Biothérapies ciblées: nouveautés dans la sclérodermie systémique

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Conflits d’intérêts

- Boehringer Ingelheim®
- Incyte®
- Lilly®
- Roche®

Introduction

- **La fibrose cutanée de la sclérodermie systémique, enfin quelques succès !**
- **La pneumopathie interstitielle diffuse associée à la sclérodermie systémique : du succès, limité, d'un seul anti-fibrosant**
- **L'avènement de critère de jugement composite: de l'ACR-CRISS au Revised CRISS**
- **ACR 2023: sélection d'abstract d'intérêt**
- **Les études en cours**
- **Les études en préparation**

Fibrose cutanée

Romilkimab

SAR156597

Brodalumab

AMG-827
KHK-4827
LP 0160

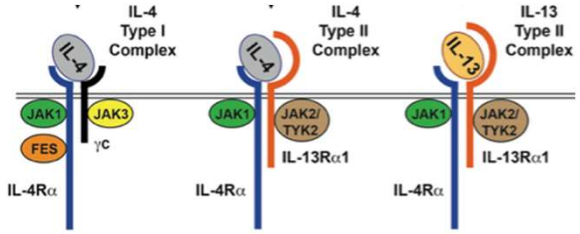
Rituximab

ziritaxestat

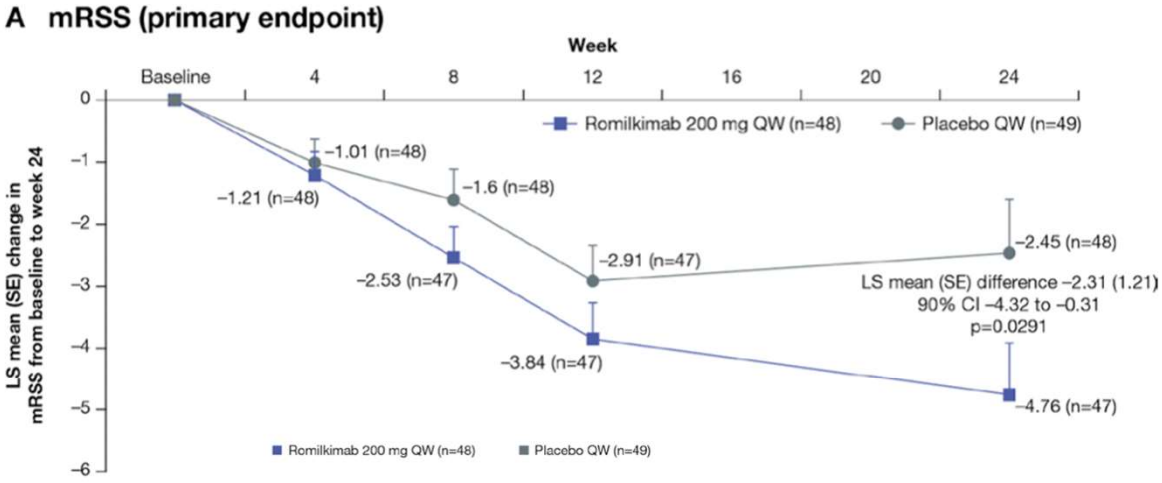
GLPG 1690

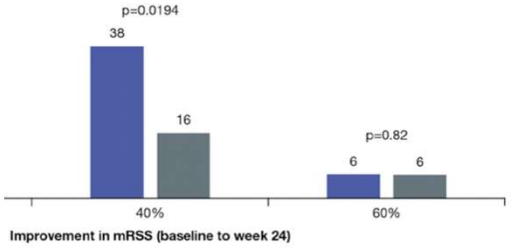
Fibrose cutanée

Romilkimab mAb bispécifique anti-IL-4/Il-13



	Placebo QW (n=49)	Romilkimab 200 mg QW (n=48)
Median Age (range)	45.0 (27–72)	53.0 (20–78)
Disease duration Median (range)	25.4 (5–36)	19.4 (6–36)
Median MRSS (range)	18.0 (10–35)	19.5 (11–35)
Median FVC (range)	91.9 (48–127)	97.3 (54–127)
PID-SSC	18 (37)	18 (38)
Methotrexate	21 (43)	12 (25)
Mycophenolate mofetil	7 (14)	10 (21)
Azathioprine	1 (2)	4 (8)





Bonne tolérance

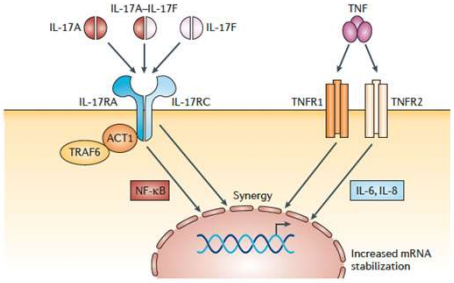
PHASE III nécessaire

Allanore et al. ARD 2020

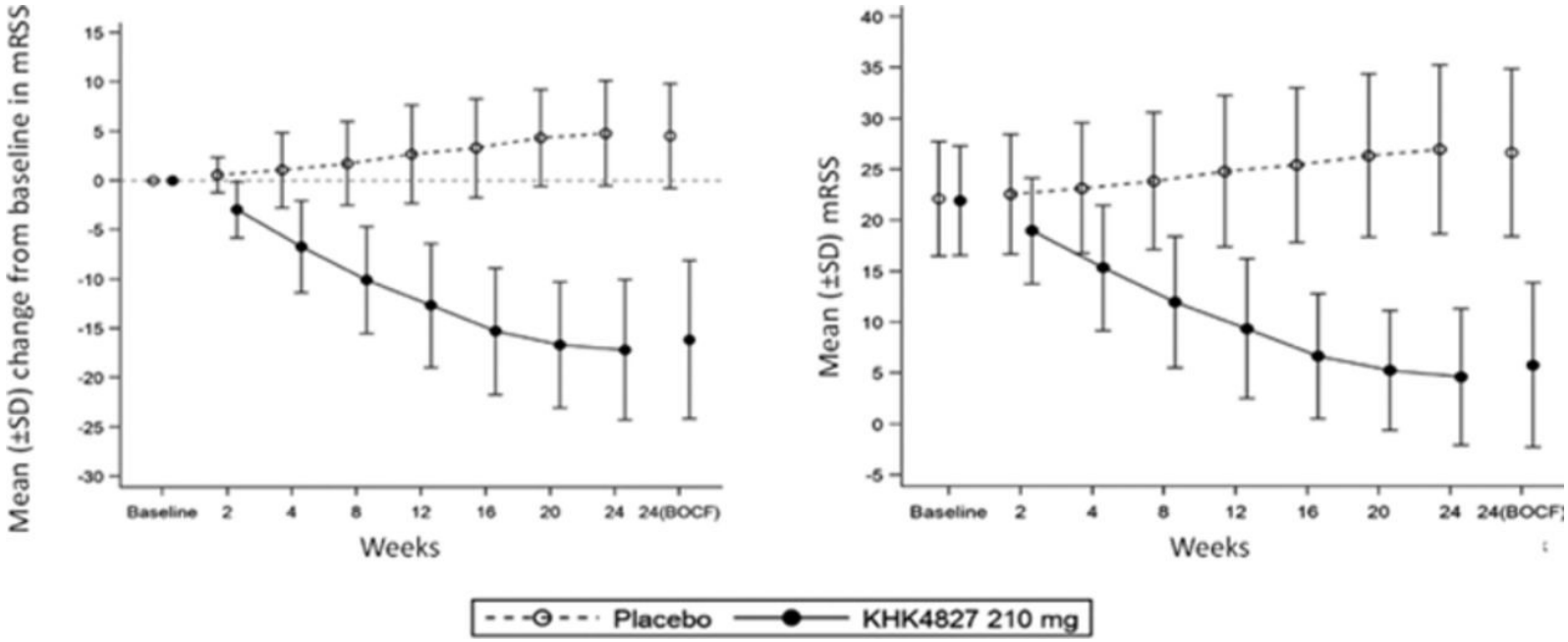
Fibrose cutanée

Brodalumab

mAb anti-RaIL17



Méthodes: mRSS:10-29, durée de maladie 60 mois
50 patients brodalumab 210 Q2W 52 semaines vs 50 placebo
Résultats: Primary endpoint (w24): mRSS: −21.2 [95% CI -23.9, 18.5]; P<0.0001)



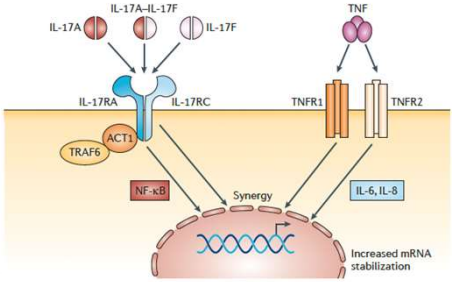
Non publiée à ce jour

Fukasawa et al. ACR 2022 – POS088

Fibrose cutanée

Brodalumab

mAb anti-RaIL17



Interleukin-17 pathway inhibition with brodalumab in early systemic sclerosis: Analysis of a single-arm, open-label, phase 1 trial

Baseline characteristics	Brodalumab 210 mg (*n* = 8)
Age, mean (SD), years	53.6 (10.6)
Women, *n* (%)	7 (87.5)
Disease duration of SSc*, mean (SD), (min-max), years	2.2 (1.9), (0.3-4.9)
Total mRSS, mean (SD), (min-max)	23.1 (5.1), (14-29)
Anti-Scl-70 antibody positive, *n* (%)	3 (37.5)
Anti-RNA polymerase III antibody positive, *n* (%)	4 (62.5)
Anti-centromere antibodies, *n* (%)	0 (0.0)
Skin thickening of both hands extending to fingers	8 (100.0)
Abnormal nail fold capillaries	8 (100.0)
Fingertip pitting scars and/or digital tip ulcers	4 (50.0)
Interstitial pattern of bilateral lower lung lobes	6 (75.0)
Medication history†	
Oral corticosteroids	6 (75.0)
Immunosuppressive agents	1 (12.5)
Other‡	1 (12.5)

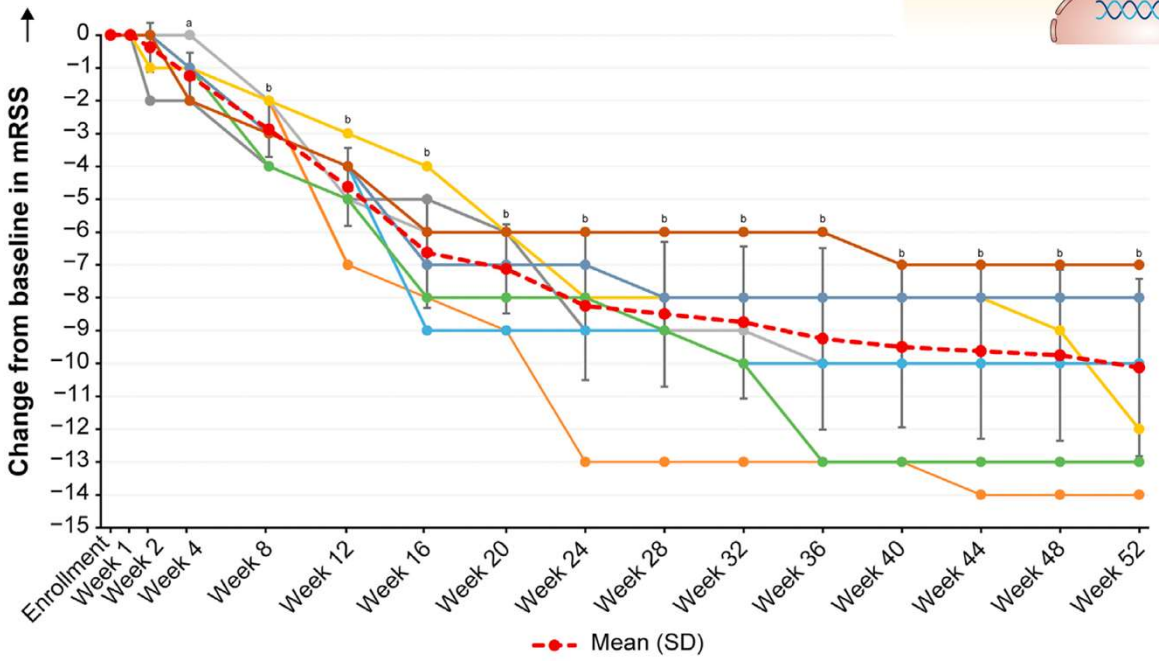


Fig 1. Mean (SD) change from baseline in mRSS over 52 weeks in patients with systemic sclerosis ($n = 8$). Each colored line represents the change for an individual patient. *mRSS*, Modified Rodnan skin score; *SD*, standard deviation. [a]$P = .002$ (week 4) and [b]$P < .001$ (weeks 8-52); paired *t*-test.

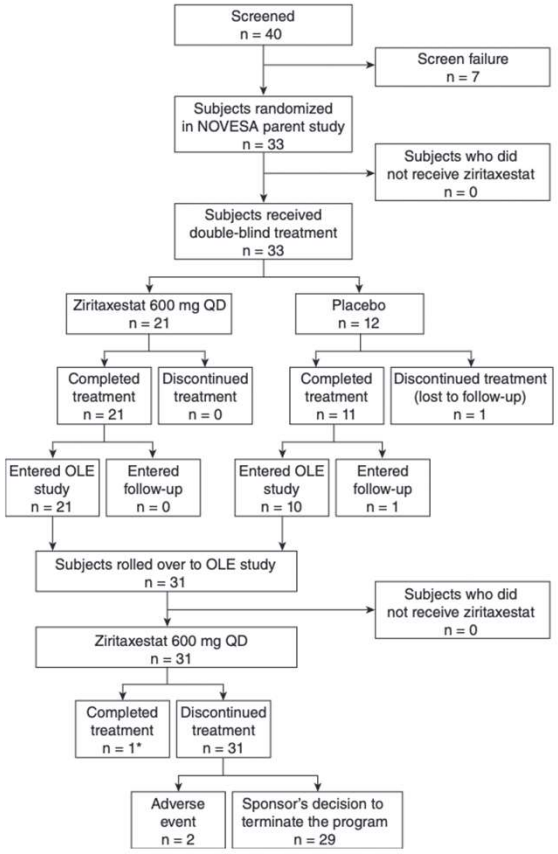
RESEARCH LETTER

Fukasawa et al. JAAD 2023

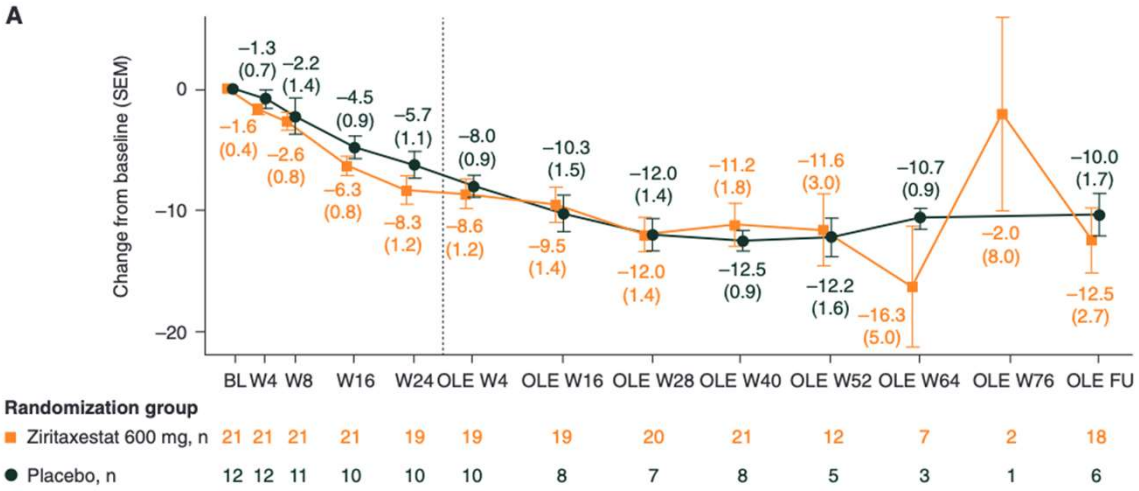
Fibrose cutanée

ziritaxestat

Inhibiteur de l'autotaxine



Arrêt du développement

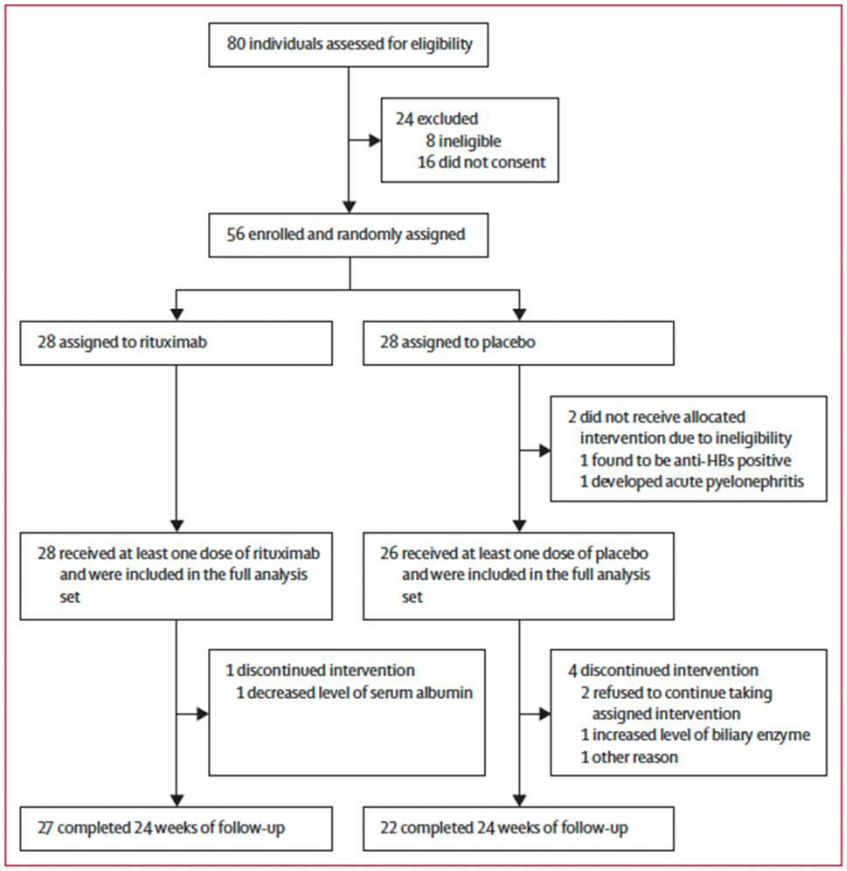


	Ziritaxestat (n = 21)	Placebo (n = 12)
Patients with TEAEs	20 (95.2)	11 (91.7)
Most frequently reported TEAEs†		
Diarrhea	7 (33.3)	2 (16.7)
Headache	5 (23.8)	2 (16.7)
Skin lesion	4 (19.0)	0
Patients with treatment-related TEAEs	12 (57.1)	6 (50.0)
Most frequently reported treatment-related TEAEs‡		
Headache	3 (14.3)	2 (16.7)
Diarrhea	3 (14.3)	0
Patients with serious TEAEs	2 (9.5)	1 (8.3)
TEAEs by worst severity		
Mild	4 (19.0)	4 (33.3)
Moderate	14 (66.7)	7 (58.3)
Severe	2 (9.5)	0
Deaths	0	0
Patients with TEAEs leading to discontinuation	0	0

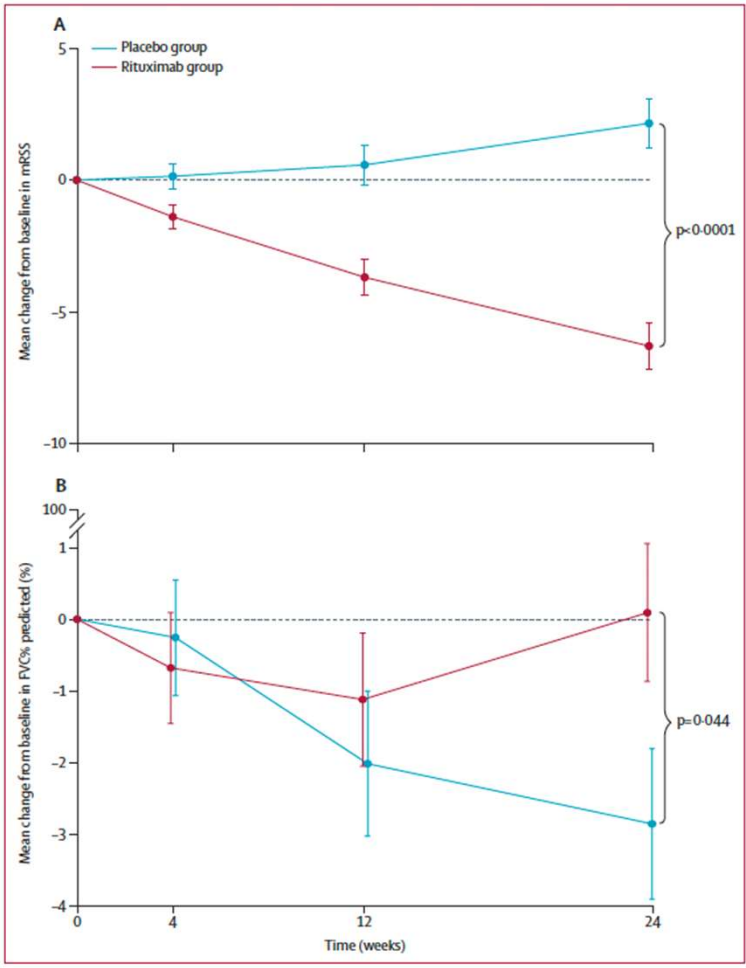
Khanna et al. A&R 2023

Fibrose cutanée

Rituximab **essai DESIRES**



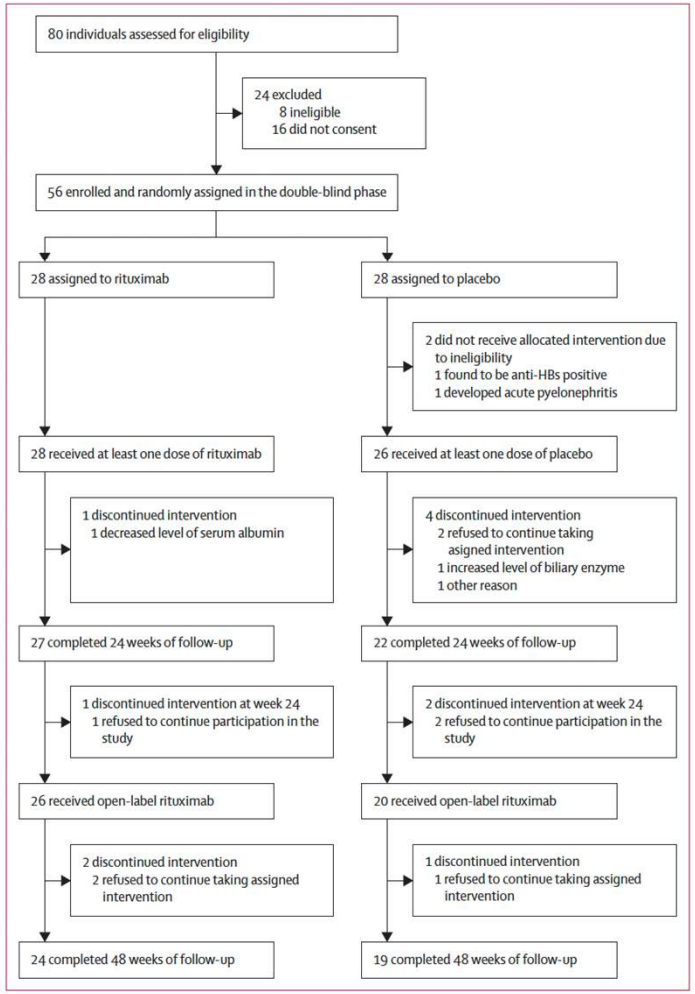
	Rituximab group (n=28)	Placebo group (n=26)
Sex		
Female	25 (89%)	24 (92%)
Male	3 (11%)	2 (8%)
Age, years	49·1 (14·4)	48·3 (9·2)
Diffuse cutaneous systemic sclerosis	23 (82%)	22 (85%)
Disease duration, months	58·5 (0–268)	52·0 (9–248)
mRSS	14·4 (3·7)	15·7 (5·5)
Interstitial lung disease present	25 (89%)	23 (88%)
FVC% predicted	87·9% (15·8)	89·4% (17·9)
%DLCO	84·1% (19·3)	80·6% (16·6)
Surfactant protein-D, ng/mL	151·3 (79·7)	166·8 (126·2)
KL-6, U/mL	678·1 (646·5)	874·4 (1066·1)
Area occupied with interstitial shadows, % of lung fields	13·64% (12·0)	15·39% (13·8)
Anti-topoisomerase I antibody positive	15 (54%)	13 (50%)
Titre of anti-topoisomerase I antibody, U/mL	125·7 (32·5)	130·7 (30·9)
Anti-centromere antibody positive	4 (14%)	4 (15%)
Anti-RNA polymerase III antibody positive	5 (18%)	3 (12%)
Concomitant systemic corticosteroid use	15 (54%)	16 (62%)
Dose of systemic corticosteroid, mg/day	6·5 (2·4)	7·3 (2·6)
Previous immunosuppressants and biologics	13 (46%)	17 (65%)



Ebata et al. Lancet Rheum 2021

Fibrose cutanée

Rituximab **essai DESIRES OLE**



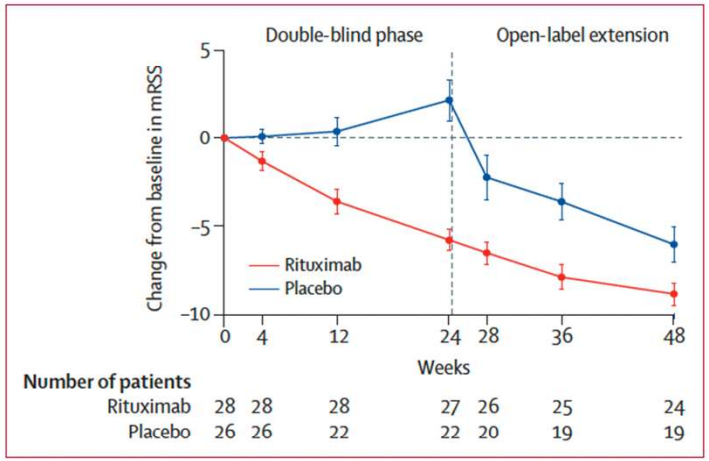


Figure 2: Patterns of change in mRSS

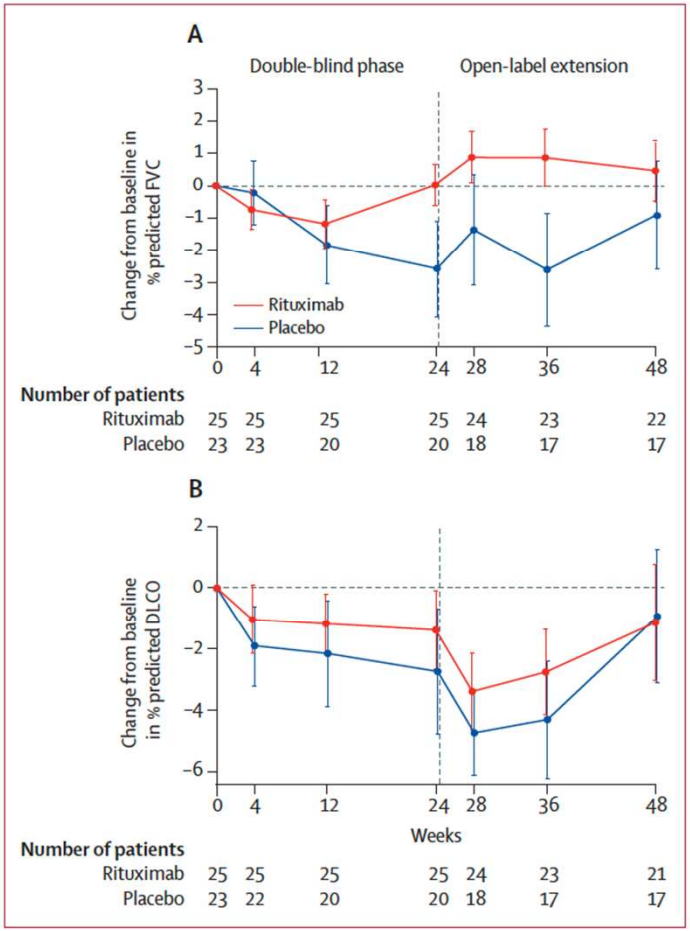


Figure 3: Patterns of change in FVC and DLCO

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Fibrose cutanée

Rituximab **essai DESIRES OLE**

	Double-blind phase		Open-label extension phase	
	Rituximab group (n=28)	Placebo group (n=26)	Rituximab–rituximab (n=26)	Placebo–rituximab (n=20)
Any adverse event	28 (100%)	23 (88%)	19 (73%)	17 (85%)
Upper respiratory infection	11 (39%)	10 (38%)	11 (42%)	8 (40%)
Pulmonary valve disease*	5 (18%)	3 (12%)	3 (12%)	0
Gastroesophageal reflux disease	2 (7%)	6 (23%)	0	1 (5%)
Enterocolitis	2 (7%)	3 (12%)	2 (8%)	2 (10%)
Increased C-reactive protein†	3 (11%)	2 (8%)	1 (4%)	0
Arthralgia	1 (4%)	4 (15%)	0	0
Skin ulceration	2 (7%)	3 (12%)	1 (4%)	1 (5%)
Diarrhoea	3 (11%)	1 (4%)	0	1 (5%)
Mucositis oral	3 (11%)	0	0	0
Decreased neutrophil count‡	3 (11%)	0	0	0
Decreased white blood cell count§	3 (11%)	0	0	1 (5%)
Dermatitis	0	3 (12%)	1 (4%)	2 (10%)
Any adverse drug reaction	21 (75%)	15 (58%)	14 (54%)	12 (60%)
Any serious adverse event¶	1 (4%)	1 (4%)	1 (4%)	1 (5%)
Serious adverse event leading to discontinuation of study treatment	1 (4%)	1 (4%)	0	0
Death	0	0	0	0
Infusion reaction	0	0	0	0

Some patients had more than one adverse event. The most common adverse events (ie, those that were reported in more than 10% of the patients in either trial group) are shown. *All pulmonary valve disease cases observed in this study were physiological pulmonary valve regurgitation that was not pathological. †>0.3 mg/ dL. ‡<1500/ µL. §<3000/ µL. ¶ Any untoward medical occurrence that: (1) results in death; (2) is life-threatening; (3) requires inpatient hospitalisation or prolongation of existing hospitalisation; (4) results in disability or incapacity; (5) might result in persistent or significant disability or incapacity; (6) any other event that might require intervention to prevent outcomes 1–5; or (7) might result in a congenital anomaly or birth defect in subsequent generations.

Table 3: Adverse events

Ebata et al. Lancet Rheum 2022

Fibrose cutanée

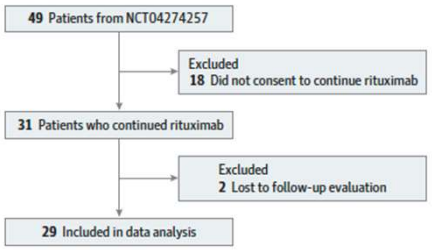
Rituximab

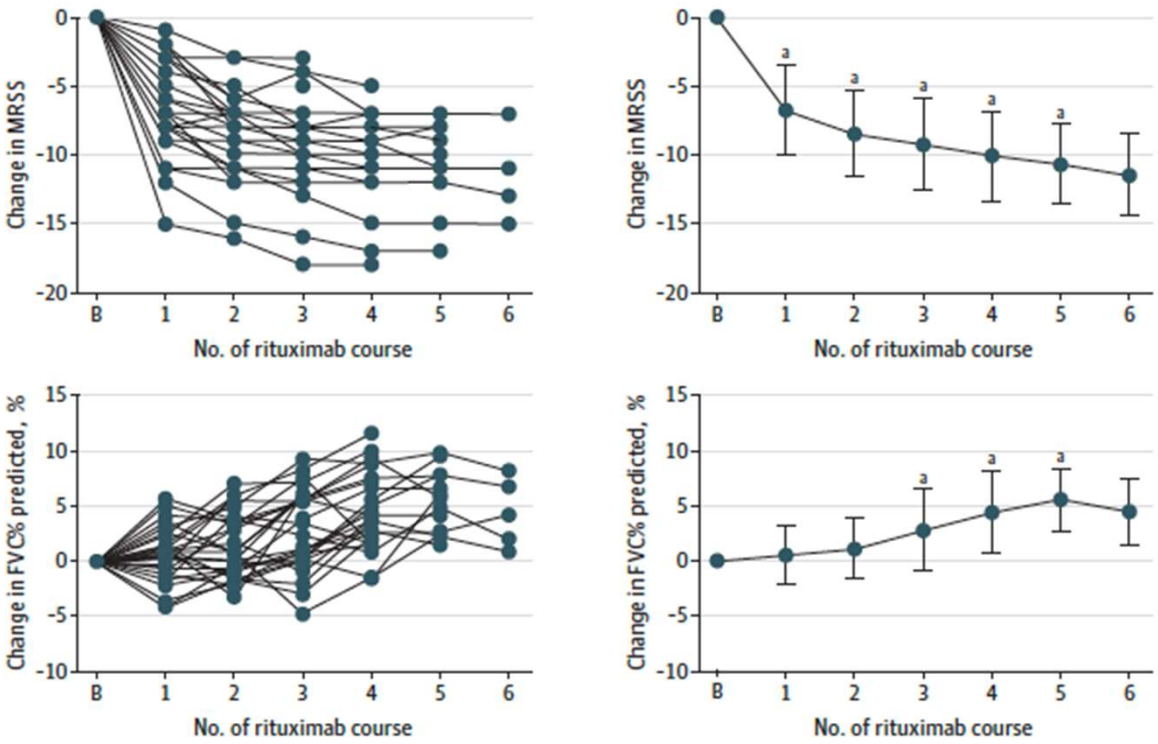
JAMA Dermatology | Original Investigation

Long-term Outcomes After Rituximab Treatment for Patients With Systemic Sclerosis

Follow-up of the DESIRES Trial With a Focus on Serum Immunoglobulin Levels

Ai Kuzumi, MD, PhD; Satoshi Ebata, MD, PhD; Takemichi Fukasawa, MD, PhD; Kazuki M. Matsuda, MD; Hirohito Kotani, MD; Asako Yoshizaki-Ogawa, MD, PhD; Shinichi Sato, MD, PhD; Ayumi Yoshizaki, MD, PhD





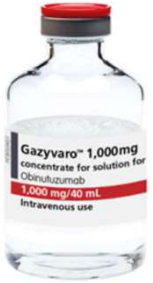
27 patients (93%): infections respiratoires

Kuzumi et al. Jama Dermatology 2023

P.H.R.C. national 2022

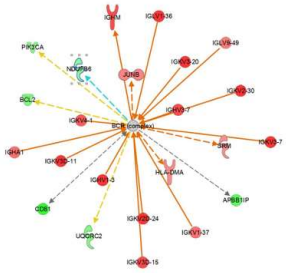
Etude OBINUSS

Investigateur principal: Dr. Benjamin Chaigne
Responsable scientifique: Pr. Luc Mouthon

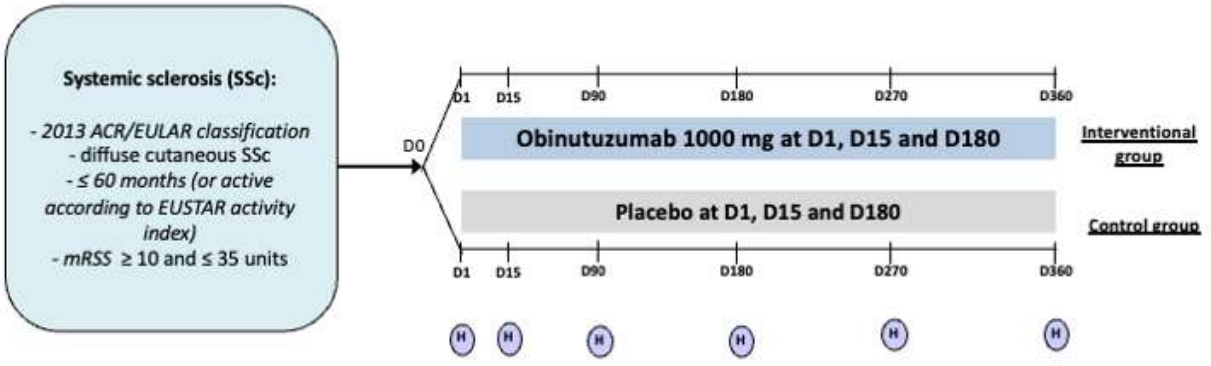


Obinutuzumab dans la sclérodermie systémique

- **Nom du protocole** : Tolérance et efficacité de l'obinutuzumab dans la sclérodermie systémique (ScS): une étude de phase II, randomisée, double-aveugle, contrôlée, *vs* placebo
- **Design :** - essai clinique, multicentrique, contrôlé, randomisé, *vs* placebo, réalisé en double-aveugle comparant l'itacitinib à un placebo dans le traitement de la ScS
  - stratification sur l'atteinte pulmonaire ou cutanée et sur les traitements reçus
  - en add-on de MTX/MMF/NTD
- **Nombre de patients à inclure** : 2*37 patients



Pour participer:
benjamin.chaigne@aphp.fr



PID-SSc

Rituximab

Nintedanib

PID(-SSc)

Rituximab vs cyclophosphamide: essai RECITAL

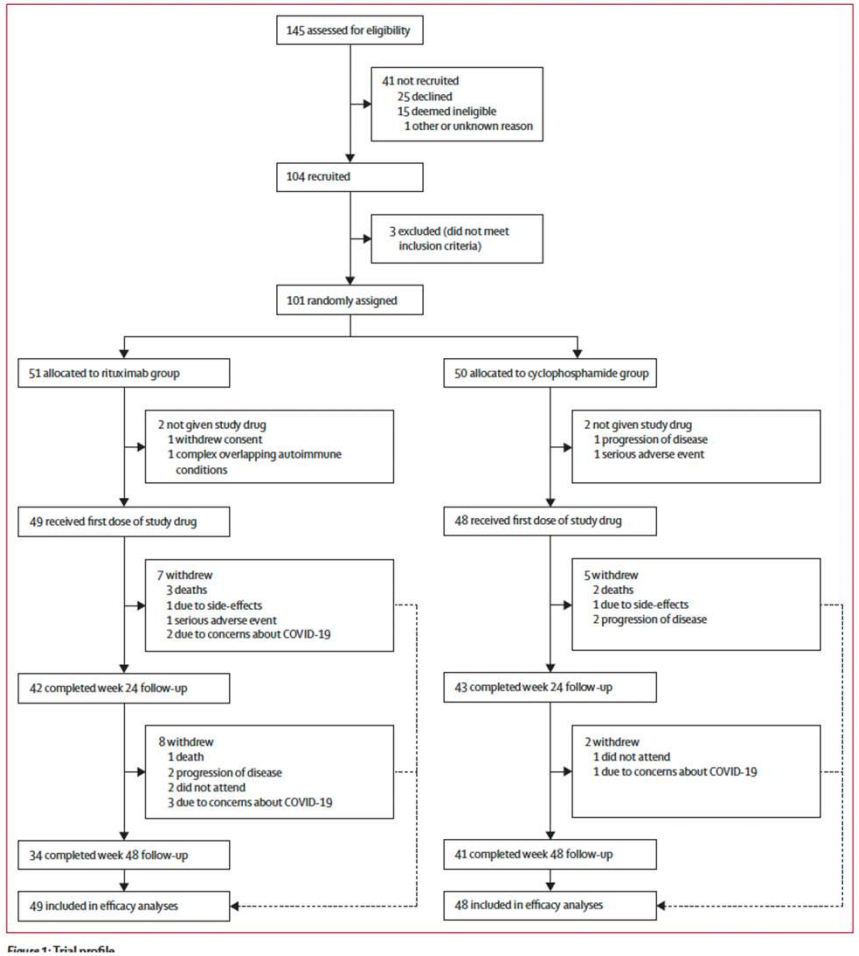
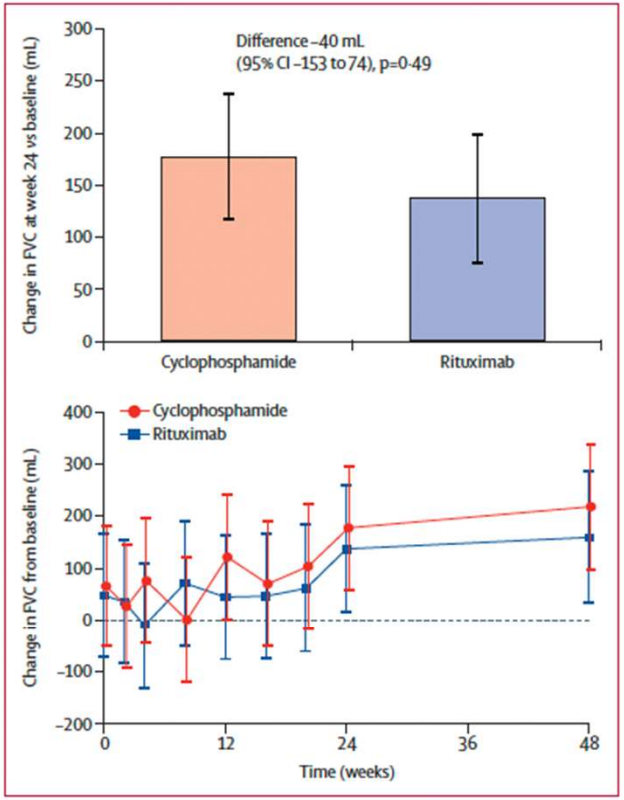


Figure 1: Trial profile

	Cyclophosphamide group (n=48)	Rituximab group (n=49)
Age, years	56·7 (11·6)	56·6 (11·4)
Sex		
Female	35 (73%)	31 (63%)
Male	13 (27%)	18 (37%)
Race and ethnicity*		
Asian	7 (15%)	9 (18%)
Black	5 (10%)	7 (14%)
White	34 (71%)	32 (65%)
Any other ethnic group	2 (4%)	1 (2%)
Connective tissue disease type		
Idiopathic inflammatory myositis	22 (46%)	22 (45%)
Systemic sclerosis	19 (40%)	18 (37%)
Mixed connective tissue disease	7 (15%)	9 (18%)
Years since onset of connective tissue disease	4·8 (6·2)	4·5 (7·6)
FVC, L	2·23 (0·85)	2·25 (0·77)
FVC, % of predicted	71% (20)	68% (17)
DL_{CO}, mL/min per kPa	3·35 (1·42), n=46	3·46 (1·33), n=45
DL_{CO}, % of predicted	40% (14), n=46	40% (14), n=45
SpO_2 on room air, %	96% (2)	97% (2)
6 min walk distance, m	363 (111)	356 (126)
EQ-5D score	55 (20)	58 (22)
GDA score	5·03 (1·76), n=40	4·58 (1·97), n=38
KBILD score	46·1 (20·3)	51 (21·2)
SGRQ score	55·8 (20·0), n=47	52·1 (17·6), n=45

Data are mean (SD) or n (%). FVC=forced vital capacity. DL_{CO}=diffusing capacity of the lung for carbon monoxide. SpO_2=arterial oxygen saturation. EQ-5D=European Quality of Life Five-Dimension. GDA=global disease activity (physician-assessed). KBILD=King's Brief Interstitial Lung Disease. SGRQ=St George's Respiratory Questionnaire. *Self-reported.

Table 1: **Baseline characteristics in the modified intention-to-treat population**



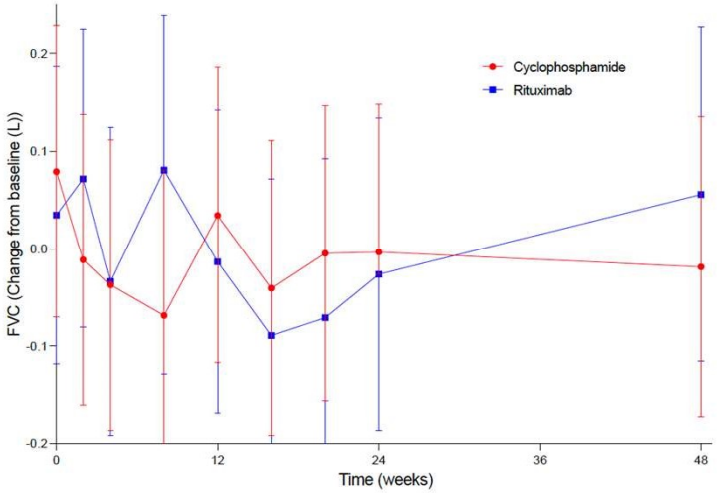
Etude de supériorité

Maher et al. Lancet Respiratory 2023

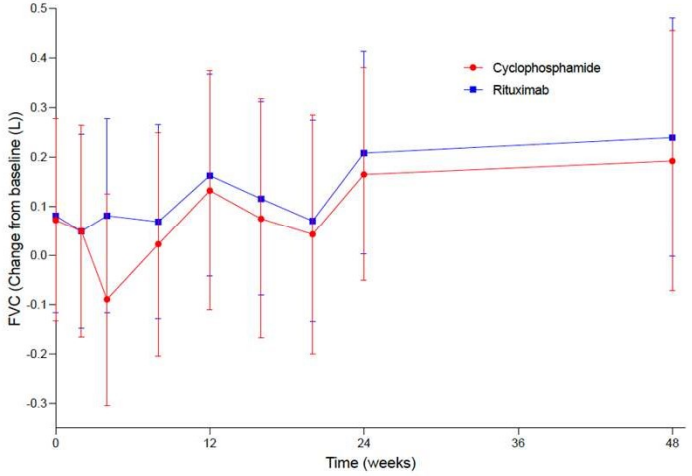
PID(-SSc)

Rituximab vs cyclophosphamide: essai RECITAL

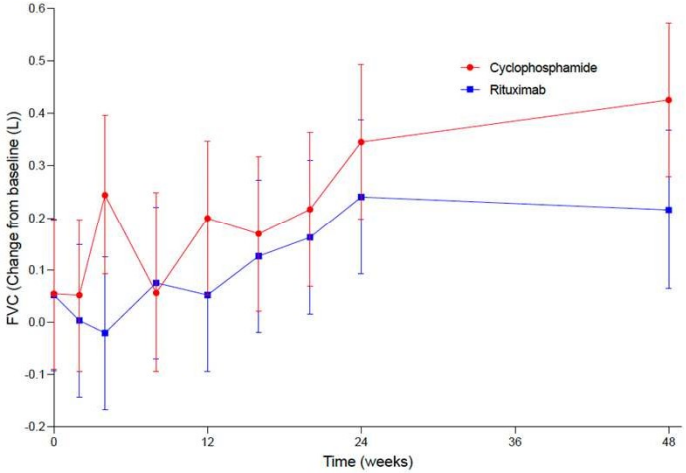
Pas de différence selon le type de connectivite



Sclérodermie
N = 37

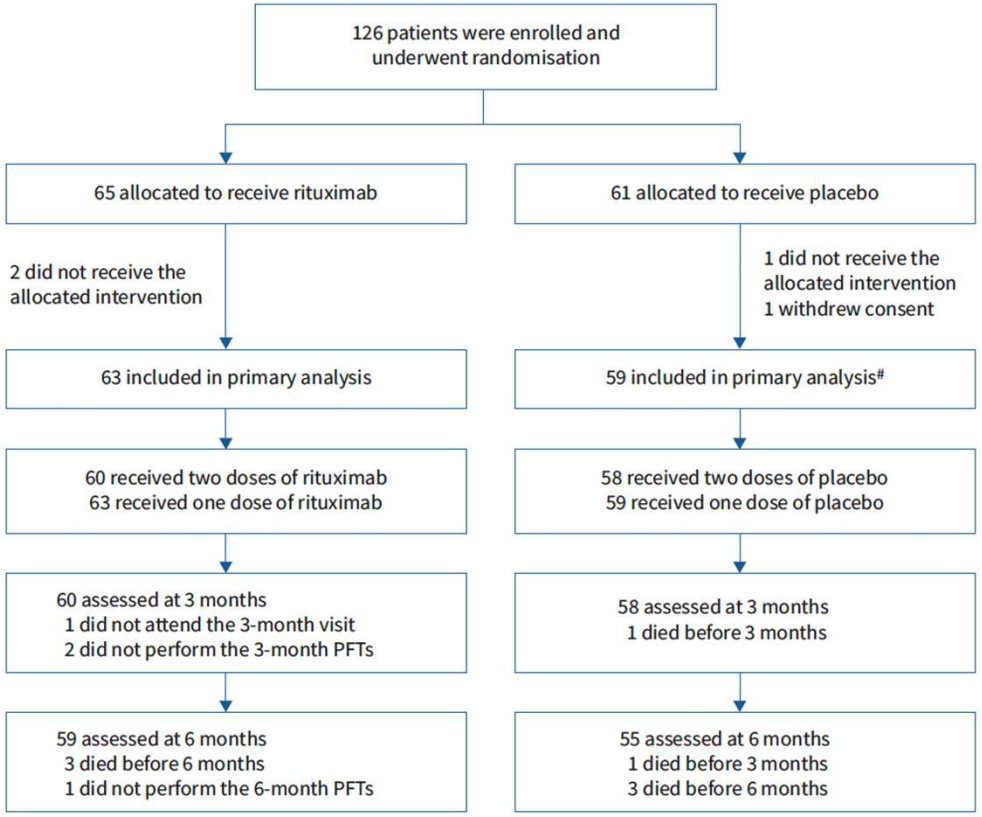


Connectivite mixte
N = 16



Myosites inflammatoires
N = 44

PID(-SSc)



Rituximab + mycophenolate mofetil: essai EVER-ILD

TABLE 1 Demographic and baseline characteristics of study participants

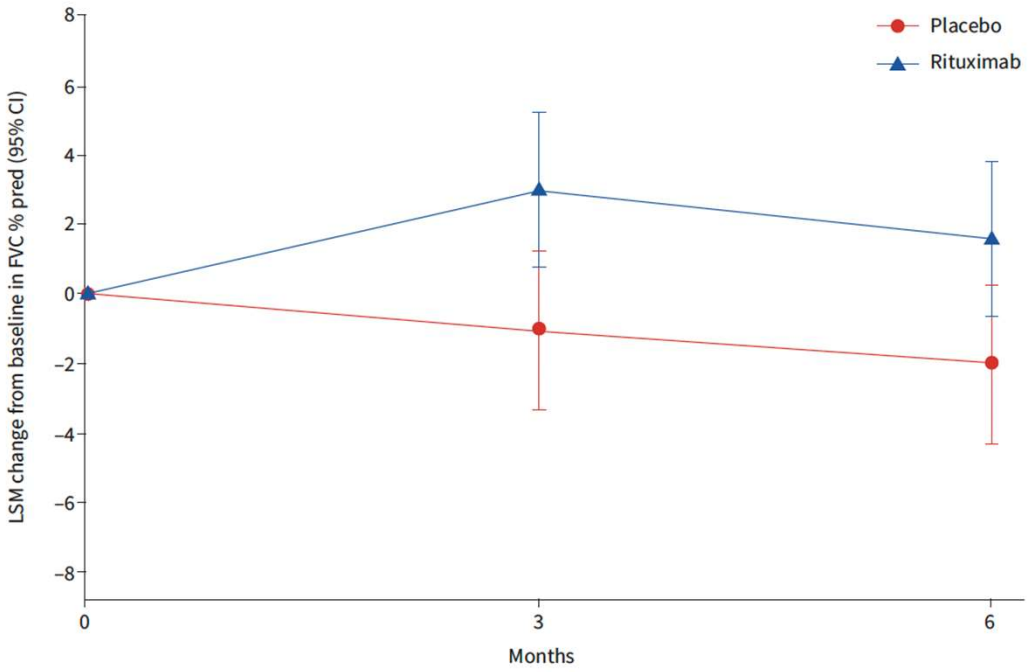
	Rituximab+MMF	Placebo+MMF
Participants	63	59
Female	35 (55.6)	38 (64.4)
Age (years)	64.7±12.1	67.5±11.9
BMI (kg·m^{-2})	29.0±5.4	28.4±5.2
Years since ILD diagnosis	3.8±4.9	2.9±2.7
FVC (% pred)	66.7±21.5	70.2±22.5
FVC (mL), n_R=63, n_P=58	2046±767	1971±724
FEV_1/FVC (%), n_R=63, n_P=57	85.7±11.0	86.9±14.0
D_{LCO}, n_R=60, n_P=55		
Unfeasible	9 (15.0)	12 (21.8)
% pred, n_R=51, n_P=43	40.1±13.5	38.6±14.8
6MWD (m), n_R=61, n_P=55	364±148	325±179
O_2 >10 h·day^{-1} at baseline	13 (20.6)	17 (28.8)
Histopathological NSIP	10 (15.8)	5 (8.5)
ILD groups		
CTD-ILD	25 (39.7)	18 (30.5)
IPAF	17 (27.0)	19 (32.2)
Idiopathic ILD	21 (33.3)	22 (37.3)
Glucocorticoids at baseline	46 (73.0)	50 (84.7)
Glucocorticoids dose at baseline (mg·day^{-1})	15 (10–20)	17.5 (10–25)
Previous treatment received for ILD#		
None¶	2 (3.2)	0
Glucocorticoids alone	36 (57.1)	33 (55.9)
Immunosuppressive agent alone	2 (3.2)	0
Glucocorticoids+immunosuppressive agent	23 (36.5)	26 (44.1)

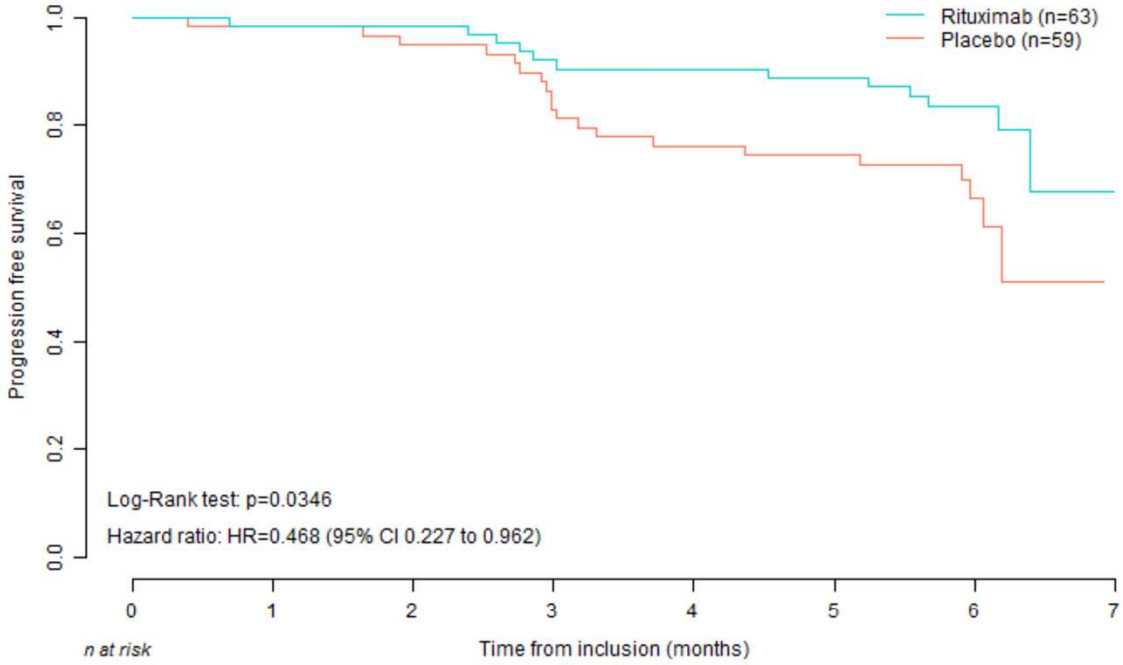
Data are presented as n, n (%), mean±SD or median (interquartile range). MMF: mycophenolate mofetil; BMI: body mass index; ILD: interstitial lung disease; FVC: forced vital capacity; n_R: number of patients assigned rituximab; n_P: number of patients assigned placebo; FEV_1: forced expiratory volume in 1 s; D_{LCO}: diffusing capacity of the lung for carbon monoxide; 6MWD: 6-min walk distance; NSIP: nonspecific interstitial pneumonia; CTD: connective tissue disease; IPAF: interstitial pneumonia with autoimmune features. #: any previous treatments were considered and are specified in supplementary table S1; ¶: patients with a contraindication to glucocorticoids.

Mankikian et al. ERJ 2023

PID(-SSc)

Rituximab + mycophenolate mofetil: essai EVER-ILD





	Rituximab+MMF	Placebo+MMF	Between-group difference (95% CI)	p-value
Participants	63	59		
LSM change in FVC % pred value from baseline to 6 months				
Primary analysis	1.60 (−0.63–3.82)	−2.01 (−4.31–0.29)	3.60 (0.41–6.80)	0.0273
Adjusted model on stratification variables[#]	1.53 (−0.69–3.76)	−2.04 (−4.35–0.26)	3.58 (0.38–6.79)	0.0288

Mankikian et al. ERJ 2023

PID(-SSc)

Rituximab + mycophenolate mofetil: essai EVER-ILD

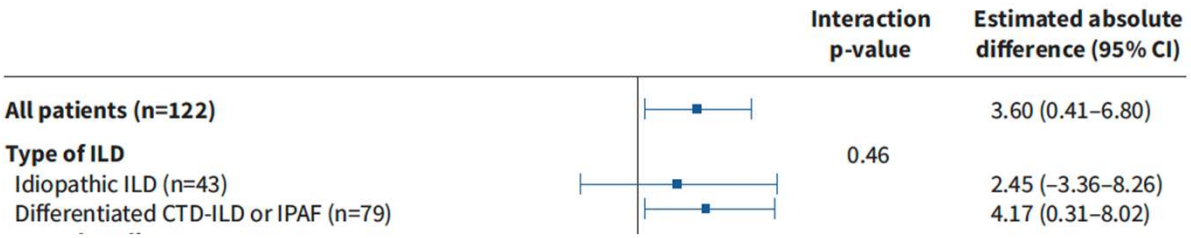


TABLE 3 Summary of all adverse events

	Rituximab+MMF	Placebo+MMF
Participants	63	59
Any adverse event	54 (86)	57 (97)
Related to study treatment	36 (57)	27 (46)
Any serious adverse event	26 (41)	23 (39)
Most common serious adverse event		
Respiratory tract disorders	3 (5)	12 (20)
Infection	9 (14)	4 (7)
Cardiac disorders	5 (8)	2 (3)
Leading to discontinuation of study treatment	3 (5)	1 (2)
Fatal adverse event	3 (5)	4 (7)
Related to study treatment	15 (24)	6 (10)
Infection	9 (14)	4 (7)
Infusion-related reaction	3 (5)	1 (2)

Data are presented as n or n (%) of patients with adverse events. MMF: mycophenolate mofetil.

Mankikian et al. ERJ 2023

Bithérapie MMF-RTX

Outcomes in progressive systemic sclerosis treated with autologous hematopoietic stem cell transplantation compared with combination therapy.

Shiri Keret[1]*, Israel Henig[2]*, Tsila Zuckerman[2], Lisa Kaly[1], Aniela Shouval[1], Abid Awisat[1], Itzhak Rosner[1], Michael Rozenbaum[1], Nina Boulman[1], Ariela Dortort Lazar[3], Yair Molad[3], Firas Sabbah [4 5], Mohammad E. Naffaa [5,6], Emilia Hardak[7], Gleb Slobodin[1], Doron Rimar[1].

	Transplantation N=16	Combination therapy N=21	P
Age	48 (9)	49 (15)	> 0.9
Gender	13 (81)	15 (71)	0.7
Autoantibodies			0.4
Scl70	8 (50)	9 (45)	
RNA Pol3	7 (44)	6 (30)	
Negative	1 (6.2)	5 (25)	
Disease duration			> 0.9
< 5 years	14 (88)	19 (90)	
SSc			**0.05**
Diffuse	15 (94)	13 (62)	
Limited	1 (6)	8 (38)	
Lung fibrosis > 10%	13 (81)	16 (76)	> 0.9
Nintedanib	**0**	**9 (43)**	**0.005**
Smoking	3 (19)	6 (29)	0.7
Baseline FVC (%)	73 (16)	70 (15)	0.8
Baseline DLCO (%)	60 (13)	58 (16)	0.8
Baseline mRSS	23 (9)	16 (14)	0.07

Primary outcomes:

1. Clinical improvement at 12 months, defined as a decrease in mRSS by more than 25%, or an absolute increase in FVC by more than 10%

2. Event-free survival (EFS) at 24 months, defined as the survival rate without the occurrence of persistent major organ failure (heart, lung, kidney)

Keret et al. Rheumatology 2023

Primary outcomes:

1. Clinical improvement at 12 months, defined as a decrease in mRSS by more than 25%, or an absolute increase in FVC by more than 10%

→ ***GREFFE: 13 (81%) COMBO:18 (86%) (p=0.7)***

2. Event-free survival (EFS) at 24 months, defined as the survival rate without the occurrence of persistent major organ failure (heart, lung, kidney)

→ ***$HR_{EFS\ -24\ mois}$ en faveur de la COMBO***
HR=0.09, 95% CI 0.009 to 0.9; P =0.04

Keret et al. Rheumatology 2023

Primary outcomes:

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$HR_{EFS\ -24\ mois}$ en faveur de la COMBO
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Mortalité associée au traitement: *GREFFE 3/16 (18.7%) vs COMBO 0 (0%)*

1 choc septique après mobilisation
1 CRS pendant le conditionnement
1 choc cardiogénique pendant le conditionnement

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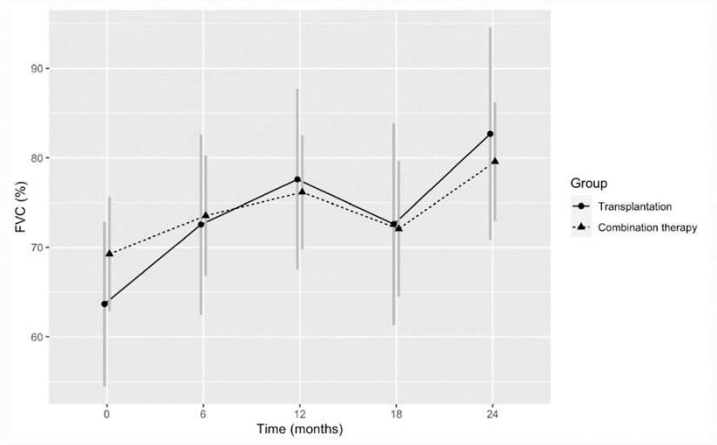
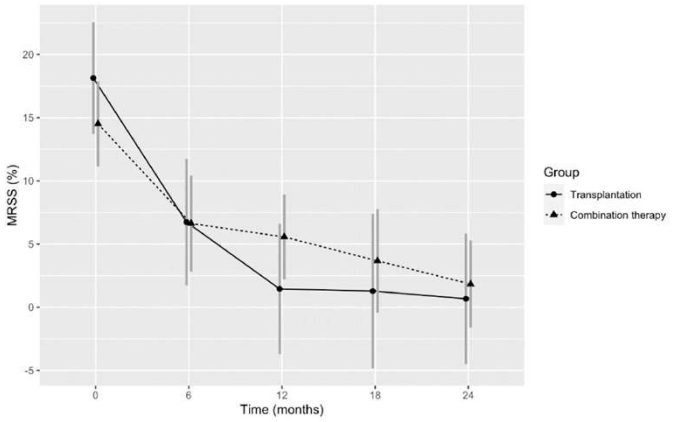




Keret et al. Rheumatology 2023

Appel à observations

Evaluation de l'association rituximab - mycophenolate mofetil dans la sclérodermie systémique : une étude rétrospective Française multicentrique

MycRiSS France et MycRiSS Europe

Design d'étude :
- étude observationnelle nationale multicentrique rétrospective et prospective

Critères d'inclusions :
- Diagnostic de ScS selon les critères de classification ACR/EULAR 2013
- Patient ayant bénéficié d'un traitement par RTX avec ou sans MMF
- Données de suivi disponibles à au moins 1 an post-introduction de traitement
- Pour chaque patient inclus ayant reçu RTX ou RTX/MMF, un patient ayant reçu MMF, apparié par centre, type de ScS, sexe et durée d'évolution de la ScS sera nécessaire

Pour participer: François Barde francois.barde@aphp.fr ; Benjamin Chaigne benjamin.chaigne@aphp.fr

N'hésitez pas à partager vos observations !

PID-SSc

AMERICAN THORACIC SOCIETY DOCUMENTS

Treatment of Systemic Sclerosis–associated Interstitial Lung Disease: Evidence-based Recommendations

An Official American Thoracic Society Clinical Practice Guideline

Ganesh Raghu, Sydney B. Montesi, Richard M. Silver, Tanzib Hossain, Madalina Macrea, Derrick Herman, Hayley Barnes, Ayodeji Adegunsoye, Arata Azuma, Lorinda Chung, Gregory C. Gardner, Kristin B. Highland, Marie Hudson, Robert J. Kaner, Martin Kolb, Mary Beth Scholand, Virginia Steen, Carey C. Thomson, Elizabeth R. Volkmann, Fredrick M. Wigley, Dee Burlile, Karen A. Kemper, Shandra L. Knight, and Marya Ghazipura; on behalf of the American Thoracic Society Assembly on Clinical Problems

This Official Clinical Practice Guideline of the American Thoracic Society was Approved May 2023

Raghu et al. AMJRCCM 2023

PID-SSc

4 revues systématiques avec méta-analyses:

- cyclophosphamide
- nintedanib seul ou associé au MMF
- rituximab
- tocilizumab

- Cyclophosphamide: 6 études (2 RCT vs PBO, 1 RCT et 2 études CYC vs MMF)

=> CYC > PBO mais CYC = MMF et effets secondaires

- Rituximab: 3 études

=> RTX stabilise la fonction pulmonaire

Niveau de preuve: « very low »

- Nintedanib: 3 études

=> NTD seul ou NTD + MMF associés à ralentissement de l'aggravation mais effets secondaires digestifs et arrêt de traitement

Niveau de preuve « very low »

- Tocilizumab: 5 études

=> TCZ moins d'aggravation et peu de toxicité

Niveau de preuve « very low »

Essais spécifiques PID-SSc nécessaires

PID-SSc

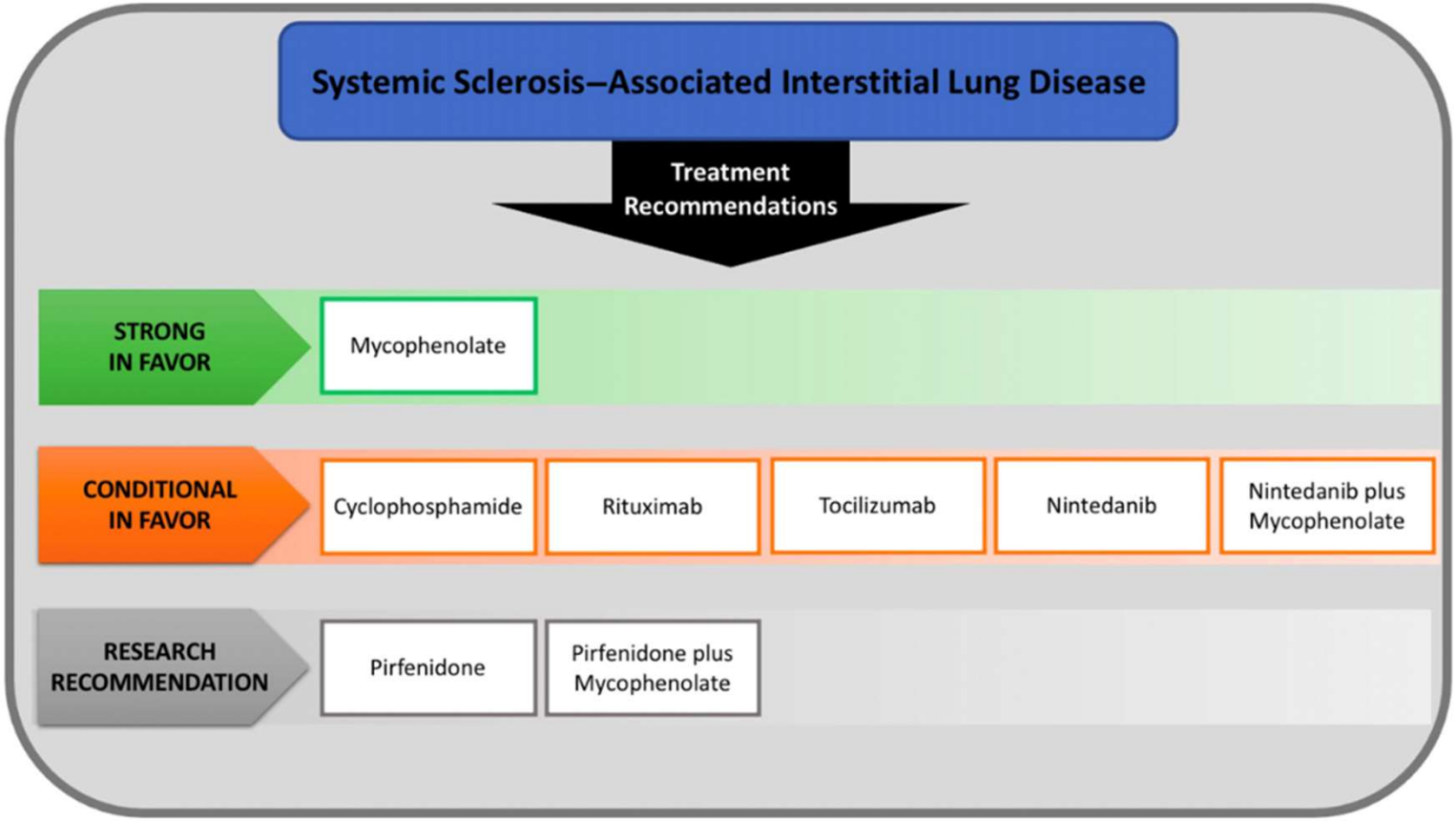
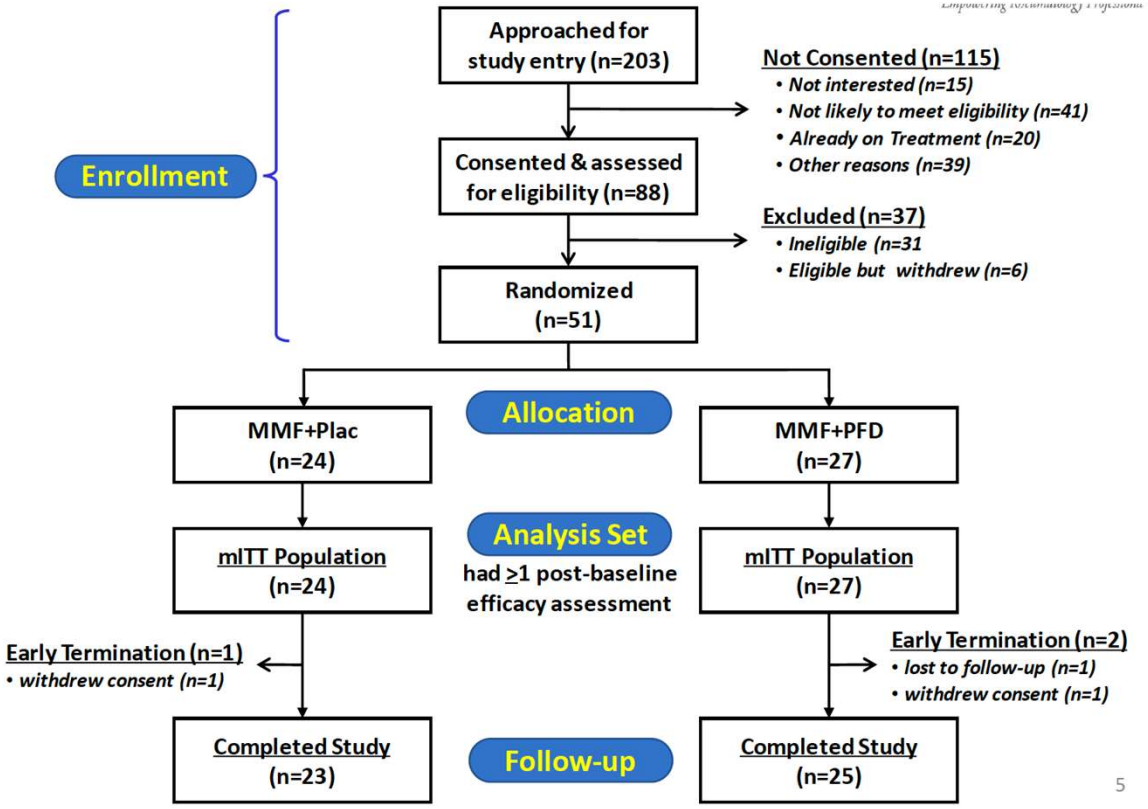


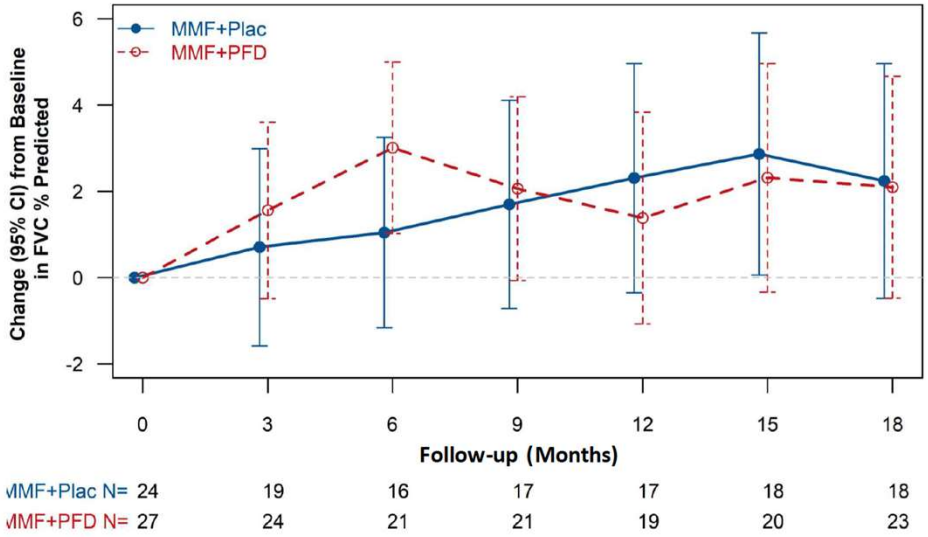
Figure 1. Summary of treatment recommendations for patients with systemic sclerosis–associated interstitial lung disease (SSc-ILD). The SSc-ILD Guideline Committee:

Raghu et al. AMJRCCM 2023

PID-SSc

Pirfenidone: scleroderma lung study III



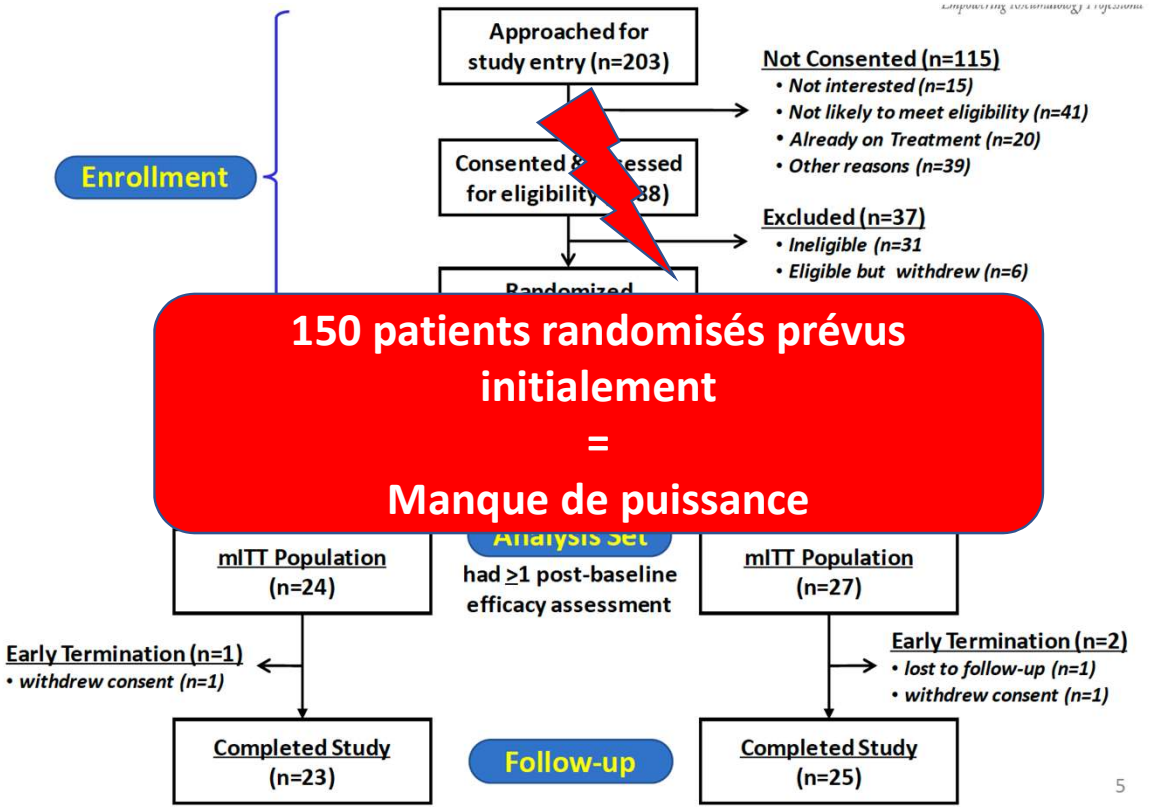


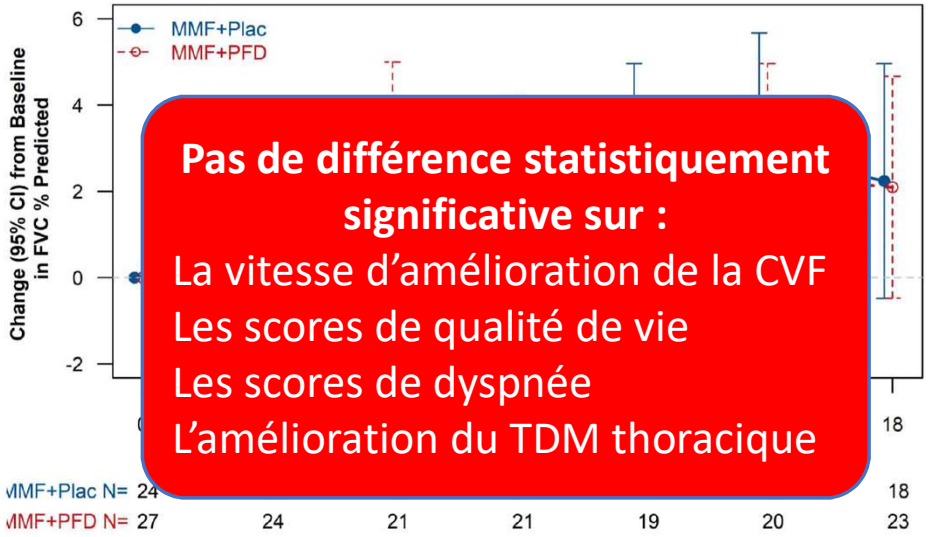
	MMF+Plac (N=24)	MMF+PFD (N=27)	(MMF+PFD) – (MMF+Plac) LSM (95% CI)
Primary analysis			
FVC % predicted • m-ITT population	**2.24** ± 1.35	**2.09** ± 1.28	**-0.14** (-3.57, 3.28)

Khanna et al. ACR CO 2023

PID-SSc

Pirfenidone: scleroderma lung study III





Pas de différence statistiquement significative sur :

La vitesse d'amélioration de la CVF

Les scores de qualité de vie

Les scores de dyspnée

L'amélioration du TDM thoracique

	MMF+Plac (N=24)	MMF+PFD (N=27)	(MMF+PFD) – (MMF+Plac) LSM (95% CI)
Primary analysis			
FVC % predicted • m-ITT population	**2.24** ± 1.35	**2.09** ± 1.28	**-0.14** (-3.57, 3.28)

Khanna et al. ACR CO 2023

ACR CRISS

CRISS is a 2-step process.

Step 1: Subjects who develop new or worsening of cardiopulmonary and/or renal involvement due to systemic sclerosis are considered as not improved (irrespective of improvement in other core items) and assigned a probability of improving equal to 0.0. Specifically if a subject develops any of the following

- **New scleroderma renal crisis (43)**
- **Decline in forced vital capacity (FVC)% predicted ≥15% (relative), confirmed by another FVC% within a month, high resolution computer tomography (HRCT) to confirm interstitial lung disease (ILD; if previous high resolution computer tomography of chest did not show ILD) and FVC% predicted below 80% predicted***
- **New onset of left ventricular failure (defined as left ventricular ejection fraction ≤45%) requiring treatment***
- **New onset of pulmonary arterial hypertension (PAH) on right heart catheterization (44) requiring treatment***. PAH is defined as mean pulmonary artery pressure ≥ 25 mm Hg at rest and an end-expiratory pulmonary artery wedge pressure ≤ 15 mm Hg and a pulmonary vascular resistance >3 Wood units

Step 2: For the remaining subjects, Step 2 involves computing the predicted probability of improving for each subject using the following equation (equation to derive predicted probabilities from a logistic regression model):

$$\frac{exp\left[-5.54-0.81*\Delta_{MRSS}+0.21*\Delta_{FVC\%}-0.40*\Delta_{Pt-glob}-0.44*\Delta_{MD-glob}-3.41*\Delta_{HAQ-DI}\right]}{1+exp\left[-5.54-0.81*\Delta_{MRSS}+0.21*\Delta_{FVC\%}-0.40*\Delta_{Pt-glob}-0.44*\Delta_{MD-glob}-3.41*\Delta_{HAQ-DI}\right]}$$

where Δ_{MRSS} indicates the change in MRSS from baseline to follow-up, Δ_{FVC} denotes the change in FVC% predicted from baseline to follow-up, $\Delta_{Pt\text{-}glob}$ indicates the change in patient global assessment, $\Delta_{MD\text{-}glob}$ denotes the change in physician global assessment, and $\Delta_{HAQ\text{-}DI}$ is the change in HAQ-DI. All changes are absolute change ($Time_2$–$Time_{baseline}$).

*= **Attributable to systemic sclerosis**

ACR CRISS

LENABASUM

Agoniste Récepteur Cannabinoïde Type 2
(Récepteur prot G)

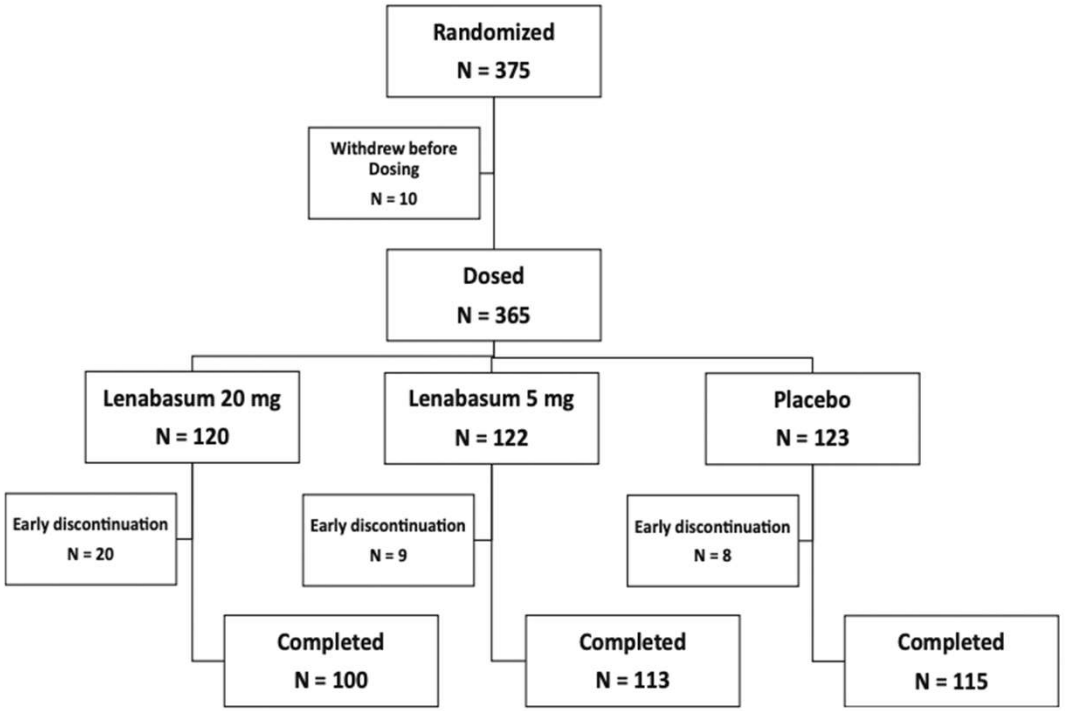
Arthritis & Rheumatology
Vol. 75, No. 9, September 2023, pp 1608–1618
DOI 10.1002/art.42510

American College of Rheumatology
Empowering Rheumatology Professionals

Efficacy and Safety of Lenabasum, a Cannabinoid Type 2 Receptor Agonist, in a Phase 3 Randomized Trial in Diffuse Cutaneous Systemic Sclerosis

Robert Spiera,[1] Masataka Kuwana,[2] Dinesh Khanna,[3] Laura Hummers,[4] Tracy M. Frech,[5] Wendy Stevens,[6] Marco Matucci-Cerinic,[7] Suzanne Kafaja,[8] Oliver Distler,[9] Jae-Bum Jun,[10] Yair Levy,[11] Piotr Leszczyński,[12] Jessica Gordon,[1] Virginia Steen,[13] Eun Bong Lee,[14] Tomasz Jankowski,[15] Irena Litinsky,[16] Lorina Chung,[17] Vivien Hsu,[18] Maureen Mayes,[19] Nora Sandorfi,[20] Robert W. Simms,[21] Stephanie Finzel,[22] Jeska de Vries-Bouwstra,[23] Scott Constantine,[24] Nancy Dgetluck,[24] Quinn Dinh,[24] Bradley J. Bloom,[24] Daniel E. Furst,[25] Barbara White,[24] and Christopher P. Denton,[26] on behalf of the RESOLVE-1 Study Group

ACR CRISS



Characteristic	Safety population (mITT population)		
	Lenabasum 20 mg (n = 120)	Lenabasum 5 mg (n = 122)	Placebo (n = 123)
Age, mean ± SD years	49.7 ± 12.87	49.7 ± 13.51	51.9 ± 12.38
Female	96 (80.0)	88 (73.3)	91 (74.0)
Race			
White	84 (70.0)	80 (66.7)	88 (71.5)
Asian	24 (20.0)	24 (20.0)	26 (21.1)
Black or African American	6 (5.0)	8 (6.7)	4 (3.3)
Multiracial, all other races	6 (5.0)	8 (6.7)	5 (4.1)
Hispanic	14 (11.7)	6 (5.0)	10 (8.1)
BMI, mean ± SD kg/m^2	25.0 ± 5.61	24.5 ± 4.96	25.1 ± 5.25
Disease duration, mean ± SD months	33.2 ± 20.32	32.6 ± 17.95	30.6 ± 17.15
Scl-70 autoantibody positive†	58 (48.3)	52 (42.8)	55 (44.7)
RNA polymerase 3 autoantibody positive†	48 (40.0)	41 (33.6)	50 (40.7)
Interstitial or restrictive lung disease‡	82 (68.3)	89 (73.0)	89 (72.4)
MRSS (0–51), mean ± SD	22.1 ± 8.55	22.0 ± 7.35	23.3 ± 8.68
Physician global assessment (0–10), mean ± SD	5.3 ± 1.46	5.4 ± 1.58	5.6 ± 1.71
Patient global assessment (0–10), mean ± SD	5.0 ± 2.10	4.8 ± 2.16	5.0 ± 2.10
HAQ DI (0–3), mean ± SD	1.12 ± 0.782	1.07 ± 0.765	1.16 ± 0.768
FVC%, mean ± SD	81.3 ± 18.83	79.5 ± 16.13	78.9 ± 15.23
Immunosuppressive/modulating therapies	107 (89.2)	94 (78.3)	103 (83.7)
Mycophenolate§	66 (54.2)	58 (47.5)	70 (56.9)
Glucocorticoids	35 (29.2)	36 (29.5)	49 (39.8)
Methotrexate	34 (28.3)	28 (22.9)	27 (21.9)
Antimalarials¶	20 (16.7)	21 (17.2)	16 (13.0)
Biologics#	13 (10.9)	8 (6.5)	10 (8.2)
Immunoglobulin	6 (4.9)	4 (3.3)	6 (4.9)
Azathioprine	5 (4.2)	4 (3.3)	3 (2.4)
Other**	2 (1.6)	1 (0.8)	2 (1.6)

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ACR CRISS

Table 2. ACR CRISS score and its core items at week 52 by cohort, mITT population, phase 3 RESOLVE-1 clinical trial*

Efficacy end point	Lenabasum 20 mg (n = 99–100)	Lenabasum 5 mg (n = 111–113)	Placebo (n = 112–115)
ACR CRISS score, median (IQR)	0.8880 (0.0610–0.9970)	0.8270 (0.0700–0.9880)	0.8870 (0.0710–0.990)
P versus placebo, ranked score, MMRM	0.4972	0.3486	
Change in MRSS, mean ± SD	−6.7 ± 6.59	−7.1 ± 6.24	−8.1 ± 7.72
P versus placebo, MMRM	0.1183	0.5036	–
Change in FVC%, mean ± SD	−1.6 ± 6.9	−2.2 ± 6.2	−1.0 ± 8.7
P versus placebo, MMRM	0.539	0.516	–
Change in HAQ DI, mean ± SD	−0.13 ± 0.44	−0.06 ± 0.39	−0.13 ± 0.47
P versus placebo, MMRM	0.745	0.322	–
Change in MDGA, mean ± SD	−1.7 ± 1.7	−1.9 ± 1.9	−1.8 ± 1.7
P versus placebo, MMRM	0.649	0.406	–
Change in PtGA, mean ± SD	−1.4 ± 2.7	−0.3 ± 2.4	−1.1 ± 2.2
P versus placebo, MMRM	0.598	0.015	–

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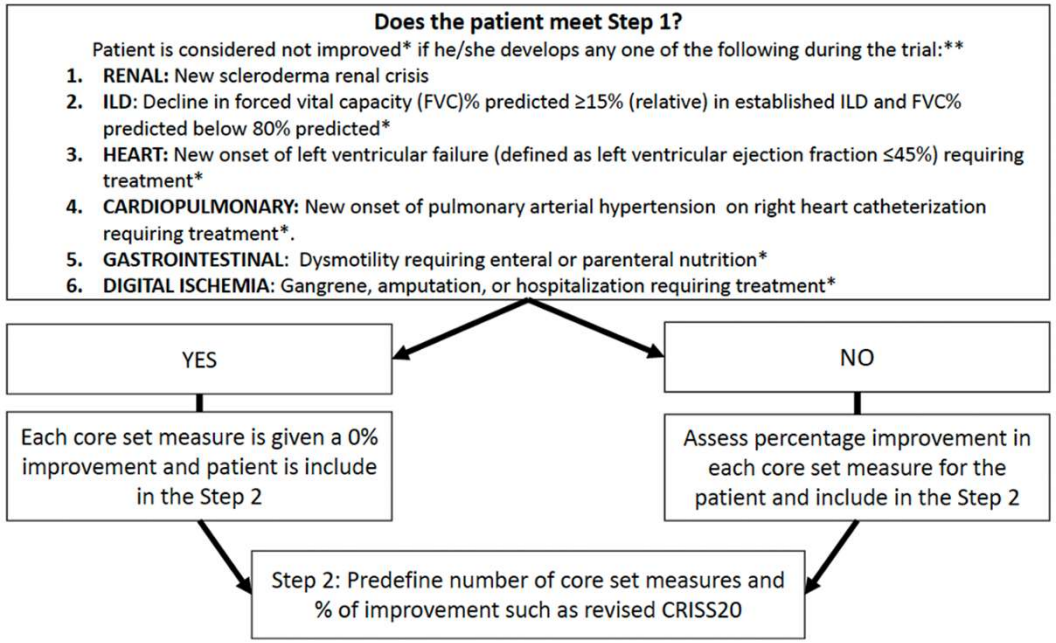
Revised CRISS

New composite endpoint in early diffuse cutaneous systemic sclerosis: revisiting the provisional American College of Rheumatology Composite Response Index in Systemic Sclerosis



*Irrespective of improvement in other core items ** Attributable to SSc

ACR 2023 - Preview

ABSTRACT NUMBER: 1699

Immunosuppression with Targeted Therapies Reduces Morbidity and Mortality in Pre-Capillary Pulmonary Hypertension Associated with Systemic Sclerosis: A EUSTAR Analysis

	ALL (n=755)	IMS no (n=377)	IMS yes (n=378)
Age, years	63 ± 11	66 ± 10	**61 ± 12**
Diffuse SSc, n (%)	223 (29)	67 (18)	**156 (41)**
Digital ulcers history, n (%)	285 (38)	146 (39)	**139 (37)**
Renal crisis history, n (%)	24 (3)	9 (2)	**15 (4)**
Muscle weakness, n (%)	120 (16)	38 (10)	**82 (22)**
Arthritis, n (%)	85 (11)	26 (7)	**60 (16)**
ILD on HRCT, n (%)	456 (60)	162 (43)	**294 (78)**
DLCO%	42 ± 15	44 ± 15	**39 ± 15**
FVC%	83 ± 23	91 ± 22	**75 ± 13**
LVEF%	60 ± 7	61 ± 6	**60 ± 7**
NYHA>2, n (%)	388 (51)	178 (47)	**210 (56)**
mPAP on RHC, mmHg	35 ± 11	35 ± 11	**35 ± 11**
Cardiac Index on RHC<2.5, n (%)	269 (36)	140 (37)	**129 (34)**
Increased BNP/NTproBNP, n (%)	516 (68)	364 (70)	**252 (67)**
6MWD<440 m, n(%)	635 (84)	318 (84)	**317 (84)**
PrecapPH profile [group 1, mild group 3, severe group 3], n (%)	299 (39) 262 (35) 194 (26)	215 (57) 123 (33) 39 (10)	**84 (22)** **139 (37)** **155 (41)**
Any csDMARD	356 (47)		**356 (94)**
Mycofelolate mofetil, n(%)	187 (25)		**187 (50)**
Any targeted therapy	68 (9)		**68 (18)**
Rituximab, n(%)	52 (7)		**52 (14)**
Tocilizuman, n(%)	21 (3)		**21 (6)**
ANY PAH medication	642 (85)	321 (85)	**321 (85)**
Follow up duration	2.9 (1.2-5.4)	2.9 (1.2-5.4)	**2.9 (1.2-5.5)**
Morbidity-Mortality, n(%)	546 (72)	261 (69)	**285 (75)**
Death, n(%)	307 (41)	148 (39)	**159 (42)**
PrecapPH worsening, n(%)	**387 (54)**	**177 (48)**	210 (58)

IMS = csDMARDS **N= 365** CTC ≥10 mg/day, CYC, MMF, AZA, MTX ou biomédicament **N=68** = abatacept, RTX, TCZ, TNFi, JAKi

WHO precapPH class =
- WHO group 1 (Absence de PID),
- mild WHO group 3 (PID– CVF ≥70%)
- severe WHO group 3 (PID and CVF< 70%).

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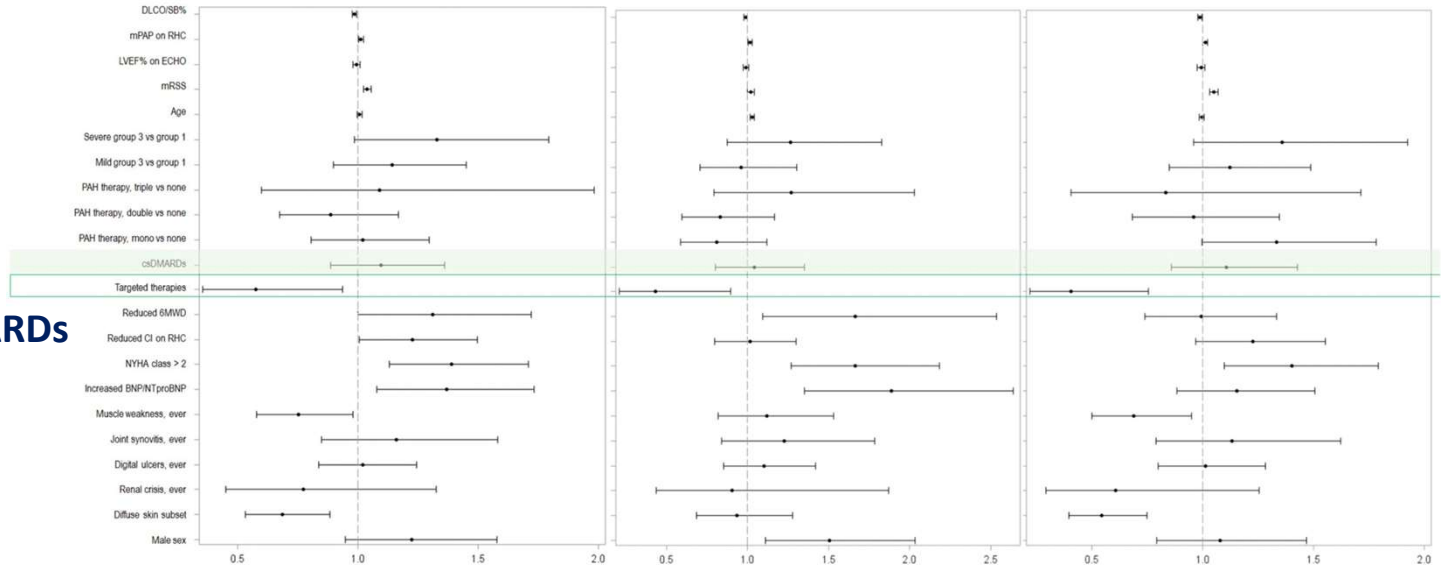
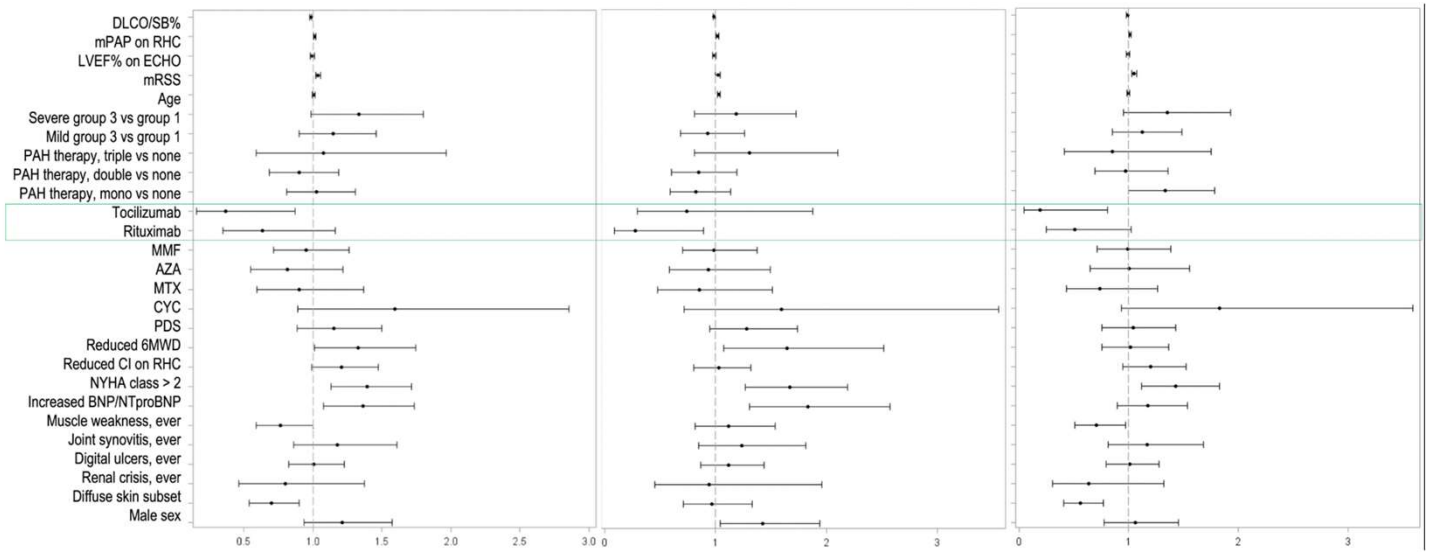
Regroupement Biothérapies vs DMARDs



Morbi-mortalité Mortalité Aggravation PH

Traitements



Bruni et al. ACR 2023

ABSTRACT NUMBER: 2595

A Randomized Controlled Trial to Compare the Efficacy and Safety of Tacrolimus with Mycophenolate Mofetil in Patients with Systemic Sclerosis – Interstitial Lung Disease (INSIST TRIAL)

Methods: single center open labelled, prospective, two-arm parallel group, randomized controlled pilot study (INSIST)

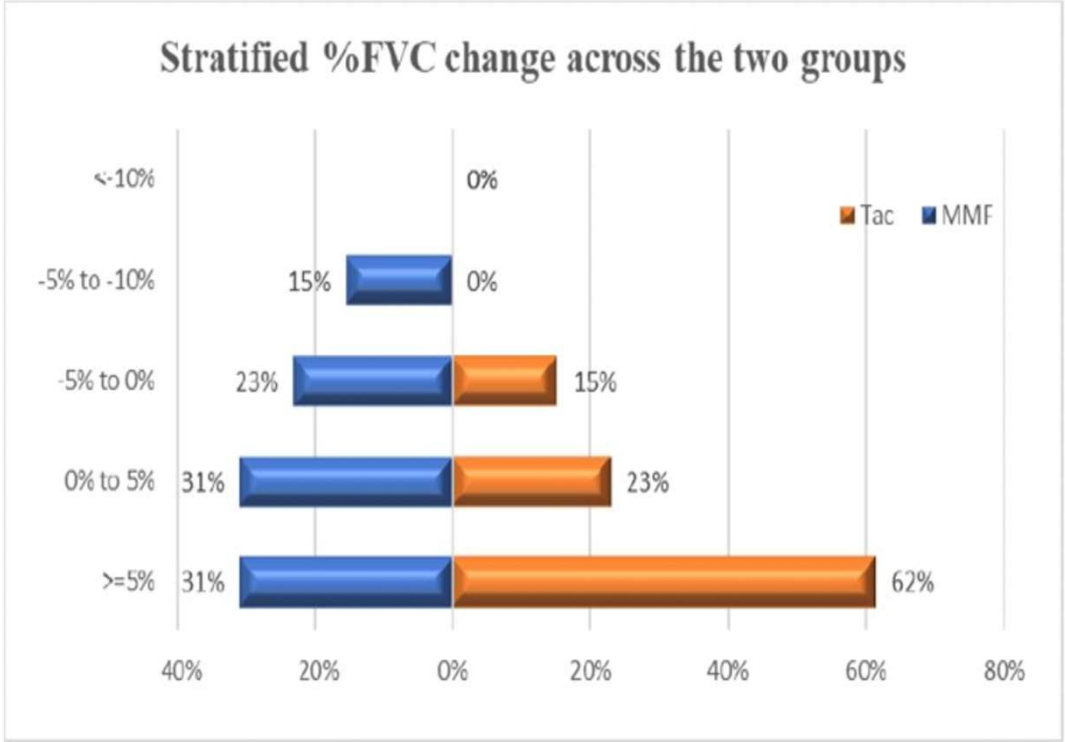
Inclusion PID-SSc (CVF decline >10%), 18-65 ans, durée de maladie < 10 ans, pas de myosite, CVF entre 40 et 85%, absence de ttt autre que CTC 10mg dans les 6 mois

Randomisation MMF (target dose 2g/j) ou tacrolimus (Max dose-0.075 mg/kg/day; target trough levels- 4- 10ng/ml) pour 24 semaines.

Primary endpoint: difference in change in FVC% at 24 weeks
Secondary outcomes: absolute change in FVC, skin scores, 6-minute walk distance, Mahler's transitional dyspnea index, ACR-CRISS and revised CRISS responses and adverse outcomes.

Khanna Sharma et al. ACR 2023

	MMF (n=13)	Tacrolimus (n=13)	P value
Change in FVC (% predicted), mean (SD)	+ 4.4 (10.6)	+ 6.92 (8.4)	Difference 2.52%, 95% CI (-10.3 to 5.18); p-0.500
Absolute change in FVC (ml), mean (SD)	+130.7 (164.6)	+176.8 (305.5)	0.636
Change in mRSS , median (IQR)	-1 (-3 to -0.5)	-1 (-1 to -0.5)	0.209
Change in 6MWD (metres), mean (SD)	63.15 (56.72)	32.67 (27.53)	0.094
Change in SGRQ score, mean (SD)	-14.83 (12.40)	-12.97 (11.78)	0.698
Focal Score TDI, median (IQR)	3 (2-4)	3 (2-4)	0.979
Change in SF-36 PCS, mean (SD)	5.59 (4.89)	4.72 (12.91)	0.823
Change in SF-36 MCS, mean (SD)	3.46 (7.86)	5.58 (5.54)	0.446
Change in PGA, median (IQR)	-2.0 (-2.5 to -1.5)	-2.0 (-2 to -1)	0.364
Change in HAQ-DI, median (IQR)	-0.23 (-0.25 to -0.19)	-0.125 (-0.25 to -0.125)	0.393
ACR-CRISS Improvement, n (%)	5 (38.5)	3 (23.1)	0.395
Revised ACR-CRISS responders; n (%)	10 (76.9)	7 (53.9)	0.416

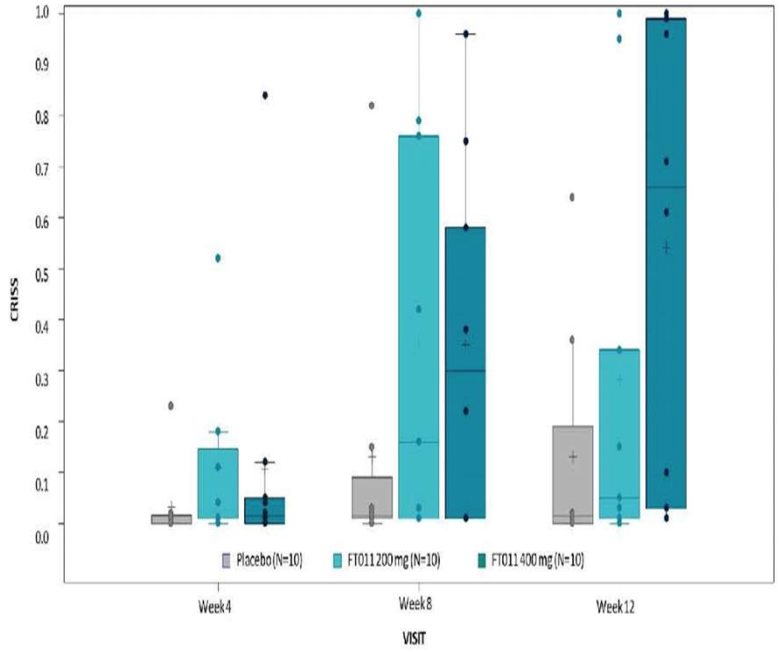


Khanna Sharma et al. ACR 2023

ABSTRACT NUMBER: 2593

FT011 for the Treatment of Systemic Sclerosis. Results from a Phase II Study

FT011= antagoniste G protein-coupled receptor 68 (GPR68)
Methods: Phase II, multi-center, randomized, double blind, placebo-controlled study of the pharmacokinetics, pharmacodynamic effects, and safety, of oral FT011 in patients with diffuse SSc (dSSc).
30 participants (n = 10/group) to placebo, FT011 200 mg or FT011 400 mg taken once daily (OD) for 12 weeks.



	Placebo	FT011 400 mg	FT011 400mg - Placebo	Nominal P-value
Parameter Visit	LS mean (95%CI)		LS Mean difference (95%CI)	
# mRSS	-1.8 (-4.57, 0.97)	-3.25 (-5.87, -0.62)	-1.45 (-5.27, 2.38)	0.443
‡ % Predicted FVC	-1.64 (-5.49, 2.21)	4.9 (1.23, 8.56)	6.54 (1.23, 11.85)	0.018
# SHAQ-DI	0.0273 (-0.145, 0.200)	-0.2636 (-0.428, -0.100)	-0.291 (-0.529, -0.053)	0.019
‡ Patient Global Assessment	8.14 (-5.60, 21.88)	9.03 (-3.70, 21.76)	0.89 (-18.01, 19.79)	0.924
# Physician Global Assessment	-4.83 (-19.52, 9.86)	-28.19 (-41.29, -15.10)	-23.36 (-43.03, -3.69)	0.022

Denton et al. ACR 2023

Essais en cours / en préparation

Essai en cours

JAK inhibitor

JAK inhibitors and systemic sclerosis: A systematic review of the literature

Clothilde Moriana [a], Thomas Moulinet [a,b], Roland Jaussaud [a], Paul Decker [a,*]

	Total ($N = 38$) % (n/N) or mean ± SD or median [IQR]	Early SSc ($N = 19$) % (n/N) or mean ± SD or median [IQR]	Late SSc ($N = 19$) % (n/N) or mean ± SD or median [IQR]
Diffuse SSc	93 (25/27)*	100 (13/13)†	86 (12/14)‡
Female sex	74 (28/38)	80 (15/19)	68 (13/19)
Age at inclusion (years)	47 ± 14	40 ± 12	53 ± 13
Disease duration at inclusion (months)	35 [15–55]	15 [12–21]	54 [42–78]
Cutaneous response	84 (32/38)	84 (16/19)	84 (16/19)†
mRSS at inclusion	25.9 ± 10.0	27.2 ± 9.4	24.5 ± 10.8
Δ mRSS before and after JAKi	−10.6 ± 5.0	−11.4 ± 5.2	−9.7 ± 4.8
FVC at inclusion (% predicted value)	77 [71–81]	75 [70.5–80]	78 [70.5–83]
Δ FVC before and after JAKi (% predicted value)	−2.2 ± 3.1	−2.7 ± 2.9	−1.7 ± 3.3
CRP level at inclusion (mg/L)	7.7 [2.4–11.6]	8.8 [3.4–12.2]	5.8 [1.7–11.2]
Δ CRP level before and after JAKi (mg/L)	−2.5 [−5.7–0.6]	−3.3 [−9.3–0.4]	−1.8 [−2.9–0.8]

	Total ($N = 59$) % (n/N) or mean ± SD or median [IQR]	« Naïve » SSc ($N = 35$) % (n/N) or mean ± SD or median [IQR]	Refractory SSc ($N = 24$) % (n/N) or mean ± SD or median [IQR]
Diffuse SSc	93 (26/28)*	100 (13/13)†	87 (13/15)‡
Female sex	74 (29/39)*	87 (13/15)†	67 (16/24)
Age at inclusion (years)	46 ± 15	45 ± 15†	46 ± 15
Disease duration at inclusion (months)	35 [15–55]	21 [15–44]†	36 [15–60]
Cutaneous response	90 (53/59)	97 (34/35)	79 (19/24)‡
mRSS at inclusion	26.2 ± 10.1	28.3 ± 8.0	24.9 ± 11.3
Δ mRSS before and after JAKi	−10 [−14.5 to −7]	−14 [−15 to −10]	−8.5 [−13 to −4]
FVC at inclusion (% predicted value)	77 [71–81]	76 [71–79.5]	81 [64–91]
Δ FVC before and after JAKi (% predicted value)	−1 [−4.3–0]	−2 [−4.5–0]	0 [−5–0]
CRP level at inclusion (mg/L)	6.8 [2.5–11.6]	8.2 [4.9–16.8]†	2.8 [0.9–11.6]
Δ CRP level before and after JAKi (mg/L)	−2.5 [−5.7–0.6]	−2.8 [−6.8–0]†	0.4 [−6.5–0.9]

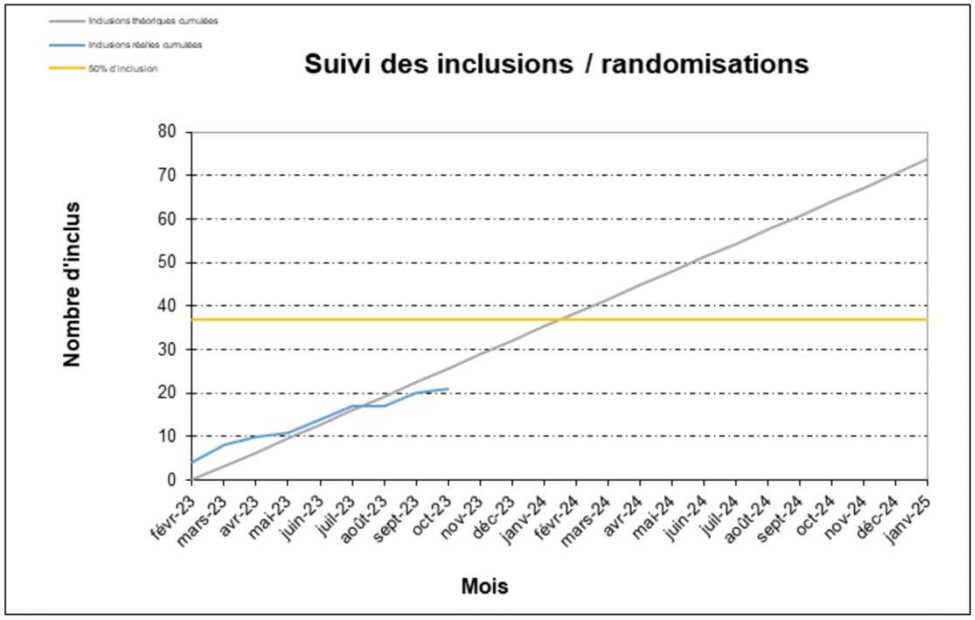
P.H.R.C. national 2018

Etude SCLERITA

Investigateur principal: Dr. Benjamin Chaigne
Responsable scientifique: Pr. Luc Mouthon

Inhibiteur de JAK 1-3 dans la sclérodermie systémique

- **Nom du protocole** : Tolérance et efficacité de l'itacitinib (JAK1-3) dans la sclérodermie systémique (ScS): une étude de phase II, randomisée, contrôlée, *vs* placebo,
- **Design :** essai clinique, multicentrique, contrôlé, randomisé, *vs* placebo, réalisé en double-aveugle comparant l'itacitinib à un placebo dans le traitement de la ScS
- **Critères d'inclusion** :
  - ScS ACR/EULAR 2013
  - Durée d'évolution ≤ 5 ans ou active selon le score d'activité EUSTAR
  - Score cutané modifié de Rodnan (mRSS) ≥ 10 et ≤ 35
- **Intervention :** itacitinib 200mg/J per os *vs* placebo (**en add-on**)
- **Critère de jugement principal** : mRSS à 360 jours
- **Nombre de patients à inclure** : 74 patients (37 dans chaque groupe)
- **Statut de l'étude** :
  - Etude ouverte depuis le 2 février 2023
  - 21 patients inclus/randomisés



P.H.R.C. national 2020

Etude SCLERIJAK-2

Investigateur principal: Dr. Benjamin Chaigne
Responsable scientifique: Pr. Luc Mouthon

Inhibiteur de JAK 2 dans la sclérodermie systémique

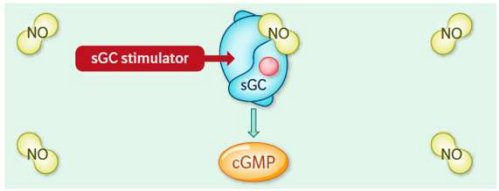
- **Nom du protocole** : Tolérance et efficacité du baricitinib (JAK2) dans la sclérodermie systémique (ScS): une étude de phase II, randomisée, contrôlée, *vs* placebo,
- **Design :** essai clinique, multicentrique, contrôlé, randomisé, *vs* placebo, réalisé en double-aveugle comparant le baricitinib à un placebo dans le traitement de la ScS
- **Critères d'inclusion** :
  - ScS ACR/EULAR 2013
  - Durée d'évolution ≤ 5 ans ou active selon le score d'activité EUSTAR
  - Score cutané modifié de Rodnan (mRSS) ≥ 10 et ≤ 35
- **Intervention :** baricitinib per os *vs* placebo (**en add-on**)
- **Critère de jugement principal** : mRSS à 360 jours
- **Nombre de patients à inclure** : 74 patients (37 dans chaque groupe)
- **Statut de l'étude** :
  - Soumission au CPP et ANSM en préparation

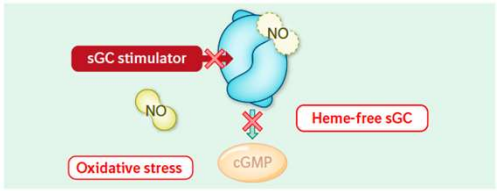
Pour participer et devenir centre :

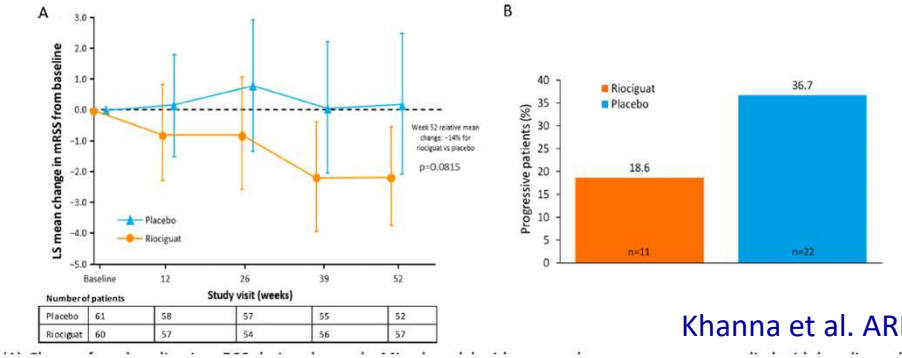
benjamin.chaigne@aphp.fr

Essais en cours

Soluble guanylate cyclase: BI 1366031







Khanna et al. ARD 2020

RCT multicentrique mondial
Phase II
Objectifs 200 patients
CJI: CVF
Fin d'étude: 2024

Country	Screened	Randomized	Screen failed	In treatment
Australia	1	0	1	0
Belgium	1	1	0	1
China	10*	1	9**	1
Italy	2	0	1	0
Japan	5	1	2	1
Korea	10*	6	4**	5
Malaysia	1	0	0	0
Philippines	2*	0	1	0
Poland	5	2	2	2
Romania	2	0	1	0
Singapore	1	1	0	1
Spain	4*	0	4**	0
Thailand	2	1	1	1
United States	1	0	0	0
Total	**47***	**13**	**26****	**12**

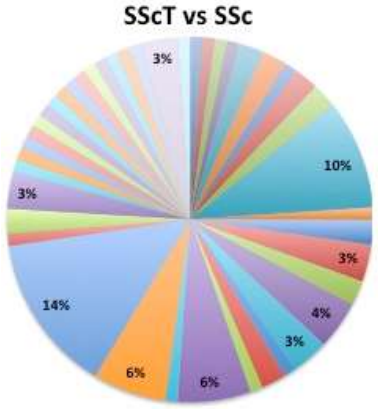
Essais en cours

Phase II
ACR-CRISS

MT-7117: dersimelagon
Agoniste oral selectif du récepteur de la melanocortine 1

	Mean (SD) or n (%)			
	Overall	North America*	Europe†	Poland
Number	73 (100 %)	17 (23.3 %)	30 (41.1 %)	26 (35.6 %)
Age (yrs)	51.6 ± 12.4	54.7 ± 12.5	52.2 ± 10.6	48.9 ± 14.2
Disease duration (yrs)	2.0 ± 1.4	1.7 ± 1.4	1.9 ± 1.3	2.2 ± 1.6
Female	55 (75.3 %)	15 (88.2 %)	22 (73.3 %)	18 (69.2 %)
White	65 (89.0 %)	11 (64.7 %)	28 (93.3 %)	26 (100 %)
Anti-RNA-Poly III positive	15 (20.5 %)	4 (23.5 %)	7 (23.3 %)	4 (15.4 %)
Anti- Scl-70 positive	37 (50.7 %)	4 (23.5 %)	16 (53.3 %)	17 (65.4 %)
Normal CRP (≤ 5.0 mg/L)	58 (79.5 %)	13 (76.5 %)	22 (73.3 %)	23 (88.5 %)
Any immunosuppressant‡	41 (56.2 %)	10 (58.8 %)	17 (56.7 %)	14 (53.8 %)
MMF	24 (32.9 %)	7 (41.2 %)	9 (30.0 %)	8 (30.8 %)
MTX	14 (19.2 %)	1 (5.9 %)	7 (23.3 %)	6 (23.1 %)
HCQ	7 (9.6 %)	1 (5.9 %)	4 (13.3 %)	2 (7.7 %)
AZA	2 (2.7 %)	1 (5.9 %)	1 (3.3 %)	0
mRSS (0-51)	24.8 ± 7.9	23.1 ± 9.2	25.3 ± 7.9	25.2 ± 7.2
FVC% predicted	88.0 ± 17.9	88.7 ± 20.2	82.0 ± 16.9	94.4 ± 15.5

En préparation



- **Anti-TGF:** phase I et phase II
- **Anifrolumab:** phase III – Etude Daisy
- **CCL24 (eotaxin-2):** CM101 – phase II

En préparation

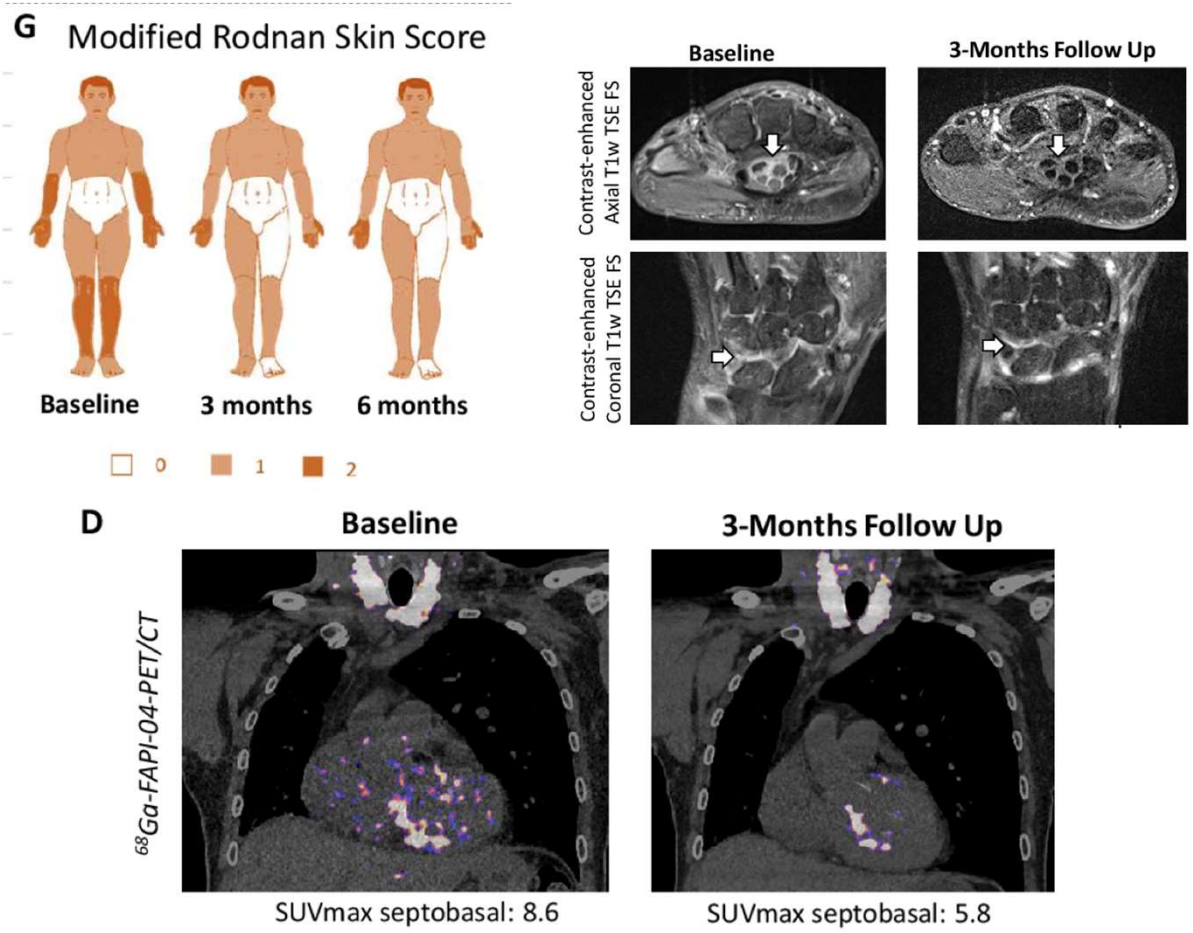
- **Disparition des anti-RP11 dès 3 mois (persistant à 6 mois)**
- **Diminution du mRSS:**

  24 vs 19 à 3 et 6 mois
- **Stabilisation de la PID à 6 mois:**

  Stabilité de la CVF (72%)

  Amélioration de la DLCO (49/52/59)
- **Pas d'aggravation de l'ETT**
- **Amélioration de l'inflammation articulaire**
- **Diminution de la fibrose intracardiaque**

CD19 CAR T



Bergmann et al. ARD 2023
Bergmann et al. ACR 2023

Conclusion

- **Des essais positifs**
- **Le retour du rituximab et des anti-B à confirmer**
- **Bithérapies: lesquelles et quand ?**
- **Beaucoup d'essais en cours et à venir**

=> Tout patient avec une forme diffuse peut vraisemblablement être inclus dans une étude de biomédicament

Merci pour votre attention !

Benjamin Chaigne

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Centre de Référence Vascularites nécrosantes et sclérodermie systémique

Assistance publique-Hôpitaux de Paris, Paris

Université Paris Descartes, Inserm U1016, Institut Cochin, Paris

Merci!
French Systemic Sclerosis Network!

Abdoul H, Agard C, Alix A, Allanore Y, Amoura Z, Andre M, Aouba A, Avouac J, Balquet MH, Barnetche T, Baudet A, Beclin A, Bellino A, Benhamou Y, Bense A, Benyamine A, Berezne A, Berthier S, Berthier S, Bertrand NM, Bienvenu B, Bonnotte B, Braun J, Cacoub P, Casadevall M, Cazalets C, Chatelus E, Chauveau-Jouve P, Clarke A, Clomenil M, Cohen P, Comarmond C, Constans J, Costedoat-Chalumeau N, Cottin V, Couderc LJ, Coutte L, Daste C, de Boysson H, De Moreuil C, Decanter L, Decker P, Desblache J, Dhote R, Dion J, Diot E, Dufour, E, Dunogue B, Duhaut P, Durant C, Durel M, Ebbo M, Fain O, Farge D, Farrines Raffoul C, Fauchais AL, Forbien S, Godeau B, Godard D, Goulenok T, Granel B, Grange C, Grange L, Guerin C, Guilpain P, Guillevin L, Hachulla E, Harle JR, Hot A, Imbert B, Jardin A, Kahn JE, Kanagaratnam A, Kardaoui H, Keraen J, Kieffer P, Lafitte B, Lambert N, Launay D, Lavigne C, Lecureur V, Le Gouellec N, Le Jeunne C, Lega JC, Legendre P, Lequellec A, Lescoat A, Lidove O, Lifermann F, Limal N, Liozon E, Lok C, London J, Machelard I, Magy-Bertrand, Maillet F, Malki E, Maria A, Martin K, Martin M, Martin T, Martins P, Martis N, Maurier F, Mékinian A, Mizzi Z, Mouthon L, Mugnier S, NGuyen C, Oukaci L, Palat S, Pennaforte JL, Perer A, Pestre V, Pique JB, Porcher R, Pugnet G, Quemeneur T, Queyrel V, Regent A, Renaud A, Richard ME, Riche A, Rivière S, Rodero M, Roriz M, Schleinitz N, Senet P, Servettaz A, Smets P, Terrier B, Thoreau B, Tieu A, Tieulie N, Truchetet ME, Uzunhan Y, Wahl D.

Et tous les autres que nous aurions oubliés ….

Appels à observations en cours

- SCLEROTRANSPLANT : Transplantation cardiaque en traitement de l'atteinte cardiaque primitive de la sclérodermie systémique en France
Contacts: Dr. Arthur Renaud arthur.renaud49@gmail.com et Pr. Christian Agard christian.agard@chu-nantes.fr

- SCLEROJAKI : Etude non interventionnelle sur données pré-existantes pour évaluer l'efficacité des inhibiteurs de JAK au cours des PID associées à la sclérodermie systémique
Contact: Dr. Paul Decker p.decker@chru-nancy.fr

- SCLEROVID: Exacerbation aiguë de fibrose pulmonaire contemporaine / dans les suites d'une infection à SARS-CoV-2 au cours de la sclérodermie systémique: étude rétrospective française
Contact: Dr. Benjamin Thoreau benjamin.thoreau@aphp.fr

- SCLEROTOX : État des lieux de la prise en charge des patients développant une sclérodermie systémique de novo sous immunothérapie anti-cancéreuse
Contact : Dr. Benjamin Chaigne benjamin.chaigne@aphp.fr

- SCLEROANTIFIBROTIC: Etude nationale multicentrique sur l'utilisation des antifibrosants en vie réelle dans la pneumopathie interstitielle diffuse liée à la sclérodermie systémique
Contacts: Pr. David Launay, Pr. Yurdagul Uzunhan, Dr Vincent Koether, david.launay@chru-lille.fr;yurdagul.uzunhan@aphp.fr; vincent.koether@univ-lille.fr

- MYCRISS : Evaluation de l'association rituximab-mycophenolate mofetil dans la sclérodermie systémique : une étude rétrospective Française multicentrique
Contacts: Dr François Barde et Dr. Benjamin Chaigne : francois.barde@aphp.fr; benjamin.chaigne@aphp.fr