ACRレポート

San Diego, CA
Nov. 12-17, 2005

藤本　学（金沢大）

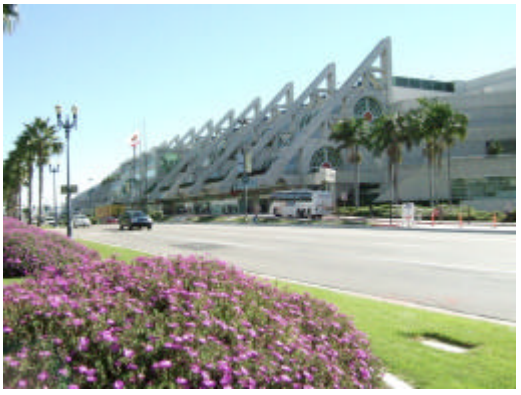
Sessions on SSc

Oral: 3 (+2) sessions, 22 abstracts (12 in 2003)

Poster: 4 sessions, 100 abstracts (60 in 2003)

Poster sessions:

- Systemic Sclerosis: Lung, Raynaoud's phenomenon and Disease Activity 32
- TGF-? and Fibrosis: Mechanisms in Scleroderma 18
- Adavances in Scleroderma 18
- Systemic Sclerosis: Genetics, QOL and Miscelleneous 32



Oral Sessions

- Plenary session, 2 abstracts
- Concurrent sessions, 6 abstracts x 3
  - Systemic sclerosis: clinical aspects
  - Recent advances in scleroderma
  - Translational approaches in scleroderma
- Late-breaking abstracts, 2 abstracts
- ACR study group

Plenary Session

- The Scleroderma Lung Study shows the beneficial effects of Cyclophsphamide over placebo in systemic sclerosis patients with active alveolitis
- Pharmacological inhibition of TGF?-induced fibrogenic response in vivo and in vitro by a novel small molecule

The Scleroderma Lung Study (SLS) Shows the Beneficial Effects of Cyclophsophamide (CYC) over Placebo (PL) in Systemic Sclerosis (SSc) Patients with Active Alveolitis

Clements P, Furst DE, Silver RM, Tashkin DP, Roth MD, Goldin J, Elashoff RM, Sterz MG, for the SLS Investigators (US).

Entry: ACR criteria for SSc, =< 7 yrs, moderate dyspnea
Oral CYC (1-2 mg/kg/day), 1 year

Changes in variables over 1 year in CYC and placebo patients (mean +/- SD)

	CYC (n=72)	PL (n=70)	p-value
FVC (% predicted)	-1.4 +/- 0.9	-3.2 +/- 0.9	0.05
TDI (focal score)	1.4 +/- 0.4	-1.3 +/- 0.5	<0.0001
Vitality (SF-36)	7.2 +/- 2.1	-2.1 +/- 2.5	0.013
Health Transition (SF-36)	-0.9 +/- 0.2	-0.4 +/- 0.2	0.0007
Skin score (all, n=142)	-3.7 +/- 0.8	-0.9 +/- 0.7	0.0048
Skin score (diffuse, n=83)	-3.9 +/- 0.3	-0.2 +/- 1.1	0.03
Skin score (limited, n=59)	-3.4 +/- 0.8	-2.1 +/- -.8	0.26
HAQ-DI	-0.11 +/- 0.42	0.15 +/- 0.49	0.0022

Conclusions: 1) CYC had a statistically significant (but clinically mild) effect on the course of FVC over one year. 2) CYC had a statistically & clinically meaningful effect on the level of dyspnea (TDI changed by => 1 unit) and the HAQ-DI (PL-corrected difference of => 0.22). 3) Skin score declined moderately, particularly in diffuse patients. 4) More toxicity (especially hematurias, leukopenias, and pneumonias) was seen with CYC therapy.

Late Breaking Abstracts

- Fibrosing Alveolitis in Scleroderma Trial (FAST) - a multi-centre prospective randomised double-blind placebo-controlled trial

- Oral Tolerance (OT) Induction to Type I Collagen (CI) Significantly Reduces the Skin Score in Patients with Diffuse Systemic Sclerosis (SSc) with Late-Phase Disease. Results of a NIAMS/NIAID Multicenter Phase II Placebo-Controlled Double Blind Clinical Trial

Fibrosing Alveolitis in Scleroderma Trial (FAST) - a multi-centre prospective randomised double-blind placebo-controlled trial

Rachel K. Hoyles1, Ross W. Ellis2, Ariane L. Herrick3, Neil J. McHugh4, Noeleen M. Foley4, Stanley B. Pearson5, Paul Emery5, Douglas J. Veale5, Christopher P. Denton1, Athol U. Wells2, Carol M. Black1, Roland M. du Bois2. 1Royal Free Hospital, London, United Kingdom; 2Royal Brompton Hospital, London, United Kingdom; 3Hope Hospital, Salford, United Kingdom; 4Royal United Hospital, Bath, United Kingdom; 5Leeds General Infirmary, Leeds, United Kingdom

45 patients (22, therapy; 23 placebo)
Prednisolone (20 mg) and 6 infusions (monthly) of Cyc (600 mg/m^2) followed by oral azathioprine (2.5 mg/kg/day)

Conclusion: The positive response of FVC to active therapy is consistent with recent data from the Scleroderma Lung Study of oral Cyc, and supports the use of Cyc with low dose prednisolone in SSc-PF [1]. The treatment advantage is likely to be understated due to the ITT analysis. Intravenous Cyc appears to confer an advantage over previous reports of toxicity with the oral regimen [2].

Systemic sclerosis: clinical aspects

- Badesch D -- Sildenafil Improves Exercise Ability and Hemodynamics in Patients with Pulmonary Arterial Hypertension Associated with Connective Tissue Disease
- Seibold JR -- Sitaxsentan, A Selective Endothelin-A Receptor Antagonist, Improves Exercise Capacity in Pulmonary Arterial Hypertension Associated with Connective Tissue Disease
- Merkel PA -- Patterns and Predictors of Change in Outcome Measures in Clinical Trials in Scleroderma
- Merkel PA -- Performance of the Modified Rodnan Skin Score in Clinical Trials of Scleroderma
- Shiozawa K -- Contribution of Mutation in Angiopoietin-1 (ang1) Gene to the Clinical Presentation of Patients with Mixed Connective Tissue Disease and Systemic Sclerosis : Genetic Association with Pulmonary Hypertension
- Warrington KJ -- Lymphocyte Activation and Upregulation of Anti-Fibrotic Cytokines by Pamidronate Treatment of Patients with Limited or Diffuse Scleroderma

Sildenafil Improves Exercise Ability and Hemodynamics in Patients with Pulmonary Arterial Hypertension Associated with Connective Tissue Disease (SUPER-1)

Mean (95% CI) changes in hemodynamic parameters and 6MWD from baseline to Week 12

	mPAP (mmHg)	Cardiac output (L/min)	PVR (dyn.s/cm^5) (m)	6MWD
Placebo	1.4	0.08	-19	-13
(n=22)*	(-0.8, 3.6)	(-0.3, 0.4)	(-106, 68)	(-36, 10)
20 mg	-4.6†	0.8	-243†	42†
(n=21)*	(-8.7, -0.6)	(-0.02, 1.5)	(-408, -77)	(20, 64)
40 mg	-2.8	0.4	-144	36†
(n=20)*	(-5.4, -0.1)	(-0.5, 1.3)	(-278, -10)	(14, 58)
80 mg	-3.2	0.2	-156	15
(n=19)*	(-7.9, 1.5)	(-0.4, 0.8)	(-267, -46)	(-24, 54)

Conclusions: Oral sildenafil, at a dose of 20 mg three times daily, improves exercise capacity and hemodynamics in patients with PAH associated with CTD.

Sitaxsentan, A Selective Endothelin-A Receptor Antagonist, Improves Exercise Capacity in Pulmonary Arterial Hypertension Associated with Connective Tissue Disease (STRIDE-1, -2, -4)

Six Minute Walk Distance (m)

	Placebo (PBO) N=28	Sitax 50mg N=26	Sitax 100mg N=39	Sitax 300mg N=17
D from Baseline	-16 ± 15.0	-2 ± 13.4	21 ± 10.4	2 ± 14
PBO-subtracted treatment effect		14.7	37.7	18.3
P-value vs PBO		NS	P=0.042	NS
N (%) Abnormal LFT >3x ULN	1 (3.6%)	0 (0%)	0 (0%)	0 (0%)

Conclusion: Sitaxsentan 100 mg improves 6MWD in patients with PAH-CTD with a low incidence of abnormal liver function tests. Selective ETA receptor antagonism appears to be an effective and well tolerated therapy for PAH associated with CTD.