapeutics I

Session Type: ACR Concurrent Abstract Session

Session Time: 4:30PM-6:00PM

Background/Purpose: Demonstrate that the course of forced vital capacity (FVC) over 2-years was better in SSc patients with symptomatic ILD treated with oral MMF for two years than with oral CYC for one year followed by placebo during the second year in a blinded randomized controlled trial.

Methods: Entry criteria: 1980 ACR criteria for SSc; disease duration of \leq 7 years from 1st non-Raynaud sign or symptom; moderate dyspnea (Level 2 of the Magnitude of Task scale of the Mahler Baseline Dyspnea Index [BDI]; %FVC between 45% and 80%; and any ground-glass opacification on chest high-resolution computed tomography (HRCT).

At

baseline and every 3 months during the 2-year trial, physical exams (including modified Rodnan skin scoring or MRSS), lung function testing and patient-reported outcomes were completed: Scleroderma Health Assessment Questionnaire (disability index [HAQ-DI] and 5 100-mm visual analogue scales); SF-36, and transition dyspnea index (TDI).

Patients

were randomized to Arm A (oral CYC 2 mg/kg/day for one year followed by

matching placebo for the second year) or Arm B (matching MMF up to 1500 mg BID for 2 years).

Results:

142 patients were randomized; 106 completed the 2-year evaluation. With the exception of MRSS, which was higher in the MMF group (15.3 in MMF vs 14.1 in CYC, $p=xxx$) the baseline characteristics were not different between treatment groups.

In preliminary analyses, the course of FVC showed comparable improvement in both treatment groups at 24 months (see figure). Improvements in both treatment groups were noted in TDI (increase of 2.24 in CYC vs 1.86 in MMF,) and in MRSS (decline of 6.1 units in CYC vs 2.9 units in MMF).

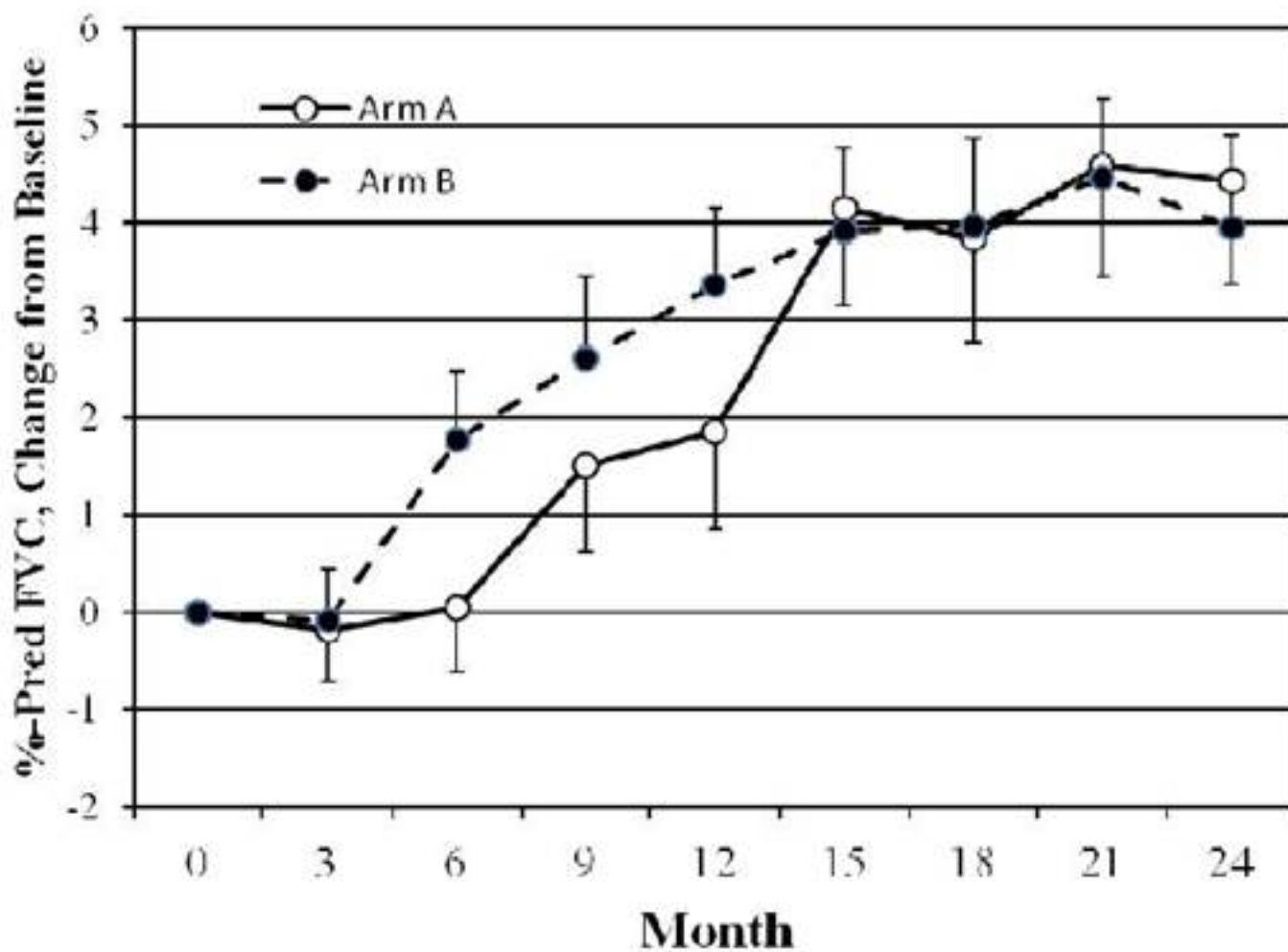
More patients in the CYC arm withdrew from study treatment prematurely (36 in CYC and 20 in MMF) ($p=0.019$). Of all the subjects with end-point data 23% assigned to CYC received alternative therapy after stopping study treatment (MMF in 8, Rituximab in 1, tocilizumab in 1 and IV-CYC in 2) and 4% assigned to MMF received alternative treatment (po CYC in 1 and IV-CYC in 1) after stopping study treatment..

Weight loss (NS) and leukopenia/thrombocytopenia ($p<0.05$) occurred more frequently in the CYC arm

Conclusion:

In this large, double blind, RTC, we found: 1) At 24 months the improvement in %FVC was comparable in the two treatment groups. 2) The TDI and MRSS improved in both treatment arms but there was a trend favoring improvements in the CYC group. 3) Significantly fewer premature withdrawals were noted in the MMF arm. 4) Leukopenia/thrombocytopenia were noted significantly less frequently in the MMF arm 5) It is unclear how the use of alternative medications in SSc patients who withdrew prematurely from study treatments, particularly in the CYC patients, could have influenced the results.

In summary both CYC and MMF are efficacious for treatment of SSc-ILD.



Disclosure: P. J. Clements, None; D. Tashkin, None; M. Roth, None; D. Khanna, Bristol-Myers Squibb, 2,EMD Serono, 2,Genentech and Biogen IDEC Inc., 2,Bayer, 5,Biogen Idec, 5,Cytori, 5,EMD Serono, 5,Forward, 5,Genentech and Biogen IDEC Inc., 5,Gilead, 5,Lycera, 5,Seattle Genetics, 5; D. E. Furst, Gilead, 2,GlaxoSmithKline, 2,NIH, 2,Novartis Pharmaceutical Corporation, 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,Genentech and Biogen IDEC Inc., 2,UCB, 2,Abbvie, 5,Actelion Pharmaceuticals US, 5,Amgen, 5,Bristol-Myers Squibb, 5,Cytori, 5,Janssen Pharmaceutica Product, L.P., 5,Gilead, 5,GlaxoSmithKline, 5,NIH, 5,Novartis Pharmaceutical Corporation, 5,Pfizer Inc, 5,Roche Pharmaceuticals, 5,Genentech and Biogen IDEC Inc., 5,UCB, 5,Abbvie, 8,Actelion Pharmaceuticals US, 8,Bristol-Myers Squibb, 2,Amgen, 2,Actelion Pharmaceuticals US, 2,Abbvie, 2,UCB, 8; C. H. Tseng, None; E. R. Volkman, None; R. Elashoff, None.

To cite this abstract in AMA style:

Clements PJ, Tashkin D, Roth M, Khanna D, Furst DE, Tseng CH, Volkman ER, Elashoff R. The Scleroderma Lung Study II (SLS II) Shows That Both Oral Cyclophosphamide (CYC) and Mycophenolate Mofetil (MMF) Are Efficacious in Treating Progressive Interstitial Lung Disease (ILD) in Patients with Systemic Sclerosis (SSc) [abstract]. *Arthritis Rheumatol.* 2015; 67 (suppl 10). <http://acrabstracts.org/abstract/the-scleroderma-lung-study-ii-sls-ii-shows-that-both-oral-cyclophosphamide-cyc-and-mycophenolate-mofetil-mmf-are-efficacious-in-treating-progressive-interstitial-lung-disease-ild-in-patients-w/>. Accessed October 2, 2015.

ACR Meeting Abstracts - <http://acrabstracts.org/abstract/the-scleroderma-lung-study-ii-sls-ii-shows-that-both-oral-cyclophosphamide-cyc-and-mycophenolate-mofetil-mmf-are-efficacious-in-treating-progressive-interstitial-lung-disease-ild-in-patients-w/>

