ΒΙΒΛΙΟΓΡΑΦΙΚΗ ΑΝΑΣΚΟΠΗΣΗ ACR 2015

ΝΙΚΟΛΑΟΣ ΚΟΥΓΚΑΣ, ΡΕΥΜΑΤΟΛΟΓΟΣ ΠΑΓΝΗ

ABSTRACT NUMBER: 1075

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

Philip J. Clements et al

PURPOSE

- Blinded randomized controlled trial
- 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

ENTRY CRITERIA

- 1980 ACR criteria for SSc
- Disease duration of =< 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%
- Any ground-glass opacification on chest high-resolution computed tomography (HRCT).

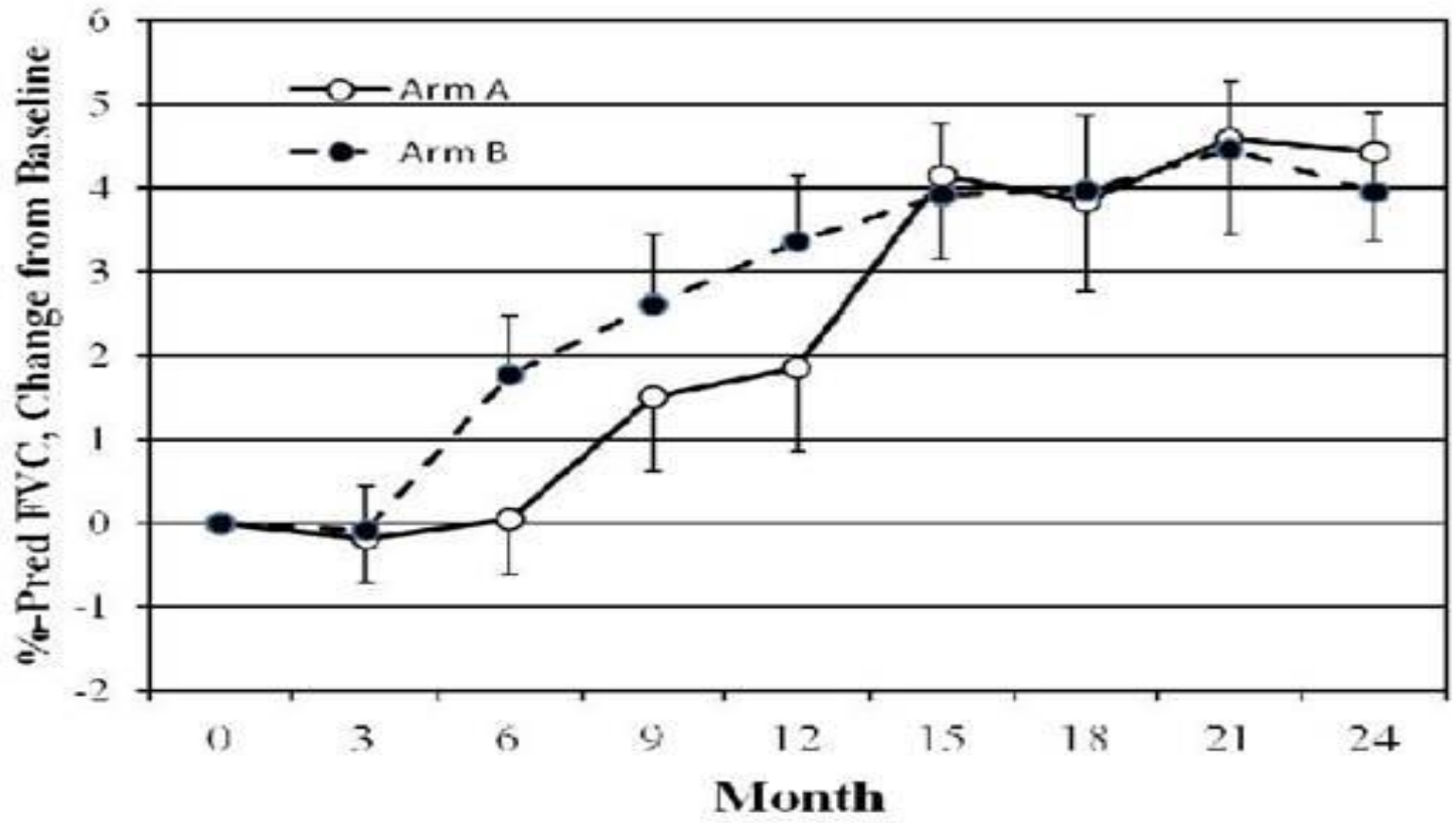
METHODS

- At baseline and every 3 months:
  - modified Rodnan skin scoring (MRSS)
  - transition dyspnea index (TDI).
  - PFT's
  - HAQ –DI and SF-36
- Arm A (oral CYC 2 mg/kg/day for one year followed by matching placebo for the second year)
- Arm B (matching MMF up to 1500 mg BID for 2 years).
- 142 patients were randomized; 106 completed the 2-year evaluation.

RESULTS

- FVC showed comparable improvement in both treatment groups at 24 months
- Improvements in both treatment groups were noted in TDI (increase of 2.24 in CYC vs 1.86 in MMF)
- 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) ($p=0.019$)
- Weight loss (NS) and leukopenia/thrombocytopenia ($p<0.05$) occurred more frequently in the CYC arm

RESULTS


Arm A
Arm B
%-Pred FVC, Change from Baseline
6
5
4
3
2
1
0
-1
-2
0
3
6
9
12
15
18
21
24
Month

CONCLUSION

- At 24 months the improvement in %FVC was comparable in the two treatment groups
- The TDI and MRSS improved in both treatment arms but there was a trend favoring improvements in the CYC group
- Significantly fewer premature withdrawals were noted in the MMF arm.
- Leukopenia/thrombocytopenia were noted significantly less frequently in the MMF arm

Abstract Number: 977

- A Randomized, Double-Blind, Active- and Placebo-Controlled Phase 3 Study of Efficacy and Safety of Ixekizumab, Adalimumab, and Placebo Therapy in Patients Naïve to Biologic Disease Modifying Anti-Rheumatic Drugs with Active Psoriatic Arthritis

  Philip J. Mease

PURPOSE

- To assess efficacy of Ixekizumab an IgG4 monoclonal antibody that binds with high affinity and specificity to the proinflammatory cytokine IL 17A in patients with PsA

ENTRY CRITERIA/METHODS

- 417 biologic disease-modifying antirheumatic drug (bDMARD)-naive patients with active PsA
- randomized to up to 24 weeks of
  - placebo (N=106)
  - adalimumab 40 mg (N=101) once every 2 weeks (Q2W; active control)
  - ixekizumab 80 mg Q2W (N=103) or Q4W (N=107) following 160 mg initial dose at Week 0

ENTRY CRITERIA/METHODS

- Endpoints:
  - ACR20 at Week 24 (primary), ACR50, ACR70
  - Improvement in Psoriasis Area and Severity Index (PASI 75/PASI 90/PASI 100)
  - DAS28-CRP
  - Leeds Dactylitis Index (LDI-B) and Enthesitis Index (LEI)
  - Health Assessment Questionnaire – Disability Index (HAQ-DI)
  - Van der Heijde modified Total Sharp (mTSS) score at 12 and 24 weeks

RESULTS

Table 1. Efficacy, Patient-Reported, and Safety Outcome Measures in Intent-to-Treat Population

	Placebo		Adalimumab 40mg Q2W		Ixekizumab 80mg Q4W		Ixekizumab 80mg Q2W	
Measure	**12 weeks**	**24 weeks**	**12 weeks**	**24 weeks**	**12 weeks**	**24 weeks**	**12 weeks**	**24 weeks**
	N=106		**N=101**		**N=107**		**N=103**	
ACR 20, %	31.1	30.2	51.5**	57.4***	57.0***	57.9***	60.2***	62.1***
ACR 50, %	4.7	15.1	29.7***	38.6***	33.6***	40.2***	39.8***	46.6***
ACR 70, %	0	5.7	17.8	25.7***	15.0	23.4***	16.5	34.0***
	N=67		**N=68**		**N=73**		**N=59**	
PASI 75, %[a]	7.5	10.4	33.8***	54.4***	75.3***	71.2***	69.5***	79.7***
PASI 90, %	1.5	6.0	22.1**	36.8***	52.1***	56.2***	57.6***	67.8***
PASI 100, %	1.5	3.0	14.7*	23.5**	31.5***	42.5***	40.7***	52.5***
LS Mean (SE) Change from baseline:								
	N=106		**N=101**		**N=107**		**N=103**	
DAS28-CRP	-0.56 (.11)	-0.85 (.13)	-1.51 (.12)***	-1.68 (.12)***	-1.58 (.11)***	-1.92 (.12)***	-1.61 (.12)***	-2.04 (.12)***
	N=39		**N=23**		**N=54**		**N=41**	
LDI-B (Dactylitis)[b]	-1.5 (.47)	-2.1 (.42)	-2.2 (.57)	-3.3 (.47)	-3.0 (.41)*	-3.4 (.35)**	-3.2 (.45)**	-3.5 (.38)**
	N=57		**N=56**		**N=70**		**N=59**	
LEI (Enthesitis)[b]	-0.8 (.24)	-0.8 (.26)	-0.8 (.24)	-0.9 (.23)	-0.9 (.21)	-1.3 (.21)	-1.5 (.24)	-1.4 (.24)
	N=106		**N=101**		**N=107**		**N=103**	
mTSS[c]	0.36 (.07)	0.49 (.09)	0.12 (.08)*	0.10 (.09)***	0.13 (.07)*	0.17 (.08)**	0.06 (.07)**	0.08 (.08)***
HAQ-DI	-0.13 (.05)	-0.18 (.05)	-0.35 (.05)***	-0.37 (.05)**	-0.37 (.05)***	-0.44 (.05)***	-0.47 (.05)***	-0.50 (.05)***
	N=106		**N=101**		**N=107**		**N=102**	
TEAE, %		47.2		64.4*		66.4**		65.7**
SAE, n (%)		2 (1.9)		5 (5.0)		6 (5.6)		3 (2.9)
Discontinue due to TEAE, %		1.9		2.0		1.9		3.9

*p≤.025, **p≤.01, and ***p≤.001 vs. placebo.
[a]: Analysis restricted to patients with baseline psoriatic lesion involving ≥3% of body surface area.
[b]: Only patients with dactylitis or enthesitis present at baseline were included in the respective analyses.
[c]: Value shown for 12 weeks was collected at 16 weeks.
Abbreviations: ACR 20/50/70=American College of Rheumatology Improvement Responder Index Improvement Response for 20/50/70%; DAS28-CRP=Disease Activity Score (28 diarthrodial joint count) based on C-reactive protein; HAQ-DI=Health Assessment Questionnaire-Disability Index; LDI-B=Leeds Dactylitis Index-Basic score; LEI=Leeds Enthesitis Index score; LS=least squares; n=number of responders; mTSS=modified Van der Heijde Total Sharp Score; PASI 75/90/100=Psoriasis Area and Severity Index Improvement Response for 75/90/100%; Q2W=once every 2 weeks; Q4W=once every 4 weeks; TEAE=treatment-emergent adverse event.

CONCLUSION

- In bDMARD-naive patients with PsA, ixekizumab showed significant, clinically meaningful improvements of disease activity and physical function, reduction in dactylitis, greater skin clearance of plaque psoriasis, and inhibition of structural progression. Ixekizumab was well tolerated with no unexpected safety findings.