ACR/ARHP 2011
レポート

東邦大学医療センター大森病院
リウマチ膠原病センター
遠藤平仁

ACR/ARHP Scientific Meeting 2011

Annual Scientific Session,Nov,5-9,2011

M^{C}CORMICK PLACE, Chicago

- 参加者　15000人
- 演題数　2600演題（抄録集2426演題）
- Systemic Sclerosis Fibrosing syndrome and Raynaud's-Clinical Aspects and Therapeutics

  Work shop　　18演題

  Poster Session 104演題

  計　　122演題

Systemic Sclerosis Fibrosing syndrome and Raynaud's- Clinical Aspects and Therapeutics

◎Basic

- Antibody ・Genome etc. 20
- Animal model 9

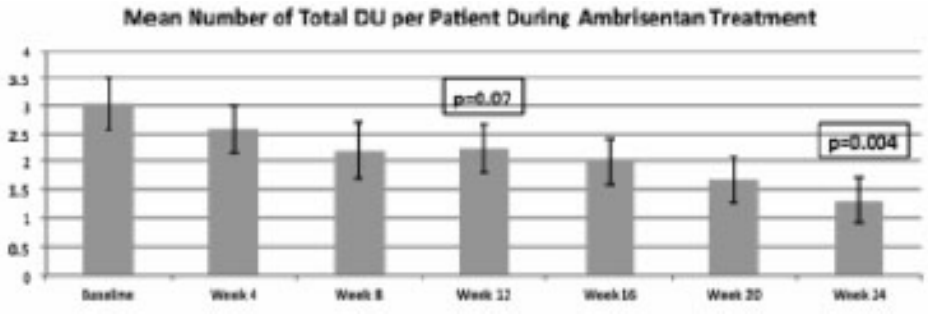
◎Clinical

- Clinical symptom and diagnosis(QOL) 19
- Treatment of Skin sclerosis 7
- Digital ulcer and vascular lesion 19
- Organ Involvement
  - Pulmonary hypertension 9
  - Lung 10
  - Heart・Kideny 5
  - GI tract 6
  - Others(Cancer, Pregnancy. etc) 26

668. Effect of the ETA Selective Endothelin Receptor Antagonist Ambrisentan on Digital Ulcers in Patients with Systemic Sclerosis:Results of a Prospective Pilot　　Brucato,A.etal. Italy

手指潰瘍病変に対するETA選択的阻害薬アンブリセンタンの効果

20症例のSSc患者　digital ulcerは平均3.05±2.11、平均3.3±1.58㎜潰瘍に対して　アンブリセンタン5mg1日1回投与
Prospective Open Label Study



24Week	N		Pvalue
Mean number of Total Digital Ulcer	20 → 16	3.05±2.11→1.75±2.02	*p*=0.004
Physician Global assessment	16 → 20	0.45±0.69→0.06±0.68	*P*=0.42
Digital ulcer diameter	16	3.3±1.58→2.01±2.13	P<0.001

Adverse Events
1. Leg edema, hand, arm, foot edema 15/20(75%)

アンブリセンタンに新たな手指潰瘍を抑制する効果は認められなかった。24週のPrimary endpointにて潰瘍数と潰瘍直径に有意な改善があった。

713.Evaluation of the Effect of Ambrisentan on digital microvascular flow in patients with systemic sclerosis using doppler pefusion imaging

- アンブリセンタン投与5mg 1か月,10mg2か月　double blind placebo control
- Laser Doppler Perfusion Imaging(LDPI):noninvasive perfusion mapping of area of skin
- Digital microvascular perfusion flow

対象：Limited SSc20例発症から7年以内,Digital ulcerは除く

mean age 50(20-70)

- 0，1，12W　visit cold challenge test（10℃）2min
- Primary outcome:mean change of blood flow in selected resion(ROI)
- Secondary outcome:Raynaud's condition score, SclerodermaHAQ,PainVAS

結果：ROI(局所血流）の有意な改善なし

RCSとP-VASは有意な改善

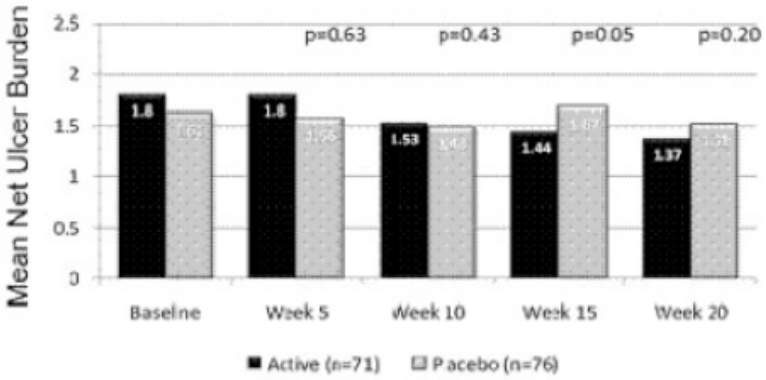
結論：より長期な血管拡張より血管のremodelingを評価が必要

2483. Digital ischmic ulcers in Scleroderma Treated with Oral Treprostinil diethanolamine:A randamized , Double Blind Controlled, Multicenter Study

- an analogue of prostacyclin
- RCT 148 SSc 48.8歳、罹病期間10.5年27Centers

  67% limitedSSc, Treprostinil 16㎎ bid
- 5週毎20週まで評価　Primary endopoint :net ulcer burden

  有意な改善なし



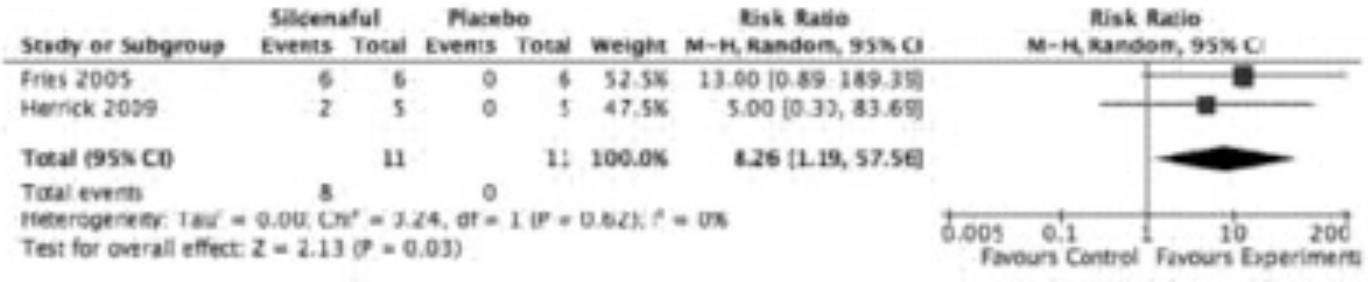
Secondary endpointのVASやSHAQ-DIで有意差あり、レイノー現象などに効果？

1449. A Meta-Analysis of Randamized Trials in treatment and prevention of digital ulcer in SSc

Digital Ulcer に関する薬剤治療のRCT

SSc 手指潰瘍に対する40 Trialのうち 21Trial がRCTであり
Iv ilioprost standard mean defference－0.77:new ulcerの出現を抑制した。
Oral prostacyclinは効果がない。
Sildenafilは完全に潰瘍を治癒させる有意な効果はない有効性はある。
Tadarafilも有効という報告が一つある。

。Sildenafil Vs. Placebo in Improvement of DU



結論
Bosentanは新しい潰瘍形成を抑制ができる、
ilioprostのIv治療は潰瘍治癒促進作用がある。
PDE-5阻害薬はおそらく有効である。

848：Prospective Observational Study of Mycophenolate Mofetil Treatment in Rapidly Progressive Diffuse Cutaneous Systemic Sclerosis of Recent Onset
Mendosa FA et al. philadelphia

- 25例の早期進行性（24か月未満）dcSScに対するMMFの効果の検討
- 平均投与量MMF2000㎎/day, 平均18.2±8.73か月投与

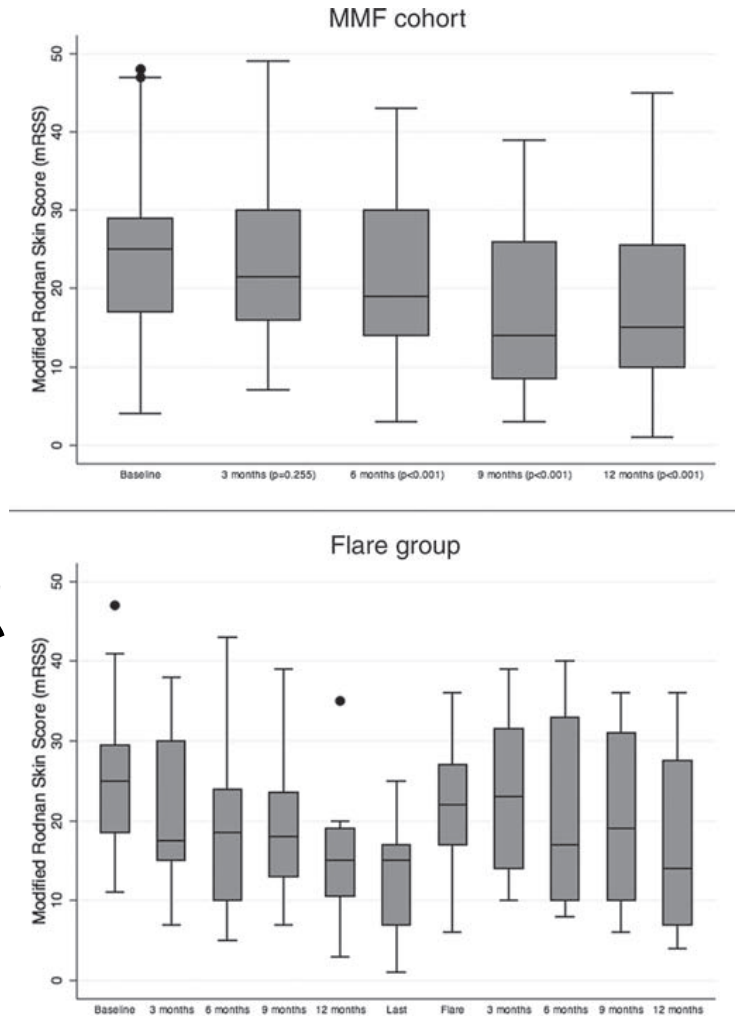
結果：mRSS 24.56±8.62→14.52±10.9（P=0.004)

- BSA(affected body surface area) 36±16%→14±13.3%（P=0.00001）
- 呼吸機能は前後で変化なし
- 3症例 皮膚生検：皮膚線維化の改善

Long-term experience of mycophenolate mofetil for treatment of diffuse cutaneous systemic sclerosis
Ann Rheum Dis.2011,70,1104-1107.
Johns Hopkins Scleroderma Center

- MMF(2g:42%,3g:52%)
- 罹病期間7.7±4.7Y
- 投与期間19.2±14M

- 12 months follow-up
- 3 months 以内で効果が認められる
- 投与12か月で有意な有効性が確認
- MMF　：－7.59±8.6
  （D-PC：　－2.47±7.12）



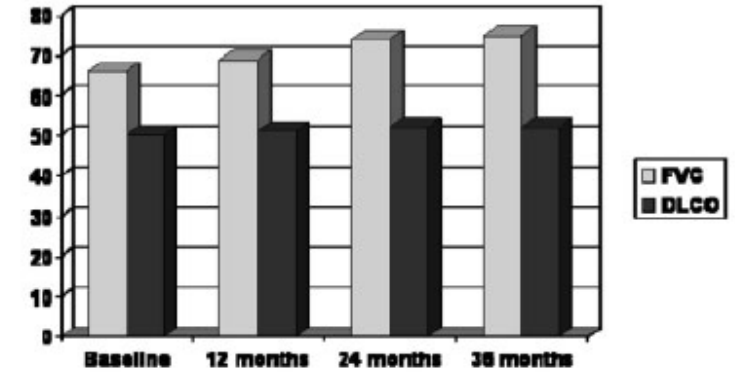
687. Mycophenolate Mofetil Is An Effective, Well-Tolerated, Steroid-Sparing Agent for a Diverse Spectrum of Connective Tissue Disease-Associated Interstitial Lung Disease.

- CTD-ILD 61例 SSc 25（41%）, anti-synthetase antibody 14 (23%),RA 6(10%)

Clinical Features of CTD-ILD patients treated with MMF

Age	**55 (21–81)**
Female gender	39 (64%)
Ethnicity	54 (89%) White, 6 (10%) Hispanic, 1 (2%) Black
Past smokers	25 (41%)
Current smokers	0
MMF discontinuation	7 (11%), symptoms of intolerability (3), leukopenia (1) abnormal liver tests (1), lymphoma (1) ILD progression (1)
Prednisone dose @ MMF start	39 patients on prednisone; mean 14 mg / d (+/−16)
Prednisone dose @ 12 months	34 patients on prednisone; mean 4 mg / d (+/−5)
FVC% @ MMF start (n=61)	66 (+/−17)
FVC% @ 12 months (n=61)	69 (+/−16)
FVC% @ 24 months (n=42)	74 (+/−17)
FVC% @ 36 months (n=29)	75 (+/−16)
DLco% @ MMF start (n=61)	50 (+/−17)
DLco% @ 12 months (n=61)	51 (+/−17)
DLco% @ 24 months (n=42)	52 (+/−17)
DLco% @ 36 months (n=29)	52 (+/−16)
Survival @ 36 months	100%

Serial pulmonary function testing in CTD-ILD patients treated with MMF



MMF therapy:平均3.5years(1-10年）3g/day 38(62%), 2g/day(34%)

PSL 14mgから4mgへ減量する効果

702. Effect and Safety of Rituximab in SS : An Analysis from the European Scleroderma Trial and Research Group

EUSTAR CohortにおいてRetorospectiveに調査：mRTSS,FVC, DAS28,CK level
Skin 12か月、Lung　6か月で判定、多施設観察研究

72例のSSc患者に27施設でRTX投与(52dcSSc、19LcSSc)disease duration 6 years (3-10years)14例MTX投与、1g day0と1gday14投与

結果: Skin :
mRTSS18.2 ±10.9→14.5±9.9（P=0.0002)
dcSSc only n=26, 26.5±6.8→20.4±8.9（P<0.0001）
European SSc activity score3.7→1.7（P＝0.01）
Organ involvement :
Lung(n=11 : FVC 57.7±9.1%→56.2±16%（P=0.5）
DLCO, HRTC有意差なし
SSc-associated arthritis(n=8) DAS28 4.8→3.7, P=0.2 ）、関節炎に効果なし
Myositis(n=11)（CK 273±177→184±139, P=0.03
副作用　Infection 14 patients, Fatigue 29 patients, Nausea 9 patients.
4症例死亡（1症例が肺炎、心不全RTX infusion後1.5か月）
結論　皮膚の線維化,筋炎に対してRTX治療は有効。RTCが必要

703.　B cell depletion Therapy in Systemic sclerosis: a follow up 4 years on Skin and Lung Involvement in Fourteen Patients

Bosello,SL,et.al. Italy

方法　14 patients：年齢 44.3±14.3歳　 dcSSc

- Rituximab 1g day0, day14 DIV
- Mean disease duration:32.9±37.1か月(8症例は1年以内の早期症例）
- RTSS, digital ulcer
- 呼吸機能（FVC, DLCO), HR-CT

結果　41.0±14.8か月Follow　RTSS　24.9±9.8→12.0±6.7（改善率 11.0-85.1％）

- Digital Ulcerの新たな出現はなく2/6例（33％）は期間中に改善
- 9例は％VCは変化せず3症例回復、2症例悪化
- HR-CT上10例は変化なし、1例のみ改善、3例悪化（早期は1例）

結論　Rituximabは皮膚硬化の進展を抑制する。肺病変の進展を抑制し特に早期症例は効果が顕著

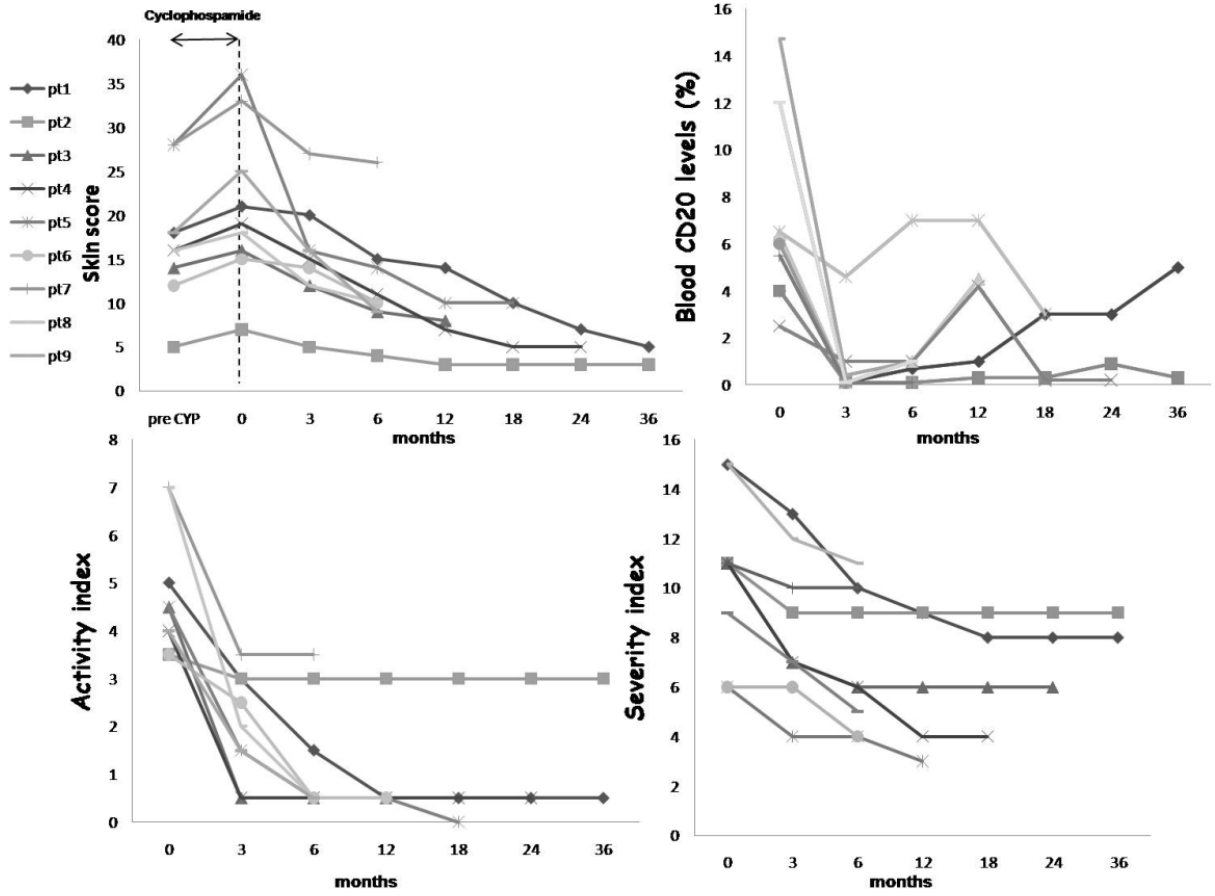
B cell depletion in diffuse progressive systemic sclerosis: safety, skin score modification and IL-6 modulation in an up to thirty-six months follow-up open-label trial

Silvia Bosello1,Bosello et al. Arthritis Research & Therapy 2010, 12:R54

9症例Clinical improvement during follow up

in nine systemic sclerosis patients treated with anti-CD20

mTSSmean21.1→4.0



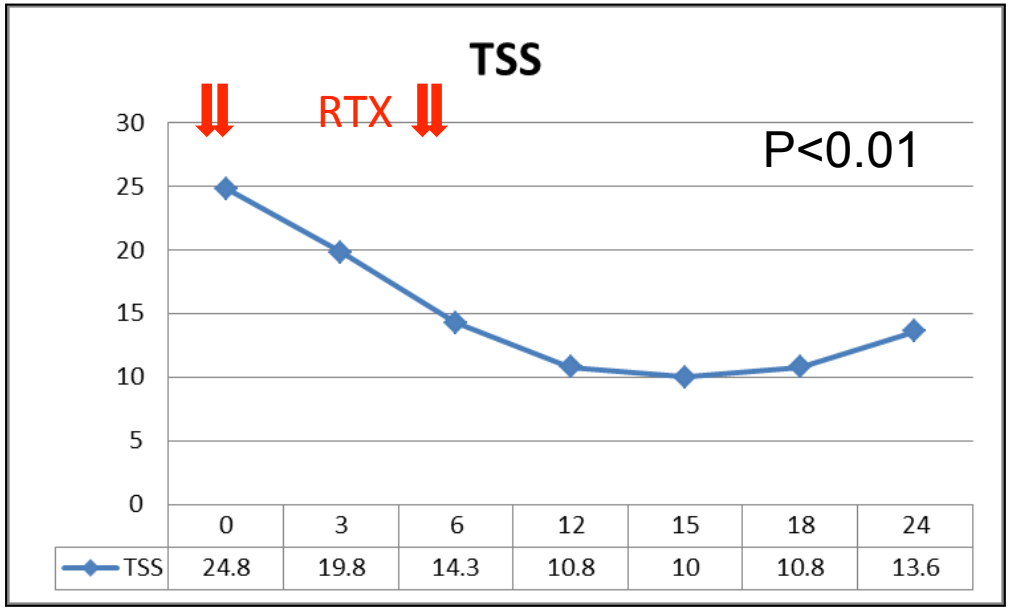
1448. Two Years Follow-up Results After Rituximub Treatment (Baseline and month 6) in Patients with ‘’ Early’’ Systemic Sclerosis with Diffuse Skin Involvement

Smith V et.al. Belgium

- 8症例の早期dcSSc (8-30M)　Open-label study
- Rituximab1000㎎DIV 0、2W、6M後（24Wと26W）
- 1000㎎ methylpredonisoloneを投与
- 0,3,6,12,15,18,24M
- mRSS, internal organ functions　(lung,　heart, kideny)　HAQ-DI,SF36

末梢血CD19count

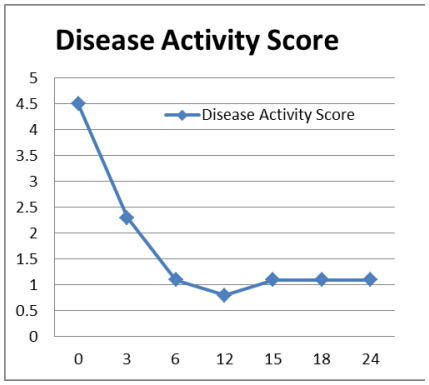
Change in Clinical and laboratory parameters in the study upon treatment with rituximab

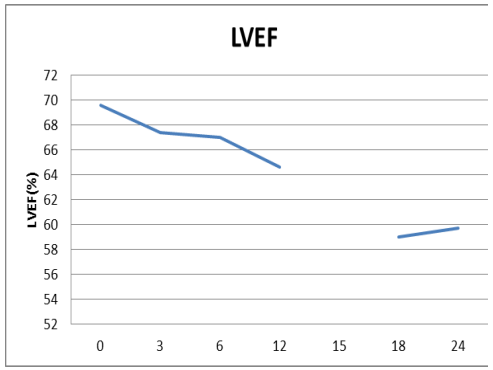


TSS3か月で低下し6か月時点で有意な低下を示した。

%DLCO, %VC,SF-36,HAQ-DI, Ccr, PAPは有意な変化はなかった

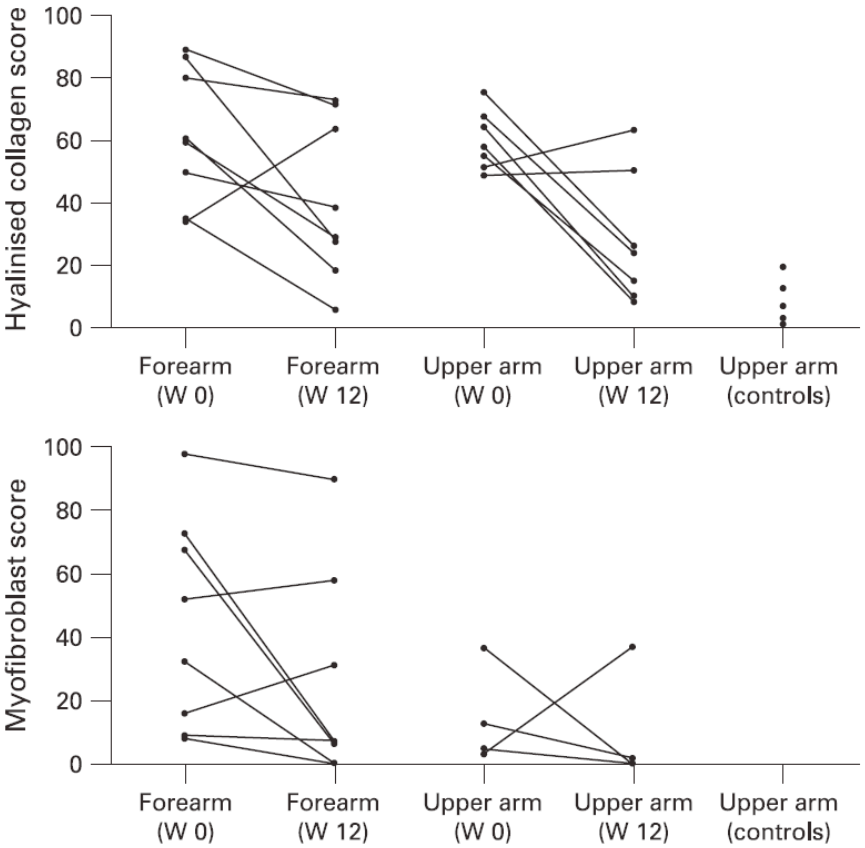
<5 CD19 cell 6M時点で全例

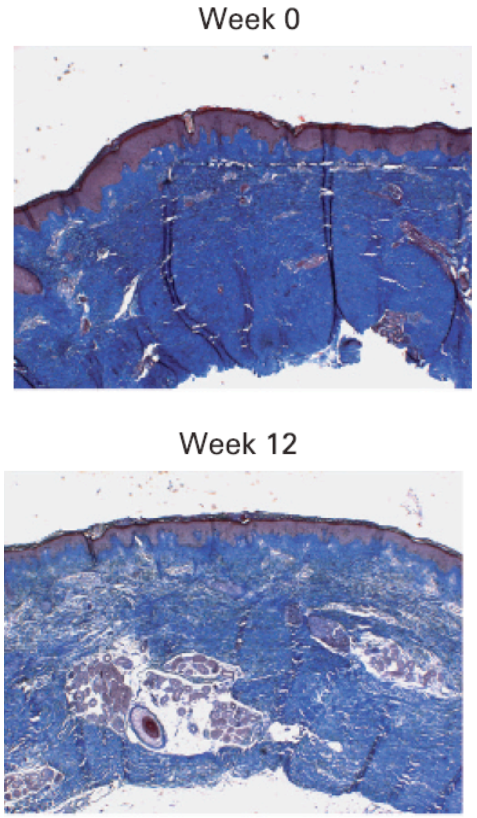




5例心筋投与前より心筋合併症あり

Smith V, Van Praet JT, Vandooren B, Van der Cruyssen B, Naeyaert JM, Decuman S, Elewaut D, De Keyser F. Rituximab in diffuse cutaneous systemic sclerosis: an open-label clinical and histopathological study. Ann Rheum Dis. 2010,69(1):193-7





1462. Outcomes of Systemic Sclerosis associated Polyarthritis patients treated by biotherapies Tocilizumb or Abadacept:A EUSTER observational study

- EUSTER networkにおけるBiologicsの効果
- 13 SSc patients
- 9 tocilizumab:8mg/kg/M

  DAS28　5.0±0.9→2.8±1.0

  mRSS　8±8→9±9　HAQ 1.4±0.5→1.7±0.7
- ４ abadacept:10mg/kg/M

  DAS28　5.2±5.0→1.2±1.8

707. A Pilot Study of Abadacept for the Treatment of patients with Systemic Sclerosis

Abadacept　通常の投与量 DIV
0W, 2W, 4W, その後4W毎投与　24Wまで

24W目にMRSSを測定する。HAQ-DI, VAS,Pulmonary function test

7人　Abadacept, 3人 Placebo

mRSSの絶対値に有意差。副作用や呼吸機能に有意差なし

Variable	Abatacept (n = 7)	placebo (n = 3)	p-value
Baseline			
Age (year, SD)	39.8 (11.4)	48.6 (13.9)	0.32
% Male	28.6	0	1
% caucasian	57.1	66.7	1
Duration (raynauds)	3.9 (3.4)	9.2 (3.2)	0.05
Duration (1st non-raynauds)	2.4 (1.6)	8.8 (3.8)	0.0042
mRSS	23.6 (6.6)	30 (3)	0.15
HAQ-DI	0.6 (0.8)	1.5 (1.1)	0.18
Physician Global VAS	37.6 (13.8)	56.3 (5.5)	0.57
Patient Global VAS	53 (35.8)	61.7 (44.8)	0.75
Patient Pain VAS	42.7 (35.3)	53 (47.8)	0.71
FVC	77.3 (19)	73.3 (27.6)	0.79
DLCO	87 (17.5)	80.3 (24)	0.65
Outcomes			
Change in HAQ-DI	−0.04 (0.2)	0.25	0.56
Absolute change in mRSS	−8.6 (7.5)	−2.3 (15.0)	0.059
% change in mRSS	−33 (29.0)	−6.2 (52.3)	0.31
Change in Physician Global	−11.9 (18.1)	−17.3 (23.2)	0.048
Change in Patient Global	−8 (7.6)	−2.7 (6.7)	0.023
Change in Patient Pain	−11.4 (8.3)	−15.0 (25.1)	0.18
Change in FVC	1.3 (8.5)	0.3 (8.5)	0.72
Change in DLCO	2.0 (6.3)	−7.4 (10.7)	0.84
# Adverse events	7	7	

Annual Scientific Meeting
2012 ACR/ARHP

Washington, DC

Friday November 9-November 14,2012.