Που θα χρησιμοποιησουμε τα Jakinibs τα επομενα χρονια

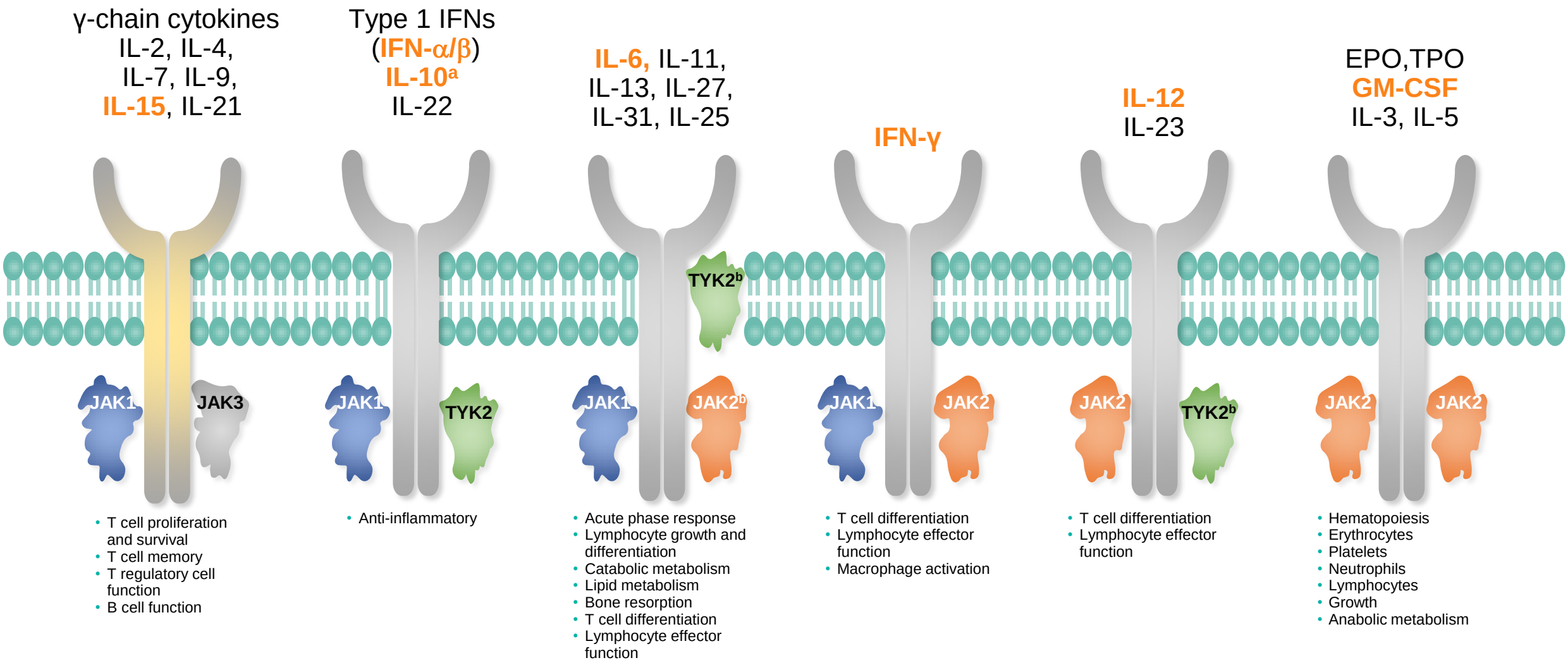
Ρεθυμνο, Σεπτ 2025

Δαούσης Δημήτρης
Αναπλ. καθηγητής Παθολογίας/Ρευματολογίας
Προεδρος Ελληνικης Ρευματολογικης Εταιρειας

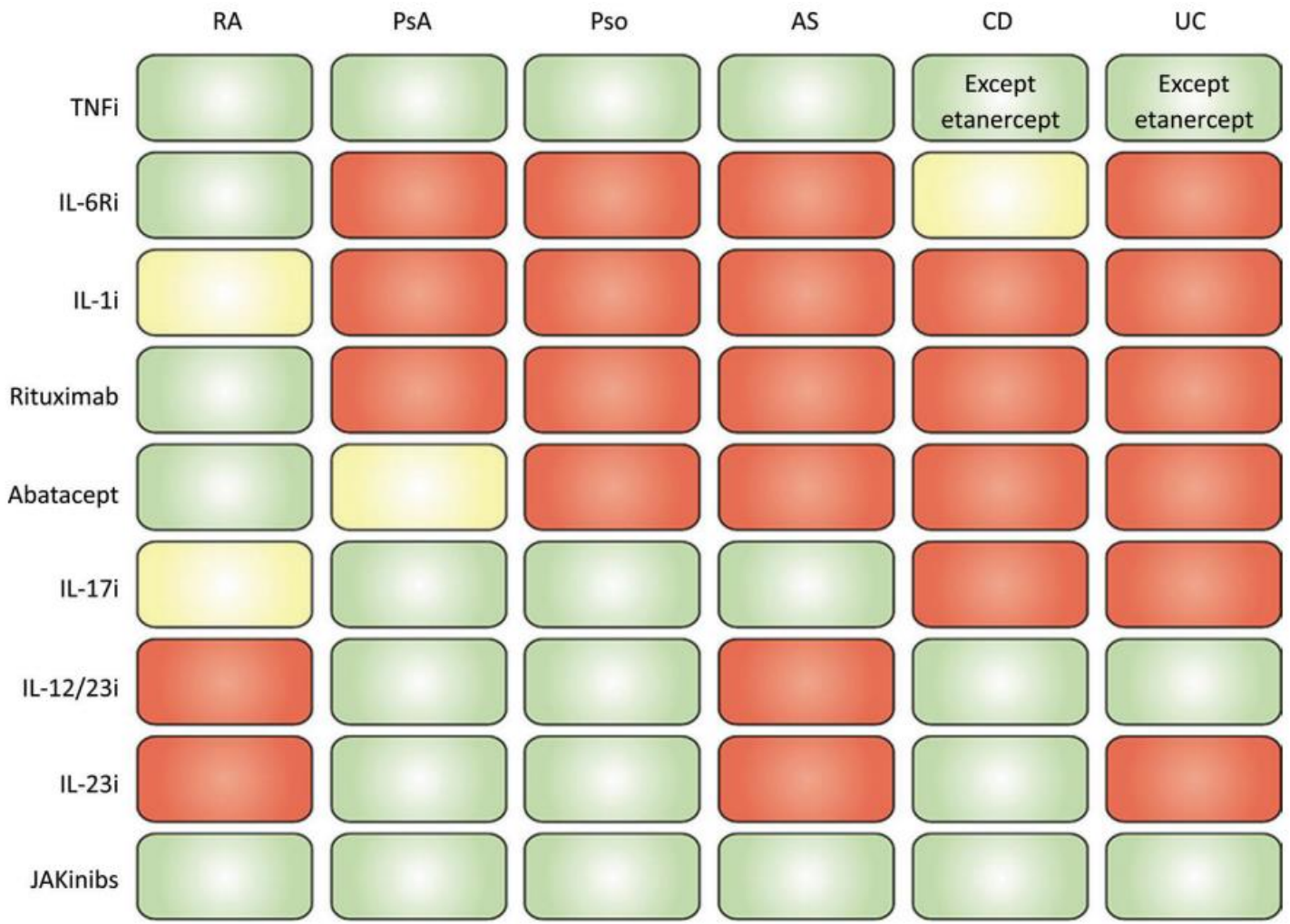
Σύγκρουση συμφερόντων

- Τιμητική αμοιβή για ομιλίες και συμμετοχή σε advisory boards από τις εταιρείες UCB, Pfizer, Novartis, BMS, MSD, Janssen, Abbvie,Lilly, Aenorasis, Boehringer, Astra Zeneca, GSK

57 κυτταροκίνες σηματοδοτούν μέσω JAK….



Μεγαλο ευρος ενδειξεων....



Alopecia areata	Ruxolitinib	JAK1/JAK2	Topical	Phase II
	Tofacitinib	JAK1/JAK3	Topical	Phase II
	Ifidancitinib	JAK1/JAK3	Topical	Phase II
Atopic dermatitis	Ruxolitinib	JAK1/JAK2	Topical	Phase III
			Topical	Phase III
			Topical	Phase I (paediatric)
			Topical	Phase I
	Delgocitinib	Pan-JAK	Topical	Phase II
			Topical	Phase I
	Tofacitinib	JAK1/JAK3	Topical	Phase II
	Brepocitinib	JAK1/TYK2	Topical	Phase II
	Ifidancitinib	JAK1/JAK3	Topical	Phase II
Chronic hand eczema	Delgocitinib	Pan-JAK	Topical	Phase III
			Topical	Phase III
			Topical	Phase II
Cutaneous GVHD	Ruxolitinib	JAK1/JAK2	Topical	Phase II
			Topical	Phase II
Discoid lupus erythematosus	Delgocitinib	Pan-JAK	Topical	Phase II
Healthy	PF-06263726	Pan-JAK	Topical	Phase I
Hidradenitis suppurativa	Ruxolitinib	JAK1/JAK2	Topical	Phase II
Lichen planus	Ruxolitinib	JAK1/JAK2	Topical	Phase II
Necrobiosis lipoidica	Ruxolitinib	JAK1/JAK2	Topical	Phase II
Psoriasis	Ruxolitinib	JAK1/JAK2	Topical	Phase II
			Topical	Phase II
			Topical	Phase II
	Tofacitinib	JAK1/JAK3	Topical	Phase II
			Topical	Phase II
			Topical	Phase II
			Topical	Phase I
	PF-06700841	JAK1/TYK2	Topical	Phase II
Vitiligo	Ruxolitinib	JAK1/JAK2	Topical	Phase III
			Topical	Phase III
			Topical	Phase III
			Topical	Phase II
			Topical	Phase II

GVHD, graft-versus-host disease; JAK, Janus kinase; JAKinibs, JAK-inhibitors.

frontiers | Frontiers in Medicine

SYSTEMATIC REVIEW
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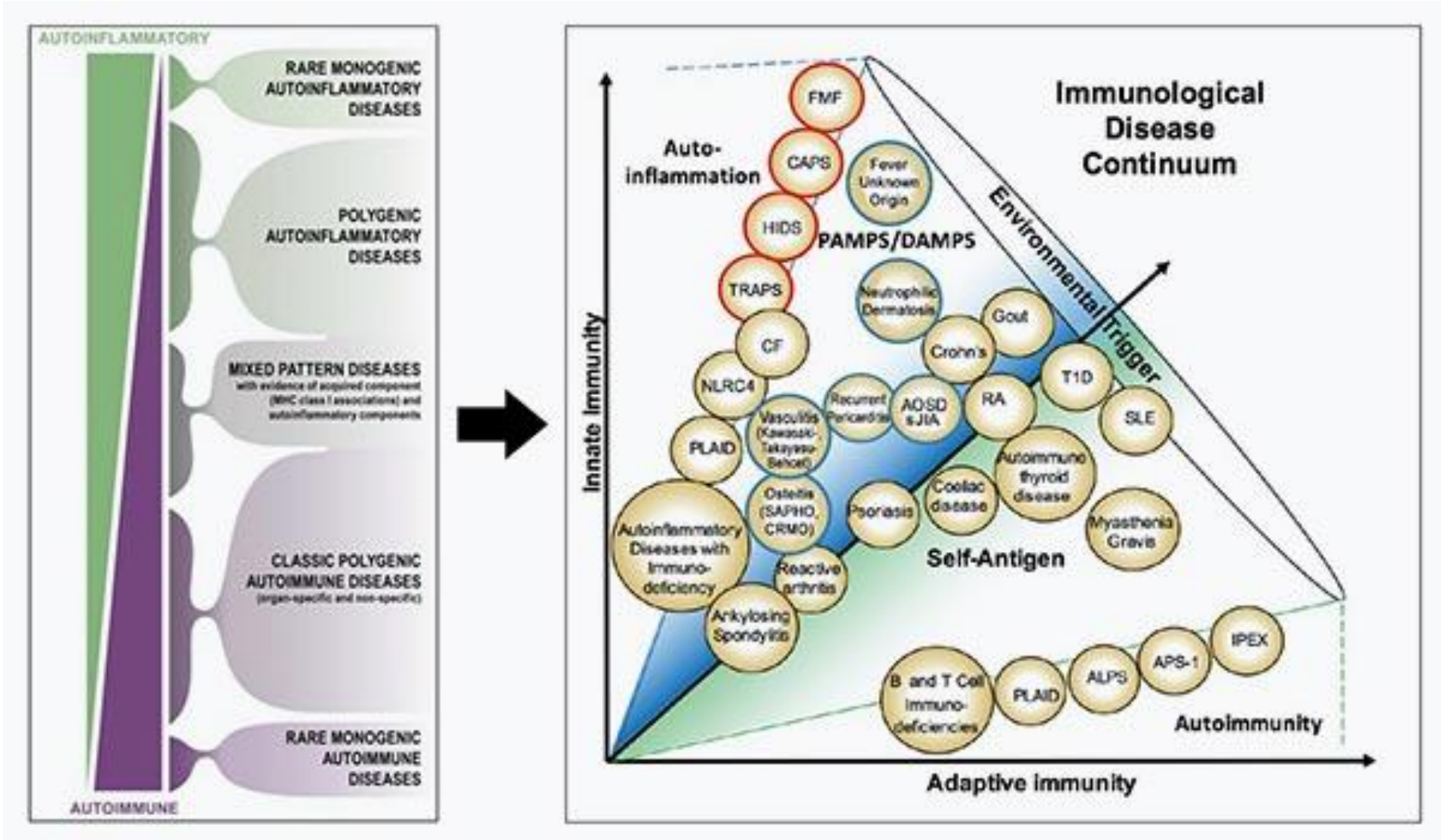
Effectiveness and Safety of JAK Inhibitors in Autoinflammatory Diseases: A Systematic Review

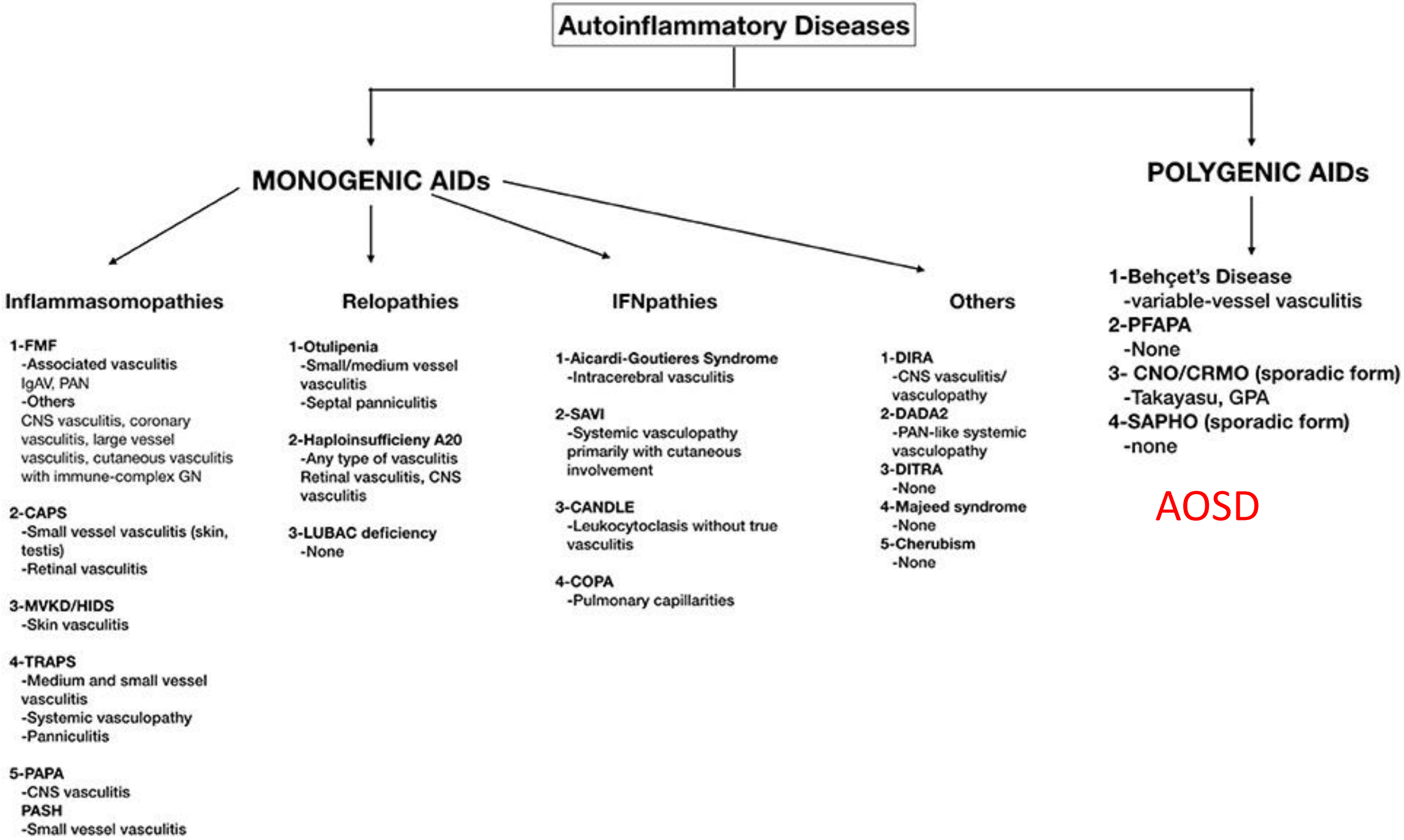
Zhivana Boyadzhieva[1], Nikolas Ruffer[2], Gerd Burmester[1], Anne Pankow[1†] and Martin Krusche[2†]*

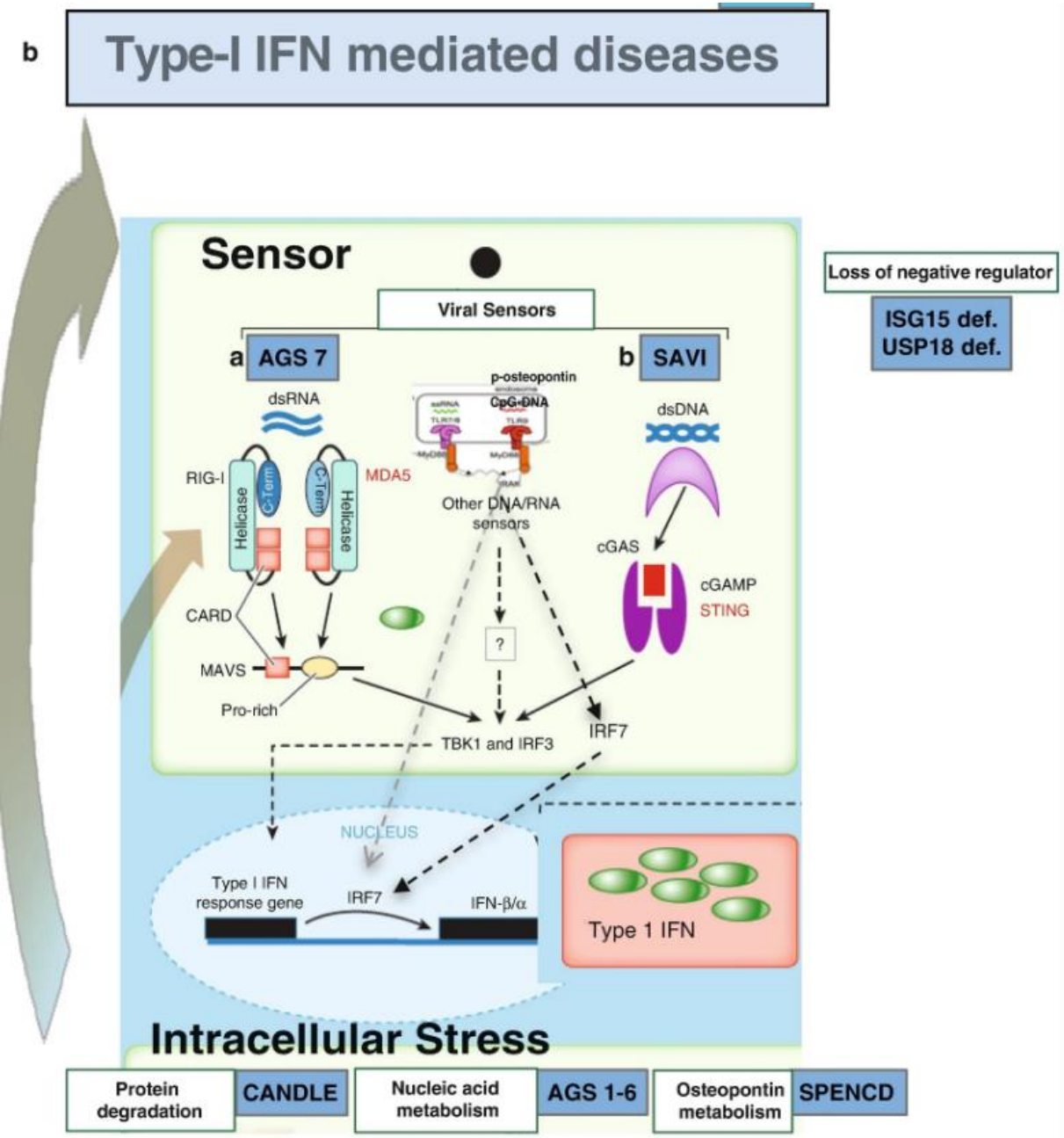
Clinical Reviews in Allergy & Immunology (2020) 59:334–351
https://doi.org/10.1007/s12016-020-08786-6

JAK Inhibitors: Prospects in Connective Tissue Diseases

Hanxiao You[1] · Dong Xu[1] · Jiuliang Zhao[1] · Jing Li[1] · Qian Wang[1] · Xinping Tian[1] · Mengtao Li[1] · Xiaofeng Zeng[1]




Autoinflammatory Diseases
MONOGENIC AIDs
POLYGENIC AIDs
Inflammasomopathies
1-FMF
-Associated vasculitis
IgAV, PAN
-Others
CNS vasculitis, coronary vasculitis, large vessel vasculitis, cutaneous vasculitis with immune-complex GN
2-CAPS
-Small vessel vasculitis (skin, testis)
-Retinal vasculitis
3-MVKD/HIDS
-Skin vasculitis
4-TRAPS
-Medium and small vessel vasculitis
-Systemic vasculopathy
-Panniculitis
5-PAPA
-CNS vasculitis
PASH
-Small vessel vasculitis
Relopathies
1-Otulipenia
-Small/medium vessel vasculitis
-Septal panniculitis
2-Haploinsufficieny A20
-Any type of vasculitis
Retinal vasculitis, CNS vasculitis
3-LUBAC deficiency
-None
IFNpathies
1-Aicardi-Goutieres Syndrome
-Intracerebral vasculitis
2-SAVI
-Systemic vasculopathy primarily with cutaneous involvement
3-CANDLE
-Leukocytoclasis without true vasculitis
4-COPA
-Pulmonary capillarities
Others
1-DIRA
-CNS vasculitis/ vasculopathy
2-DADA2
-PAN-like systemic vasculopathy
3-DITRA
-None
4-Majeed syndrome
-None
5-Cherubism
-None
1-Behçet's Disease
-variable-vessel vasculitis
2-PFAPA
-None
3- CNO/CRMO (sporadic form)
-Takayasu, GPA
4-SAPHO (sporadic form)
-none
AOSD



DIAGNOSIS

The manifestation of specific interferonopathies is presented below (see 'Selected interferonopathies' below). In general, an interferonopathy should be considered in patients presenting with manifestations including the following:

- Persistent systemic inflammation with fever, reflecting the role of type I IFNs as endogenous pyrogens.
- Cutaneous small-vessel vasculitis with acral localization (fingers, toes, ears, nose, cheeks). Initial lesions can resemble chilblains (see "Pernio (chilblains)"). The localization appears to reflect exacerbation of inflammation by cool temperatures.
- Basal ganglia calcifications resembling those observed in in utero infection with TORCH organisms (Toxoplasmosis, Other [syphilis], Rubella, Cytomegalovirus [CMV], Herpes simplex virus). These calcifications can cause seizures or neurocognitive impairment but may also be asymptomatic.
- Unexplained recurrent inflammation affecting the lung, colon, and/or skin.
- Poor response of clinical manifestations to interleukin (IL) 1 inhibition.

Jakinibs in autoinflammatory diseases…

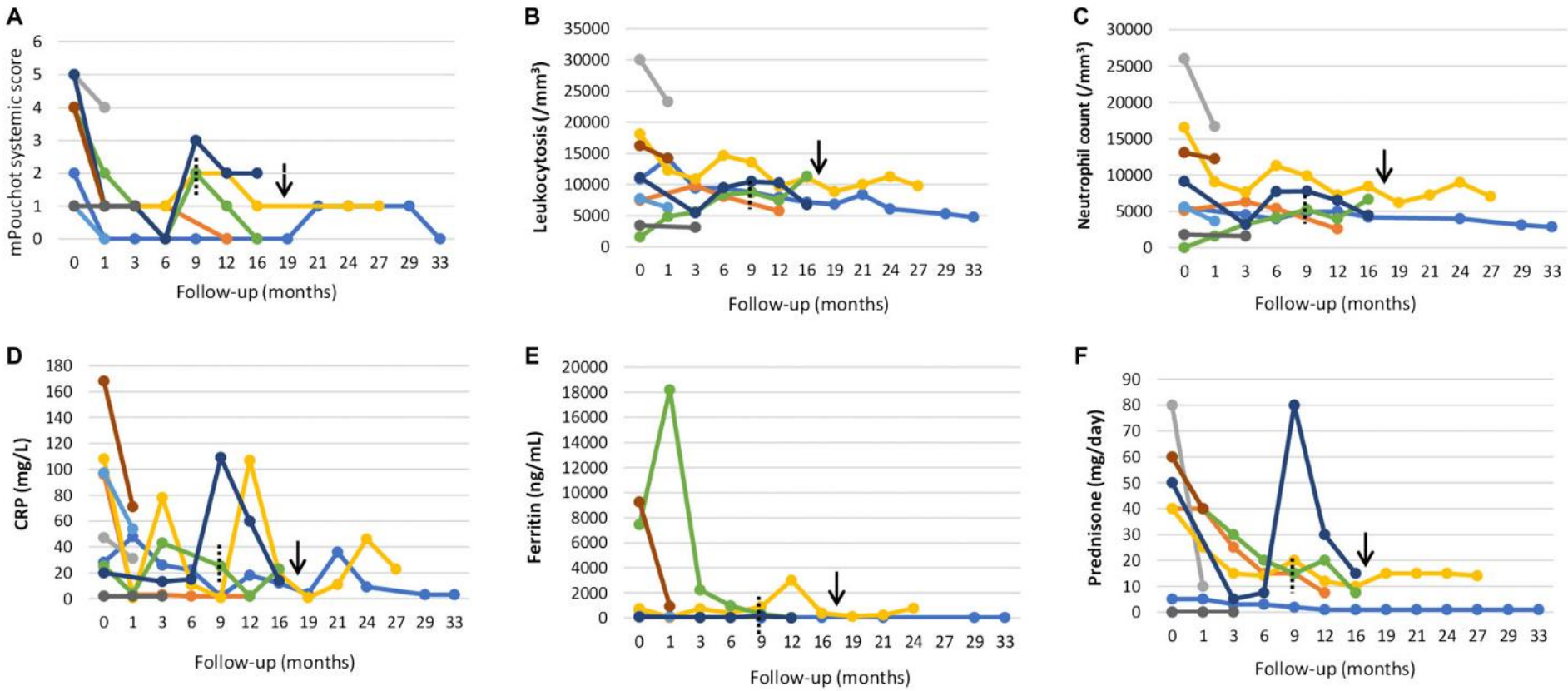
TABLE 2 | Overview of adverse events.

Disease	CANDLE	SAVI	AGS	Other type I interferonopathies	AOSD	sJIA	FMF	BS	Total
Number of patients treated	14	28	3	7	26	4	6	13	101
Adverse events—*n**	26	17	1	9	4	0	0	2	59
JAKi dose reduction	–	2	–	–	–	–	–	–	2
JAKi discontinuation	1	2	–	–	1	–	–	2	6
requiring hospitalization	3	4	–	2	–	–	–	–	9
Deaths	–	4**	–	–	1***	–	–	–	5
Types of adverse events									

Clinical science

JAK inhibitors in difficult-to-treat adult-onset Still's disease and systemic-onset juvenile idiopathic arthritis

Louise Gillard[1], Jacques Pouchot[2], Fleur Cohen-Aubart[3], Isabelle Koné-Paut [4,5], Gaël Mouterde[6], Martin Michaud[7], Héloïse Reumaux[8], Léa Savey[9], Alexandre Belot [10,11,12], Bruno Fautrel[1,5,13,†] and Stéphane Mitrovic [1,5,14,†,*]; on behalf of the CRI (Club Rhumatismes et Inflammation)



Jakinibs in CTDs. Dermatomyositis

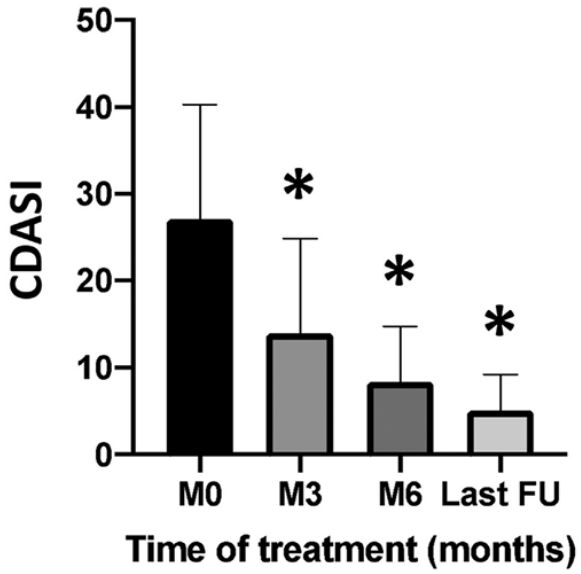
https://doi.org/10.1016/j.jaad.2022.10.054

JAK inhibitors for the treatment of adult dermatomyositis: A pilot study

Table I. Characteristics of patients with dermatomyositis at baseline and treatment response to JAK inhibitor at 3-month

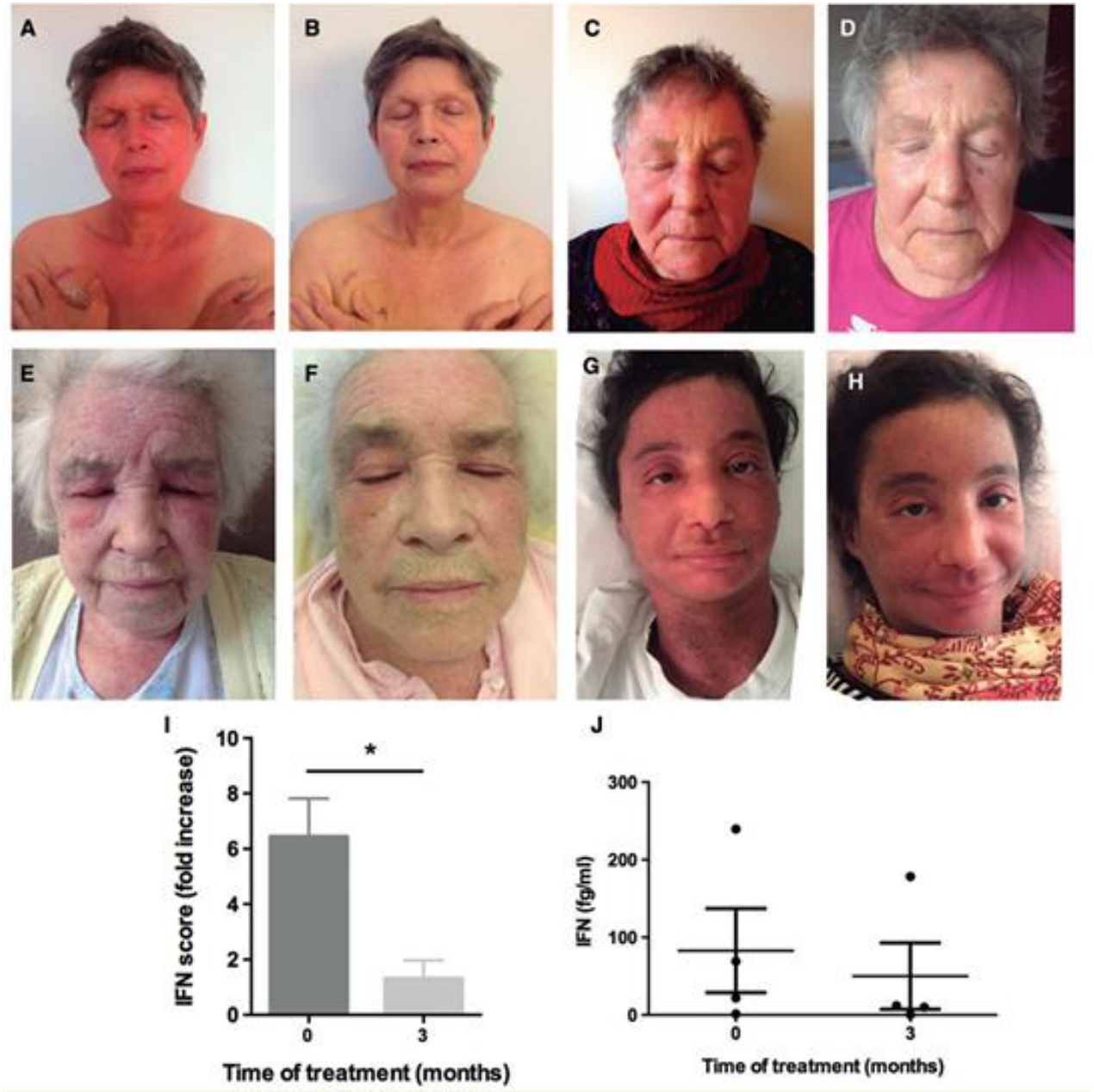
Patients	Age (yrs)	Sex	Disease duration (yrs)	Myositis-specific antibody	Previous treatment	JAKinh Molecule, dose (mg/day)	CDASI activity		IFN-α (fg/mL)		MMT8		CK level (IU/L)	
							Baseline	M3	Baseline	M3	Baseline	M3	Baseline	M3
1	59	F	5	Anti-TIF1γ	CS, HCQ, IVIg, PLEX, MTX, AZA	Ruxolitinib, 30	26	15	68 ± 19	23 ± 4	145	145	65	183
2	79	F	4	Anti-SAE	CS, MTX, IVIg, MMF	Ruxolitinib, 30	27	7	18 ± 3	12 ± NA	150	148	79	181
3	84	F	1	Anti-TIF1γ	CS, MTX, AZA, IVIg	Ruxolitinib, 20	44	14	NA	NA	NA	NA	2559	226
4	29	F	4	Anti-TIF1γ	CS, HCQ, MTX, AZA, MMF, IVIg	Ruxolitinib, 20	49	30	144 ± 12	62 ± 3	131	143	49	40
5	61	F	7	Anti-TIF1γ	CS, MTX, AZA, MMF, IVIg, RTX, TAC	Baricitinib, 2	49	39	48 ± 13	92 ± 4	146	144	110	219
6	50	F	37	Seronegative	CS, MTX, MMF, IVIg, Cic	Baricitinib, 4	30	22	NA	NA	150	146	172	236
7	75	F	14	Seronegative	CS, HCQ, MTX, AZA, IVIg, RTX	Baricitinib, 2	29	17	221 ± 15	59 ± NA	69	93	110	89
8	56	F	6	Anti-SAE	CS, HCQ, MTX, AZA, IVIg, RTX	Baricitinib, 2	34	11	19 ± 5	4 ± 1	131	145	56	67
9	57	F	1	Anti-TIF1γ	CS, HCQ, MTX, IVIg	Baricitinib, 4	10	7	8 ± 0	3 ± 3	150	150	NA	97
10	38	F	4	Seronegative	CS, HCQ, AZA, MMF, IVIg	Baricitinib, 4	17	1	NA	NA	150	150	NA	NA
11	30	M	8	Seronegative	CS, MTX, AZA, MMF, IVIg, RTX	Baricitinib, 4	5	NA	NA	NA	144	NA	418	NA
12	71	F	2	Anti-MDA5	CS, HCQ, MMF, IVIg	Baricitinib, 2	20	7	12,292	10,564	150	150	84	61
13	74	F	0.1	Anti-MDA5	None	Baricitinib, 2	18	7	NA	NA	79	78	83	61
14	18	F	0.9	Anti-NXP2	CS, MTX, IVIg	Baricitinib, 2	0	0	NA	NA	109	124	221	100
15	45	F	29	Anti-NXP2	CS, MTX, MMF, TAC, IVIg	Baricitinib, 4	16	6	NA	NA	135	144	341	NA
16	61	F	0.5	Anti-MDA5	CS, Cic, CYC	Baricitinib, 4	10	4	NA	NA	150	150	27	58

AZA, Azathioprin; *CDASI*, Cutaneous Dermatomyositis Disease Area and Severity Index; *Cic*, cyclosporine; *CK*, creatine kinase; *CS*, corticosteroids; *CYC*, cyclophosphamide; *HCQ*, hydroxychloroquine; *IFN*, interferon; *IVIg*, intravenous immune globulin; *JAKinh*, JAK inhibitor; *MDA*, melanoma differentiation-associated protein; *MMF*, mycophenolate mofetil; *MMT8*, manual muscle testing 8; *MTX*, methotrexate; *NA*, not available; *NXP2*, nuclear matrix protein; *PLEX*, plasma exchange; *RTX*, rituximab; *SAE*, small ubiquitin like modifier activating enzyme heterodimer; *TAC*, tacrolimus; *TIF-1γ*, transcriptional intermediary factor.



JAK inhibitor improves type I interferon induced damage: proof of concept in dermatomyositis

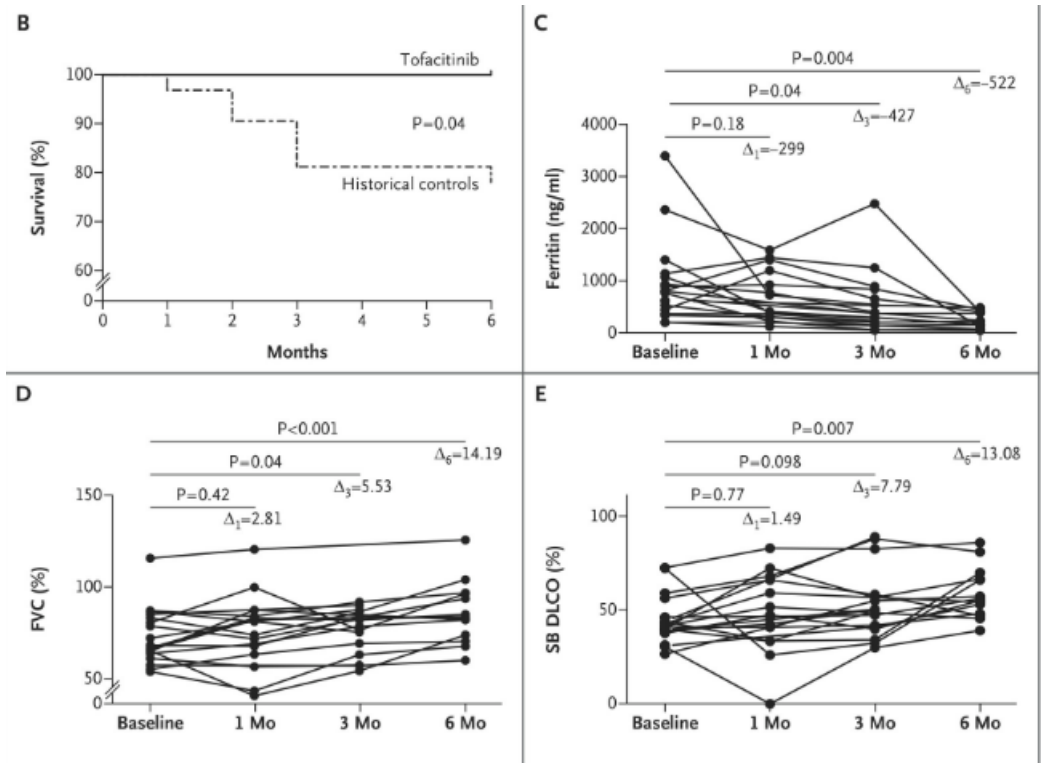
Leandro Ladislau,[1,2,*] Xavier Suárez-Calvet,[1,3,4,*] Ségolène Toquet,[1,#] Océane Landon-Cardinal,[1,#] Damien Amelin,[1] Marine Depp,[5] Mathieu P. Rodero,[5] Denisa Hathazi,[6] Darragh Duffy,[7] Vincent Bondet,[7] Corinna Preusse,[8] Boris Bienvenu,[9] Flore Rozenberg,[10] Andreas Roos,[6,11] Claudia F. Benjamim,[2] Eduard Gallardo,[3,4] Isabel Illa,[3,4] Vincent Mouly,[1] Werner Stenzel,[8] Gillian Butler-Browne,[1] Olivier Benveniste[1] and Yves Allenbach[1]



Tofacitinib in Amyopathic Dermatomyositis–Associated Interstitial Lung Disease

A

	Tofacitinib (N=18)	Historical Controls (N=32)	P Value
Age — yr	47.6±13.8	52.5±10.6	0.16
Female sex — no. (%)	11 (61)	25 (78)	0.33
History of smoking — no. (%)	2 (11)	2 (6)	0.61
Duration of ILD — mo	1.4±0.7	1.7±1.3	0.45
FVC — % of predicted value	73.4±15.2	71.9±15.3	0.76
SB DLCO — %	44.8±12.8	47.3±16.1	0.59
High-resolution CT score	118.2±13.2	127.2±24.8	0.16
Ferritin level — ng/ml	936.9±798.1	737.8±631.6	0.34
Creatine kinase level — U/ml	86.7±98.2	50.6±43.5	0.09
Albumin level— g/liter	33.5±5.3	31.8±3.3	0.18
Lactate dehydrogenase level — IU/liter	362.8±294.4	317.5±149.0	0.49
ESR — mm/hr	31.0±19.0	29.9±21.1	0.85
Maximum dosage of glucocorticoid — mg/day	78.0±54.4	87.9±81.8	0.65
Exposure to immunosuppressant — no. (%)			
Cyclosporine	2 (11)	19 (59)	
Mycophenolate mofetil	1 (6)	6 (19)	
Cyclophosphamide	0	2 (6)	
Azathioprine	0	1 (3)	
Exposure to pirfenidone — no. (%)	1 (6)	12 (38)	0.02



pharmaceuticals

MDPI

Review

Jak Inhibitors for Treatment of Autoimmune Diseases: Lessons from Systemic Sclerosis and Systemic Lupus Erythematosus

SSc

Przemysław Kotyla [1,*], Olga Gumkowska-Sroka [2], Bartosz Wnuk [3] and Kacper Kotyla [1]

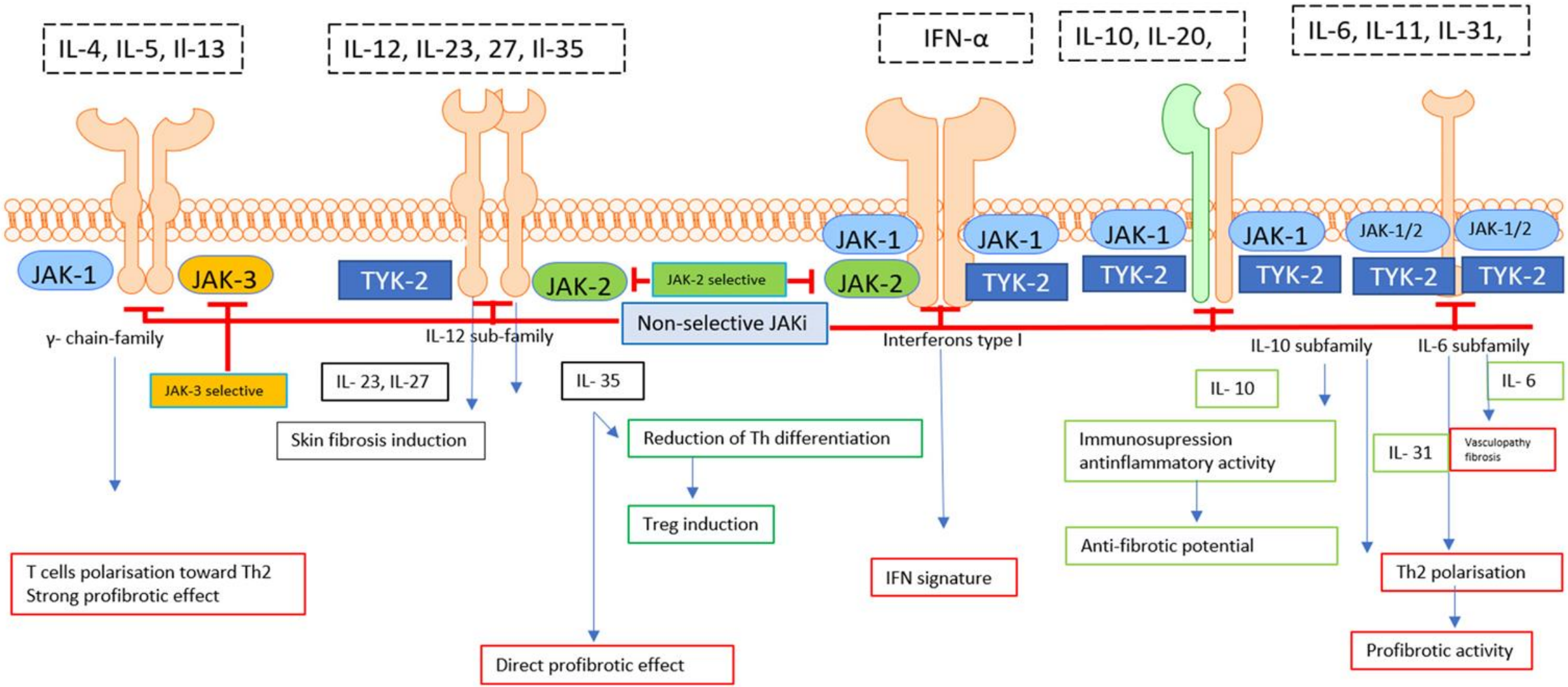
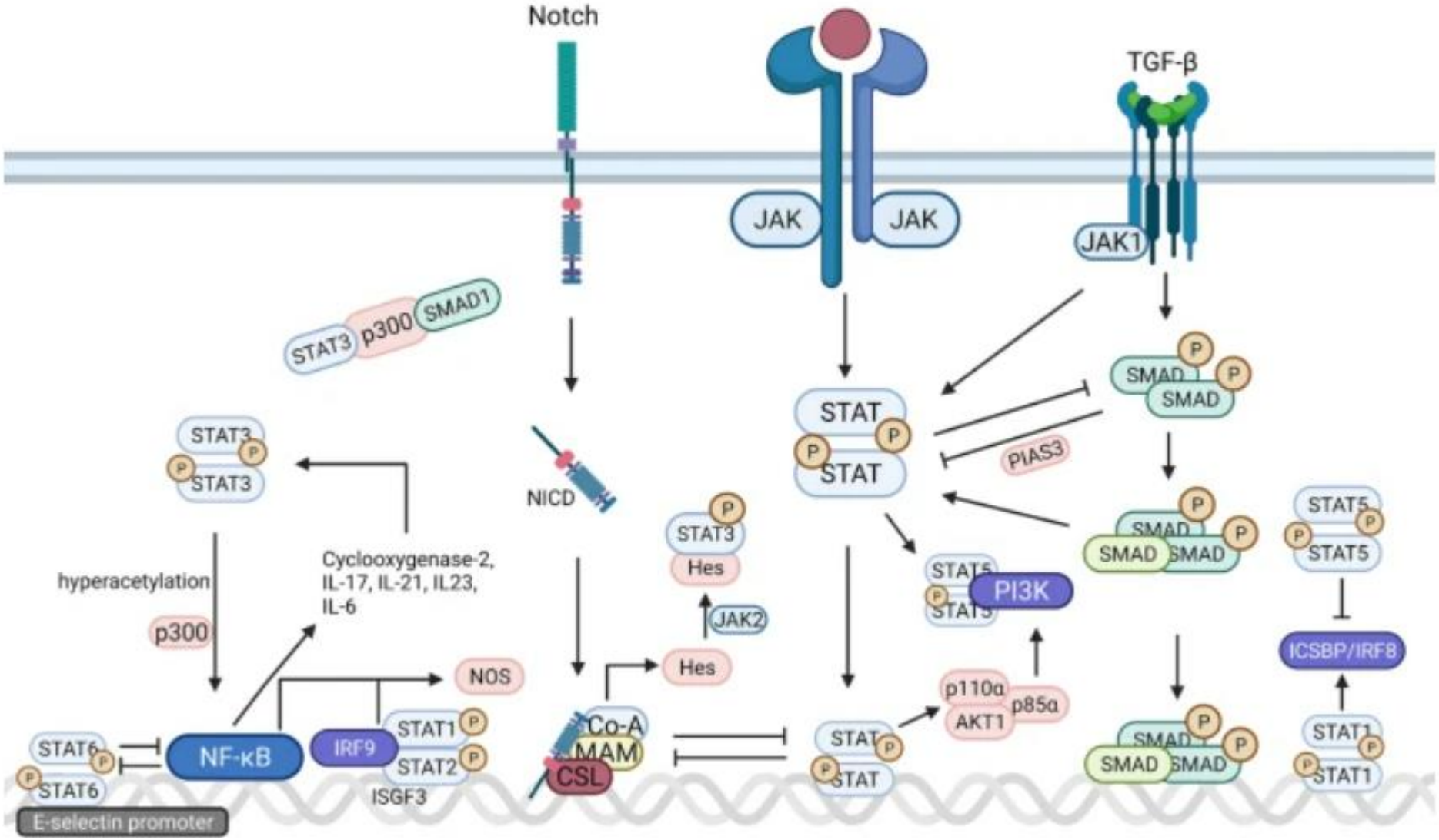


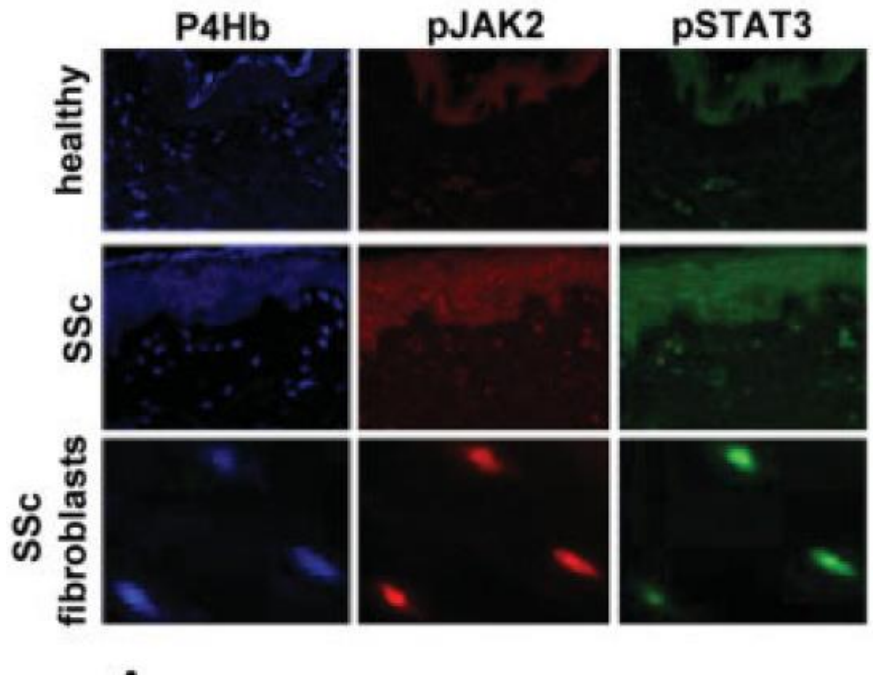
Fig. 4


Notch
TGF-β
JAK
JAK
JAK1
STAT3
p300
SMAD1
STAT3
STAT3
NICD
STAT
STAT
PIAS3
SMAD
SMAD
hyperacetylation
p300
Cyclooxygenase-2,
IL-17, IL-21, IL23,
IL-6
STAT3
Hes
JAK2
Hes
NOS
PI3K
STAT5
STAT5
STAT5
STAT5
ICSBP/IRF8
p110α
AKT1
p85α
STAT6
STAT6
NF-κB
IRF9
STAT1
STAT2
ISGF3
Co-A
MAM
CSL
STAT
STAT
STAT1
STAT1
E-selectin promoter

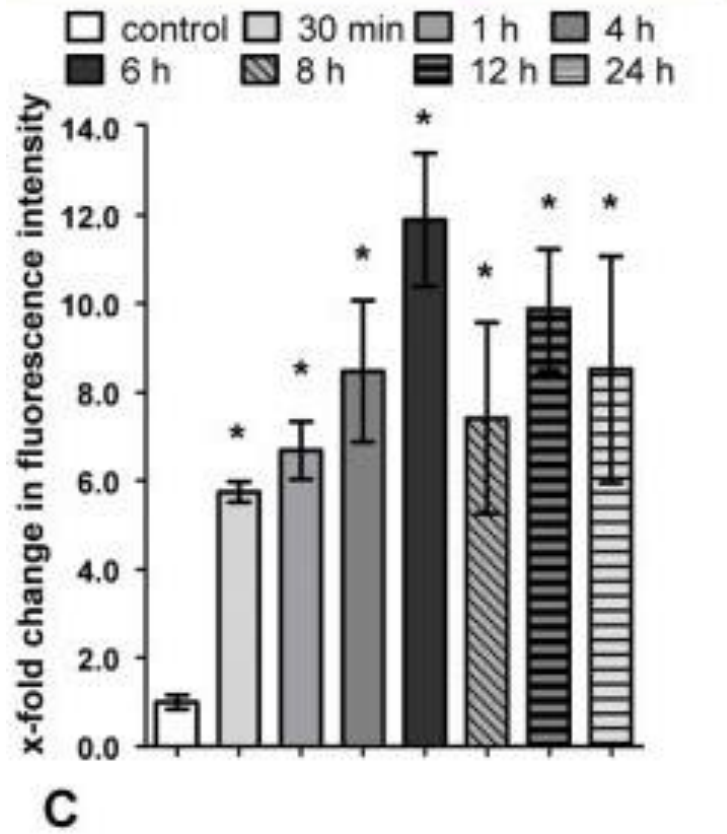
ARTHRITIS & RHEUMATISM
Vol. 64, No. 9, September 2012, pp 3006–3015
DOI 10.1002/art.34500

JAK-2 as a Novel Mediator of the Profibrotic Effects of Transforming Growth Factor β in Systemic Sclerosis

Clara Dees,[1] Michal Tomcik,[2] Katrin Palumbo-Zerr,[1] Alfiya Distler,[1] Christian Beyer,[1] Veronika Lang,[1] Angelika Horn,[1] Pawel Zerr,[1] Jochen Zwerina,[1] Kolja Gelse,[1] Oliver Distler,[3] Georg Schett,[1] and Jörg H. W. Distler[1]



Normal fibroblasts



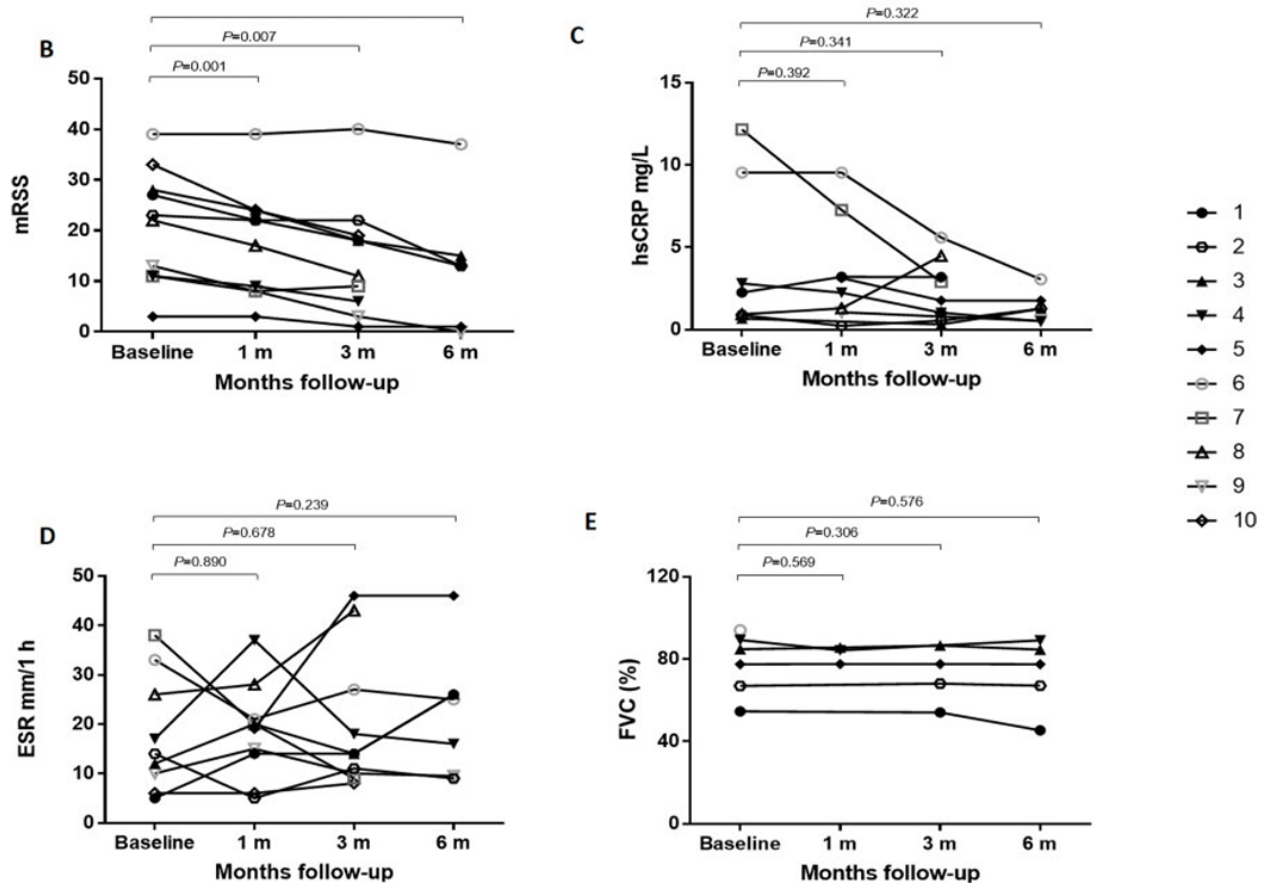
RHEUMATOLOGY

Rheumatology 2021;60:2472–2477
doi:10.1093/rheumatology/keaa613
Advance Access publication 14 November 2020

Concise report

Tofacitinib as a possible treatment for skin thickening in diffuse cutaneous systemic sclerosis

Hanxiao You [1]*, Dong Xu [1]*, Yong Hou [1], Jiaxin Zhou[1], Qian Wang[1], Mengtao Li [1] and Xiaofeng Zeng [1]



Tyk2) attached to IFNR. The hypothesis on the usefulness of JAK inhibitors is currently undergoing testing in three clinical trials from China (Baricitinib- NCT05300932), France (Ruxolitinib-NCT04206644), and the USA (Tofacitinib- NCT03274076). The completed study from the USA did not show the superiority of Tofacitinib versus a placebo towards skin improvement (measured as a change in mRSS), nor an improvement in CRISS (Combined Response Index Systemic sclerosis). This is in contrast to previously published data, where

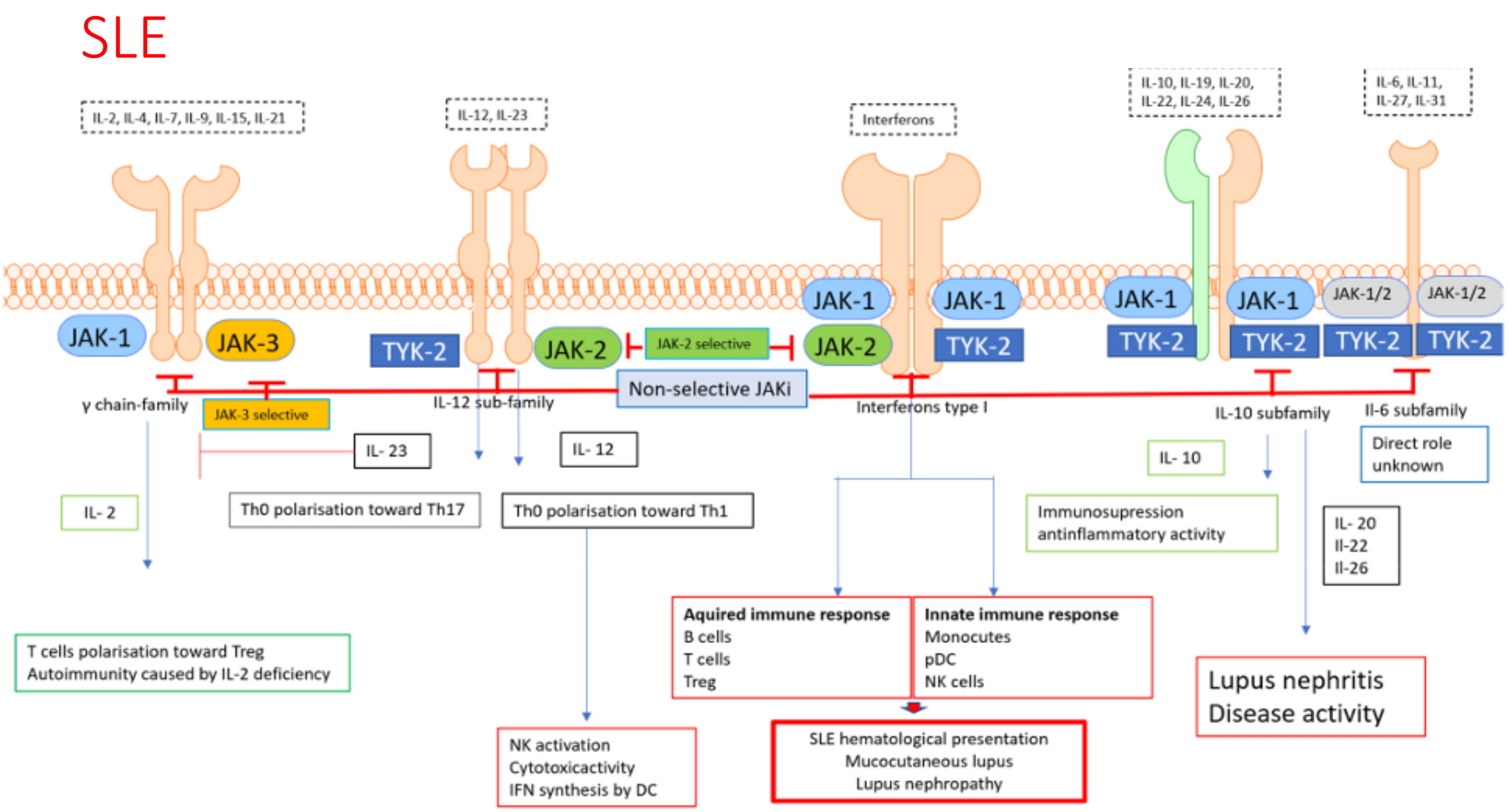


Figure 2. The role of cytokines in SLE.

Baricitinib for systemic lupus erythematosus: a double-blind, randomised, placebo-controlled, phase 3 trial (SLE-BRAVE-I)

Eric F Morand, Edward M Vital, Michelle Petri, Ronald van Vollenhoven, Daniel J Wallace, Marta Mosca, Richard A Furie, Maria E Silk, Christina L Dickson, Gabriella Meszaros, Bochao Jia, Brenda Crowe, Inmaculada de la Torre, Thomas Dörner

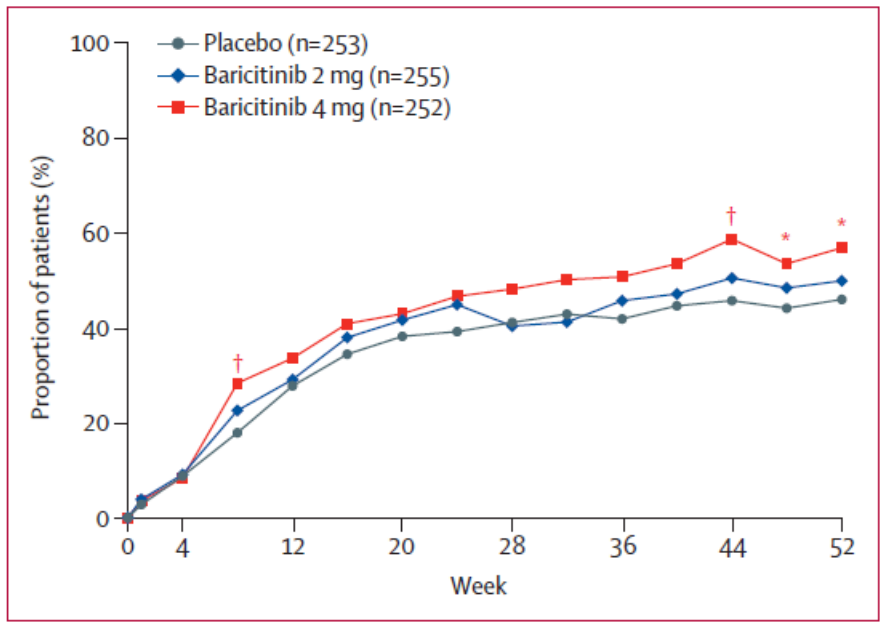


Figure 2: SRI-4 response through 52 weeks in overall study population

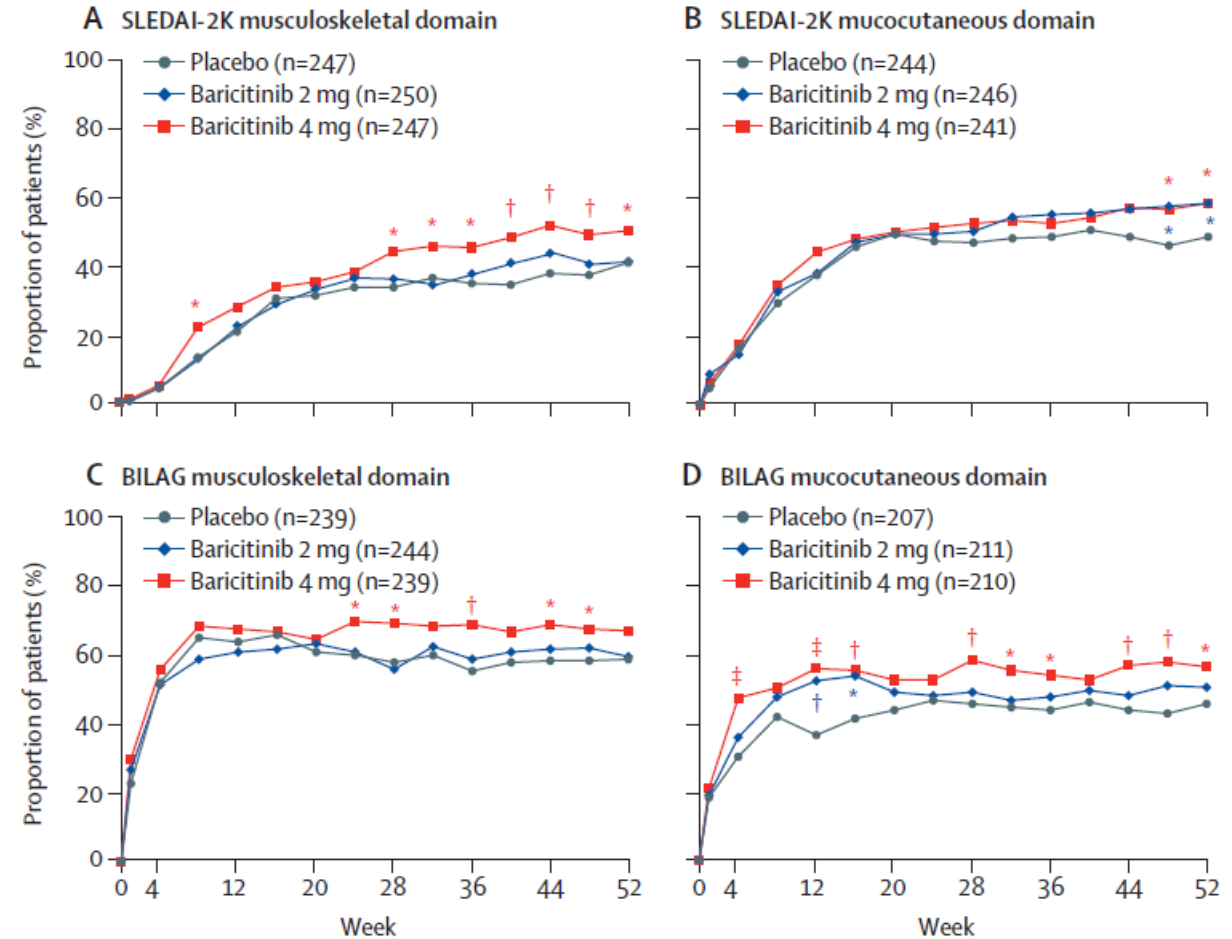


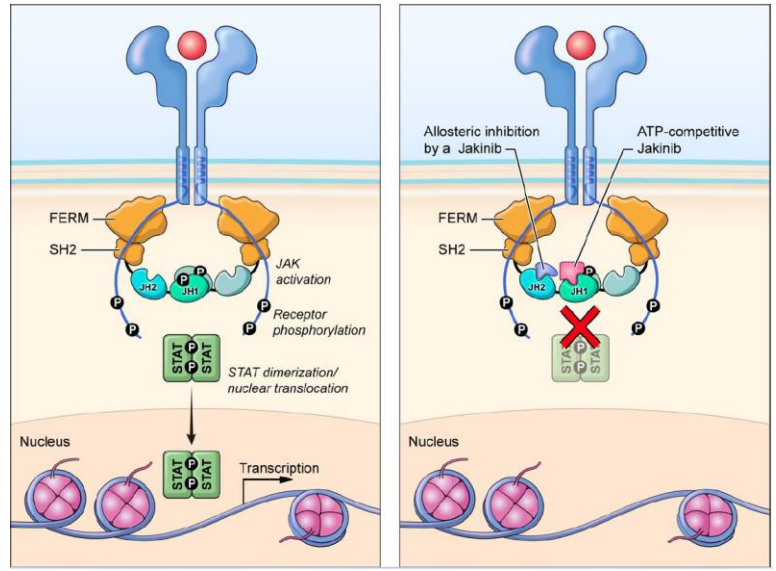
Figure 3: Improvement from baseline in SLEDAI-2K and BILAG organ systems through 52 weeks

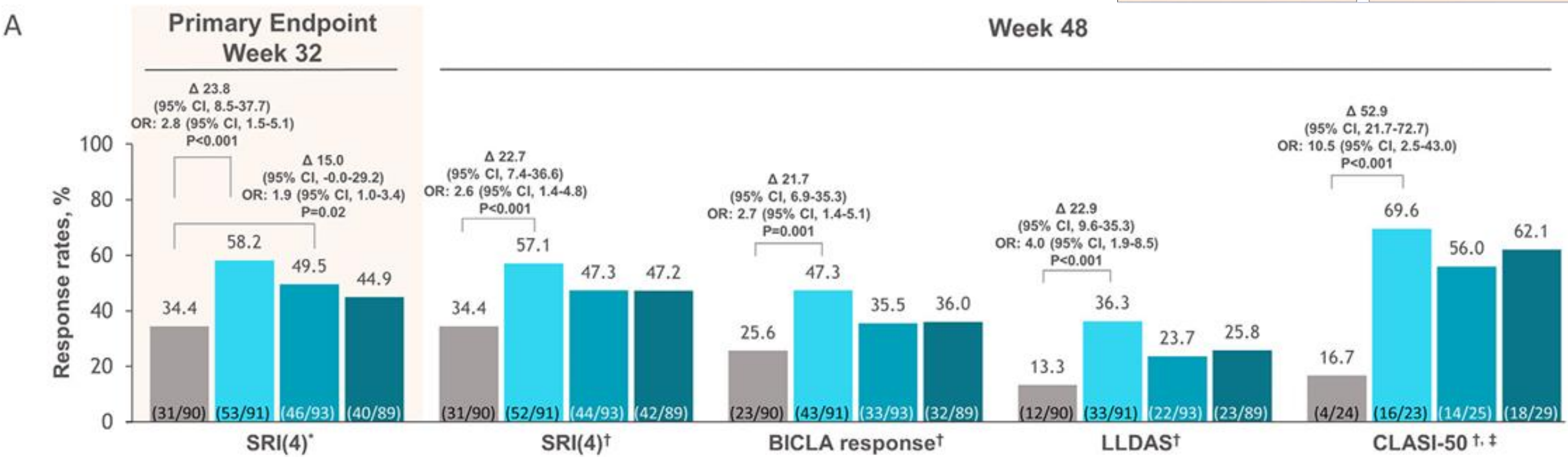
Arthritis & Rheumatology
Vol. 75, No. 2, February 2023, pp 242–252
DOI 10.1002/art.42391

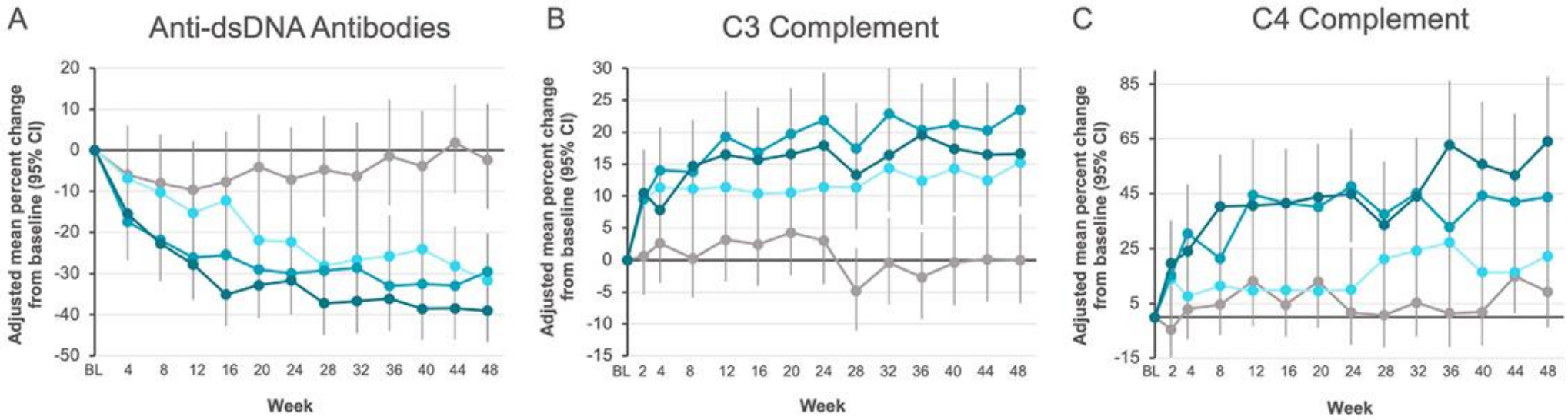
American College of Rheumatology
Empowering Rheumatology Professionals

Deucravacitinib, a Tyrosine Kinase 2 Inhibitor, in Systemic Lupus Erythematosus: A Phase II, Randomized, Double-Blind, Placebo-Controlled Trial

Eric Morand,[1] Marilyn Pike,[2] Joan T. Merrill,[3] Ronald van Vollenhoven,[4] Victoria P. Werth,[5] Coburn Hobar,[6] Nikolay Delev,[6] Vaishali Shah,[6] Brian Sharkey,[6] Thomas Wegman,[6] Ian Catlett,[6] Subhashis Banerjee,[6] and Shalabh Singhal[6]







Interferon signature

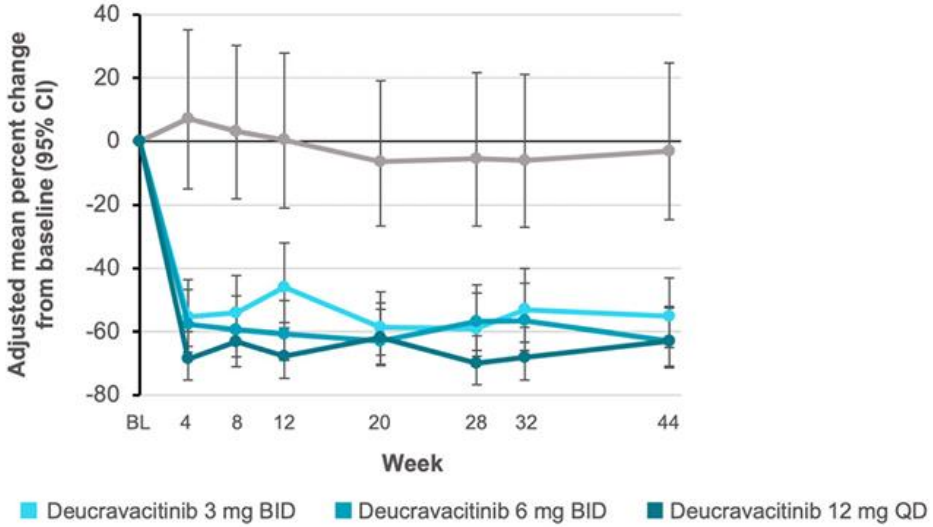


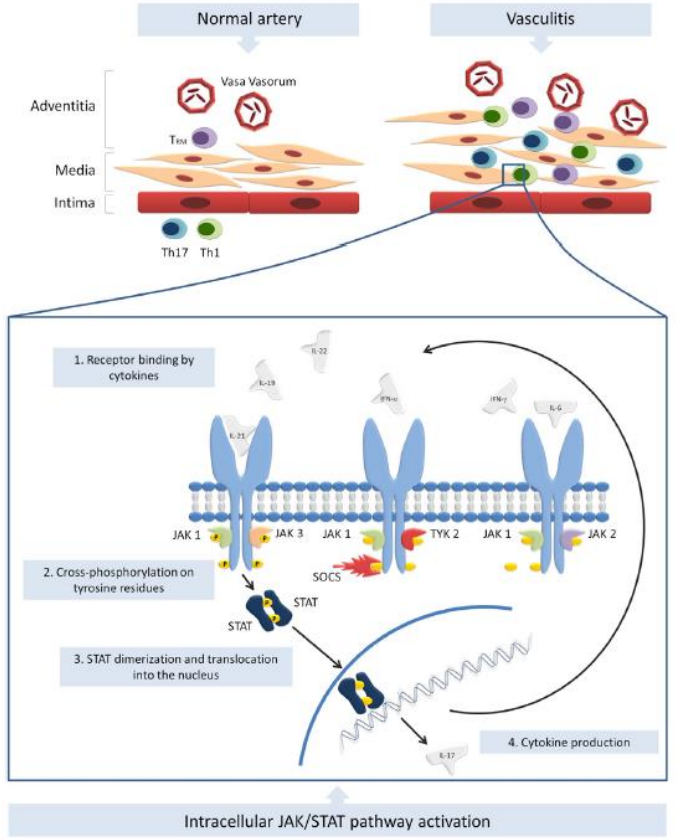
Table 2. Summary of adverse events in patients in the deucravacitinib treatment groups and placebo group over the course of weeks 0 to 48*

	Deucravacitinib 3 mg twice daily (n = 91)	Deucravacitinib 6 mg twice daily (n = 93)	Deucravacitinib 12 mg once daily (n = 89)	Placebo (n = 90)
Deaths	0	0	0	0
Adverse events	85 (93.4)	81 (87.1)	75 (84.3)	79 (87.8)
Serious adverse events	7 (7.7)	8 (8.6)	7 (7.9)	11 (12.2)
Serious infections/infestations	1 (1.1)†	2 (2.2)‡	1 (1.1)§	1 (1.1)¶
Adverse events leading to treatment discontinuation	8 (8.8)	6 (6.5)	11 (12.4)	3 (3.3)

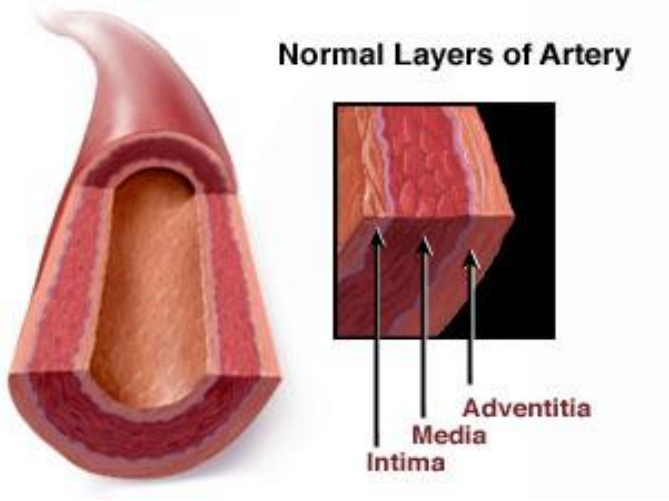
Jakinibs in large vessel vasculitides

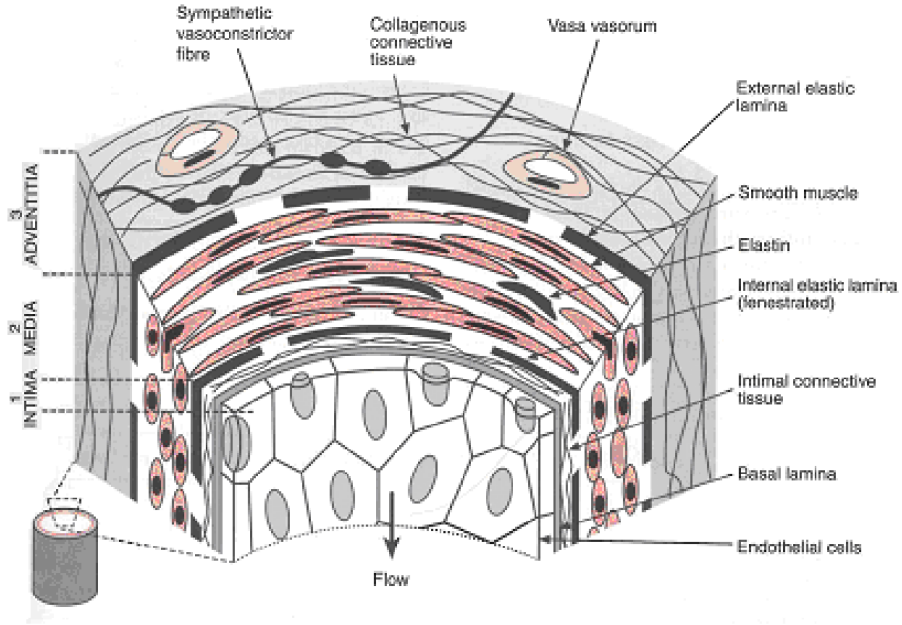
Contribution of Janus-Kinase/Signal Transduction Activator of Transcription Pathway in the Pathogenesis of Vasculitis: A Possible Treatment Target in the Upcoming Future

*Roberto Bursi†, Giacomo Cafaro†, Carlo Perricone, Ilenia Riccucci, Santina Calvacchi, Roberto Gerli and Elena Bartoloni **

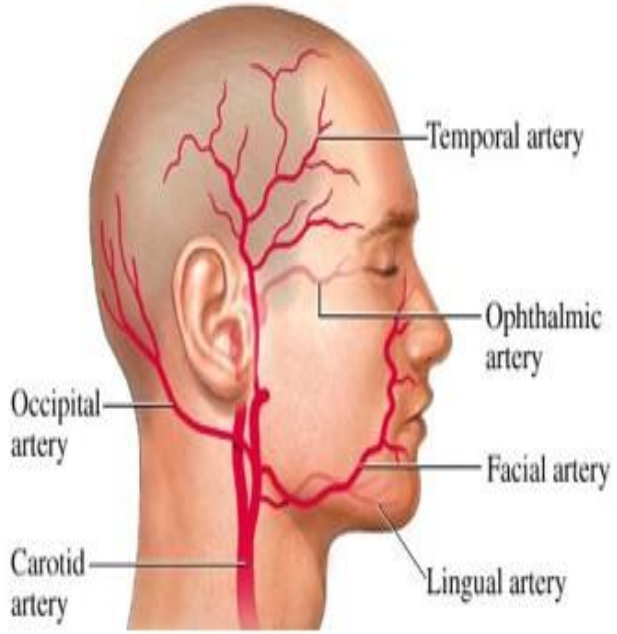


Τι διαφορετικό έχουν τα μεγάλα αγγεία??

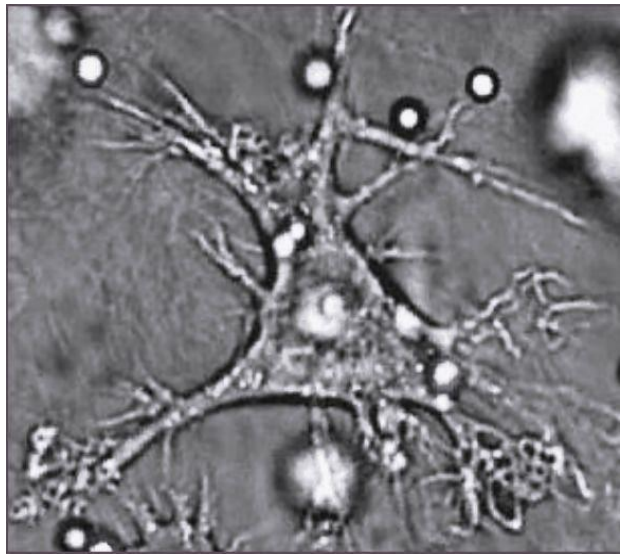


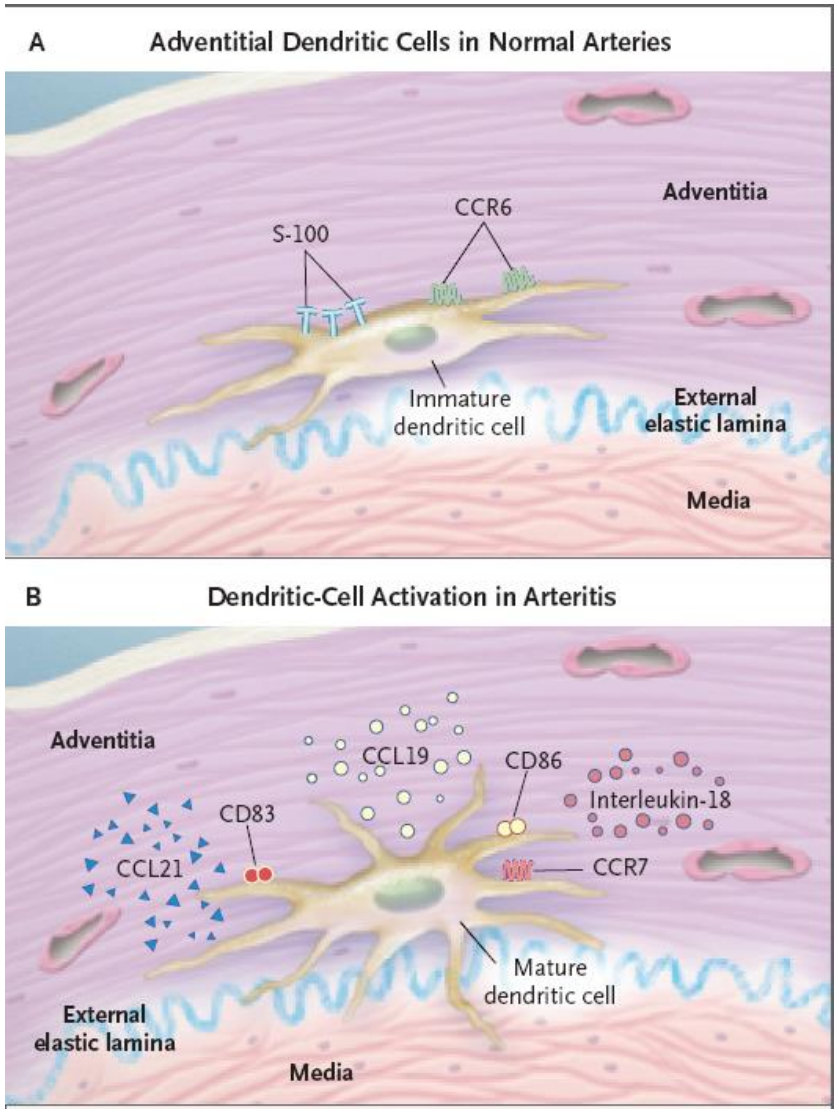


- Έχουν τροφοφόρα αγγεία
- Έχουν δικό τους λεμφικό ιστό (vascular-associated lymphoid tissue)



- Στην adventitia υπάρχουν μόνιμα τοποθετημένα δενδριτικά κύτταρα
- Τα κύτταρα αυτά έχουν αισθητήρες (Toll like receptors)

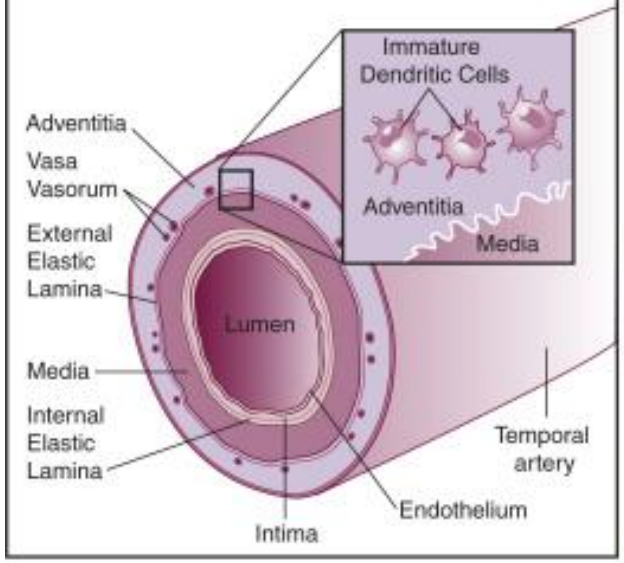




Ανώριμα- Προωθούν την ανοσολογική ανοχή

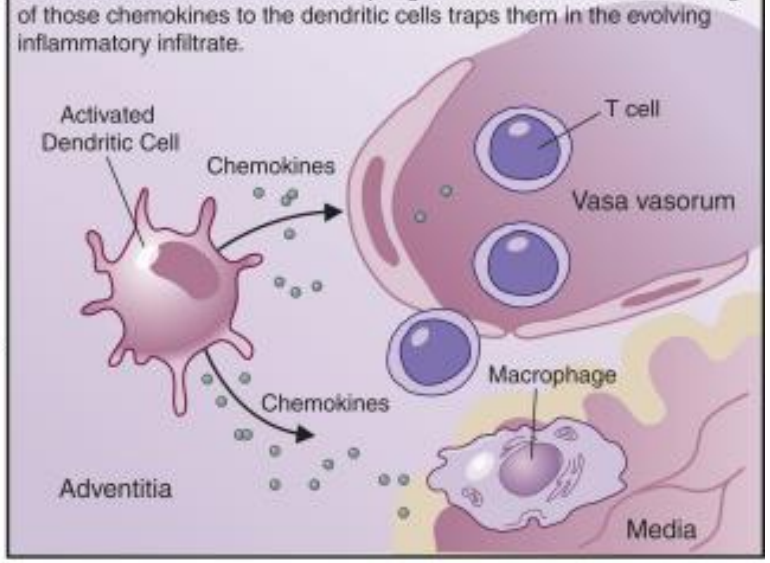
Διεγερμένα. Προσελκύουν και διεγείρουν τα Τ λεμφοκύτταρα

In **healthy medium-sized arteries,** immature, nonactivated dendritic cells reside in the adventitia near the adventitia-media border. When immature dendritic cells present antigen to T cells, the T cells are inhibited, which may be important in maintaining immune tolerance.

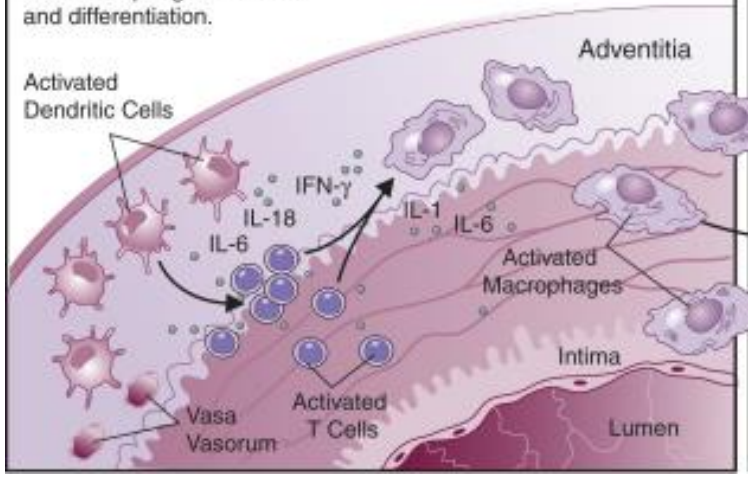


In **temporal arteritis,** a triggering antigens (e.g., an infectious agent, drug, toxin, or autoantigen) activates dendritic cells resident in the arterial wall.

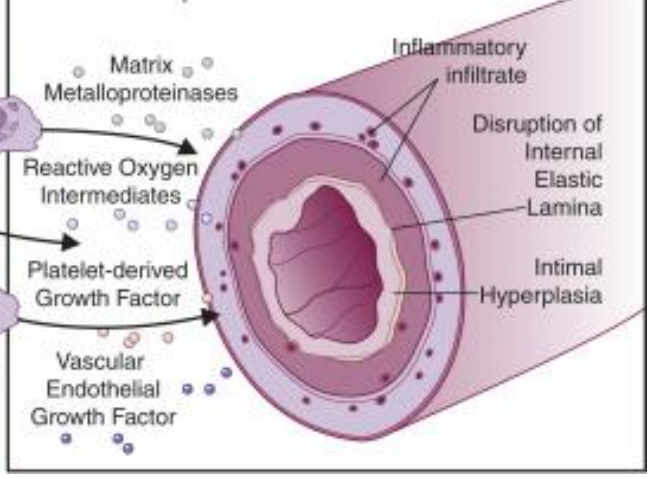
The activated dendritic cells release chemokines that attract T cells from the vasa vasorum and macrophages into the arterial wall. Binding of those chemokines to the dendritic cells traps them in the evolving inflammatory infiltrate.



The activated dendritic cells express receptors and release inflammatory cytokines (interleukin [IL] 6, IL-18) that promote activation of T cells and vascular inflammation. IL-18 up-regulates the release of interferon (IFN) γ from T cells. IFN-γ released from activated T cells promotes inflammation, granuloma formation, and macrophage activation and differentiation.



Activated macrophages produce a variety of mediators that lead to progressive vascular inflammation, endothelial damage, disruption of the internal elastic lamina, and intimal hyperplasia. Macrophages also release cytokines (IL-1, IL-6) that may contribute to systemic features of temporal arteritis.

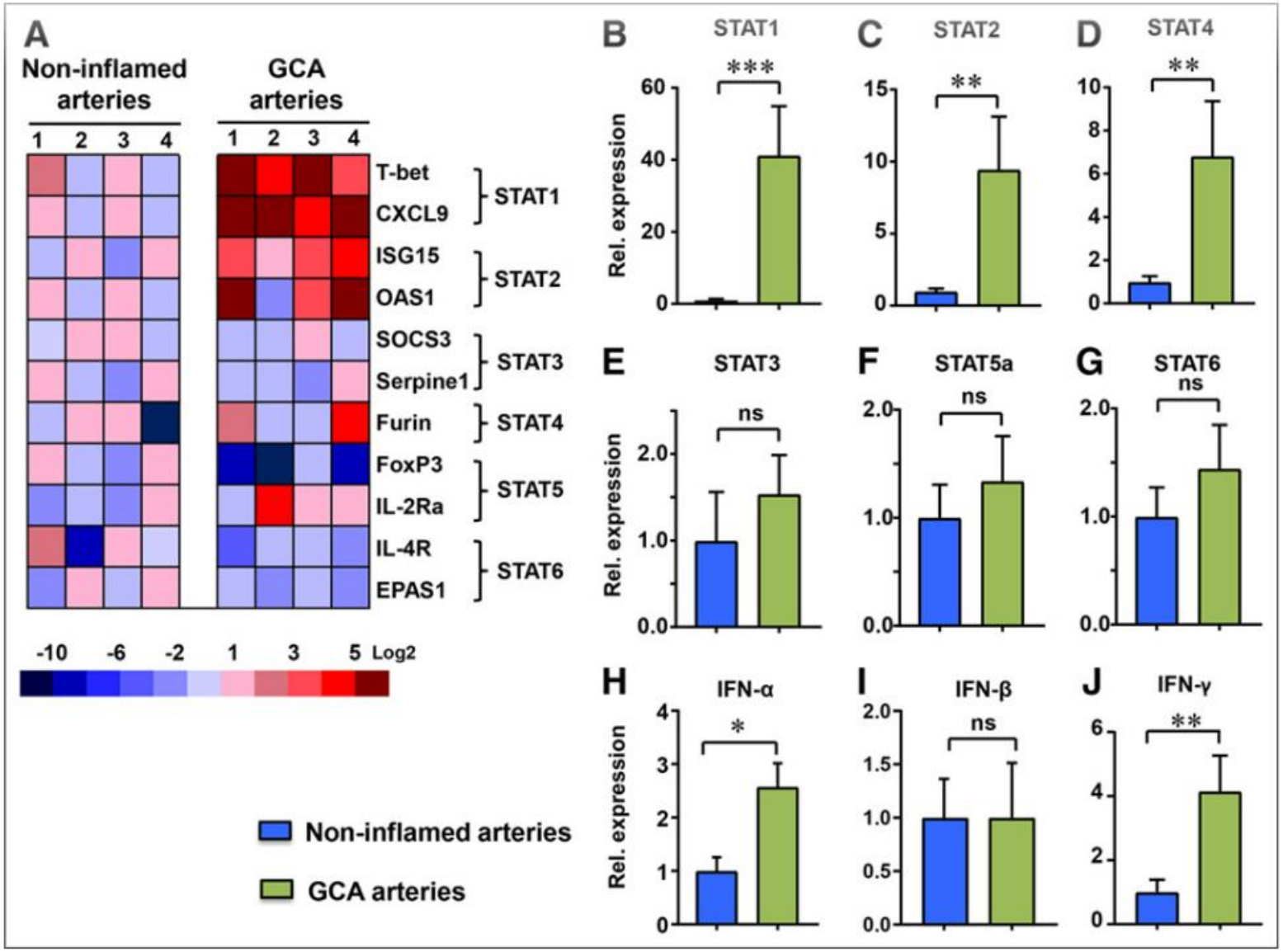


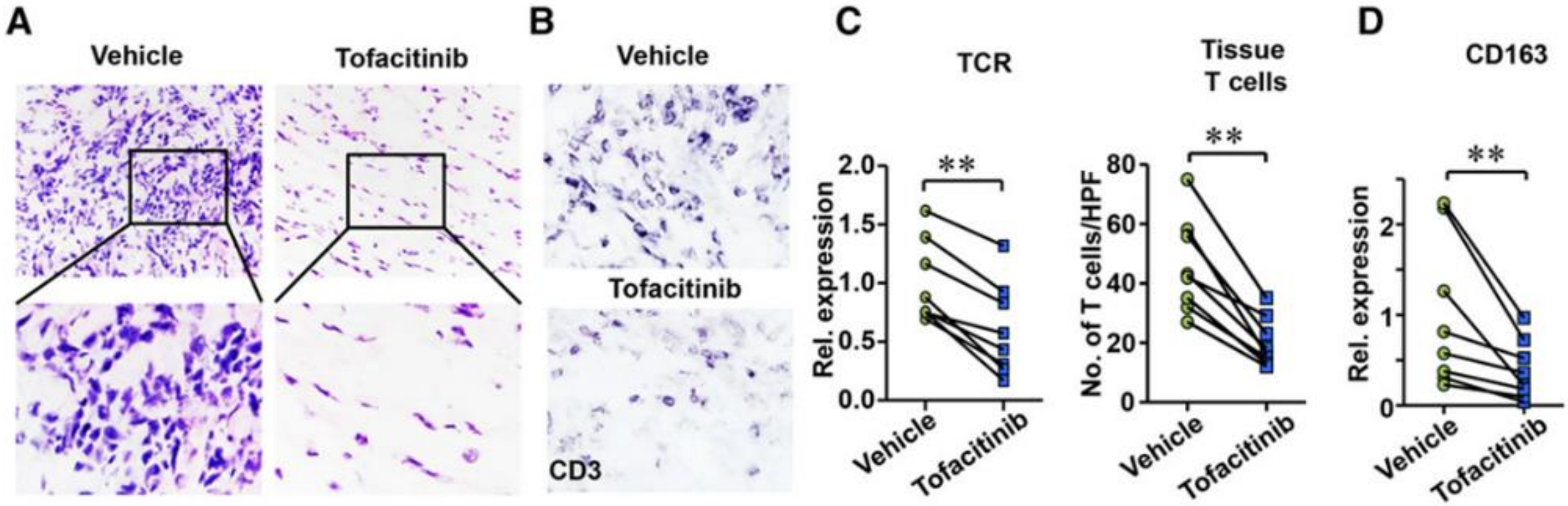
Circulation
Volume 137, Issue 18, 1 May 2018; Pages 1934-1948
https://doi.org/10.1161/CIRCULATIONAHA.117.030423

ORIGINAL RESEARCH ARTICLE

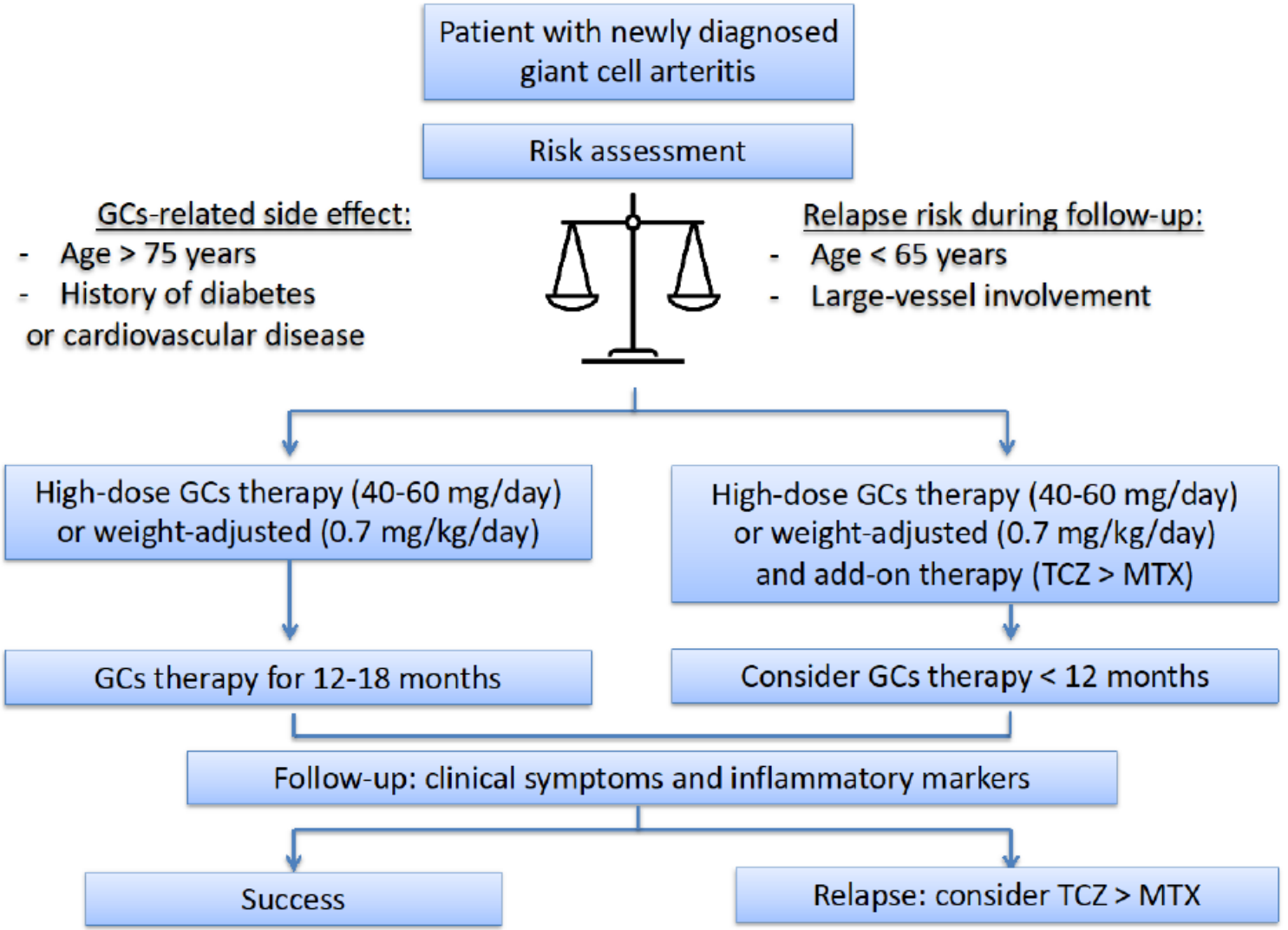
Inhibition of JAK-STAT Signaling Suppresses Pathogenic Immune Responses in Medium and Large Vessel Vasculitis

Hui Zhang, MD, PhD, Ryu Watanabe, MD, PhD, Gerald J. Berry, MD, Lu Tian, PhD, Jörg J. Goronzy, MD, PhD, and Cornelia M. Weyand, MD, PhD




A
Vehicle
Tofacitinib
B
Vehicle
Tofacitinib
CD3
C
TCR
Rel. expression
2.0
1.5
1.0
0.5
0.0
**
Vehicle
Tofacitinib
Tissue
T cells
No. of T cells/HPF
80
60
40
20
0
**
Vehicle
Tofacitinib
D
CD163
Rel. expression
2
1
0
**
Vehicle
Tofacitinib

GCA-Standard of care



The NEW ENGLAND JOURNAL of MEDICINE

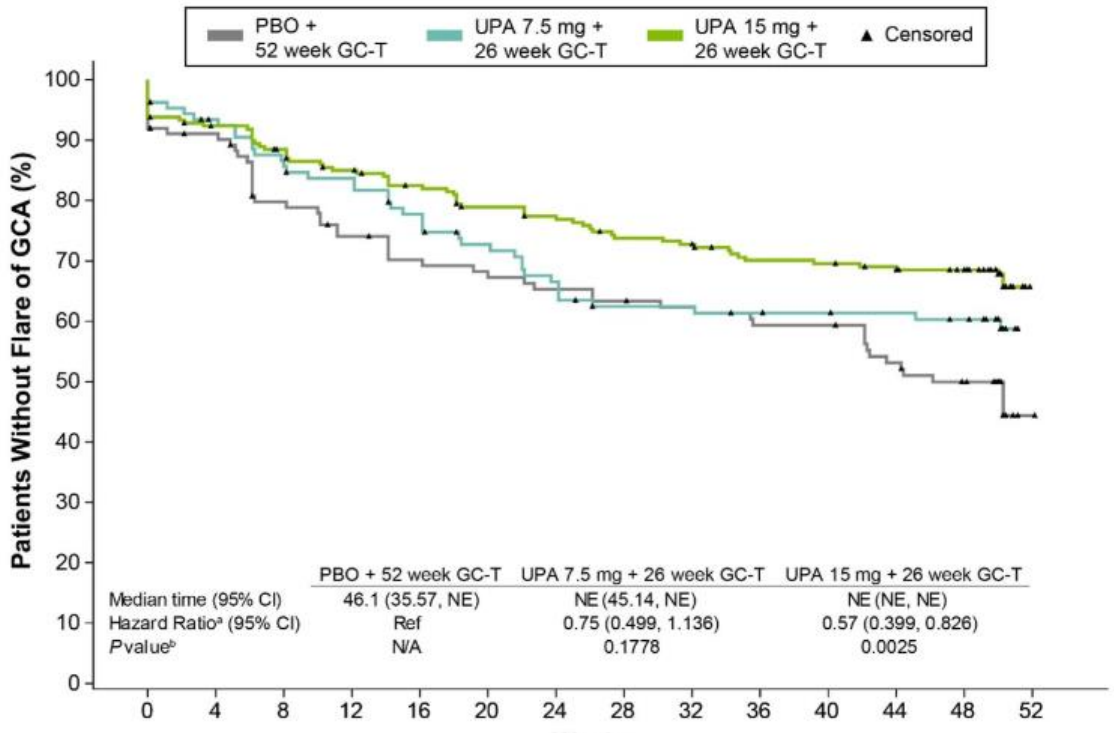
CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis

Authors: Daniel Blockmans, M.D., Ph.D., Sara K. Penn, M.D., Arathi R. Setty, M.D., M.P.H., Wolfgang A. Schmidt, M.D., M.A.C.R., Andrea Rubbert-Roth, M.D. , Ellen M. Hauge, M.D., Ph.D., Helen I. Keen, M.B., B.S., Ph.D., +11 , for the SELECT-GCA Study Group* Author Info & Affiliations

Figure. Kaplan-Meier Curves for Time to First Disease Flare Through Week 52



Conclusions: In patients with giant-cell arteritis, upadacitinib at a dose of 15 mg - but not 7.5 mg - with a 26-week glucocorticoid taper showed efficacy superior to that of placebo with a 52-week glucocorticoid taper. (Funded by AbbVie; SELECT-GCA ClinicalTrials.gov number, NCT03725202.).

Email: jimdaoussis@hotmail.com

Χρήσιμα διδάγματα από πειραματικά μοντέλα

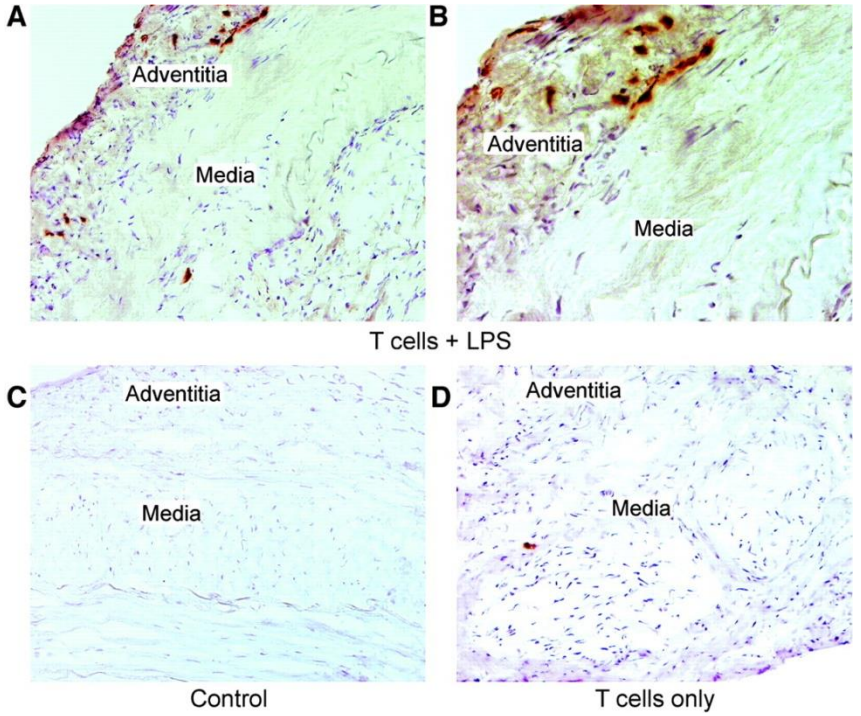
Φυσιολογική κροταφική

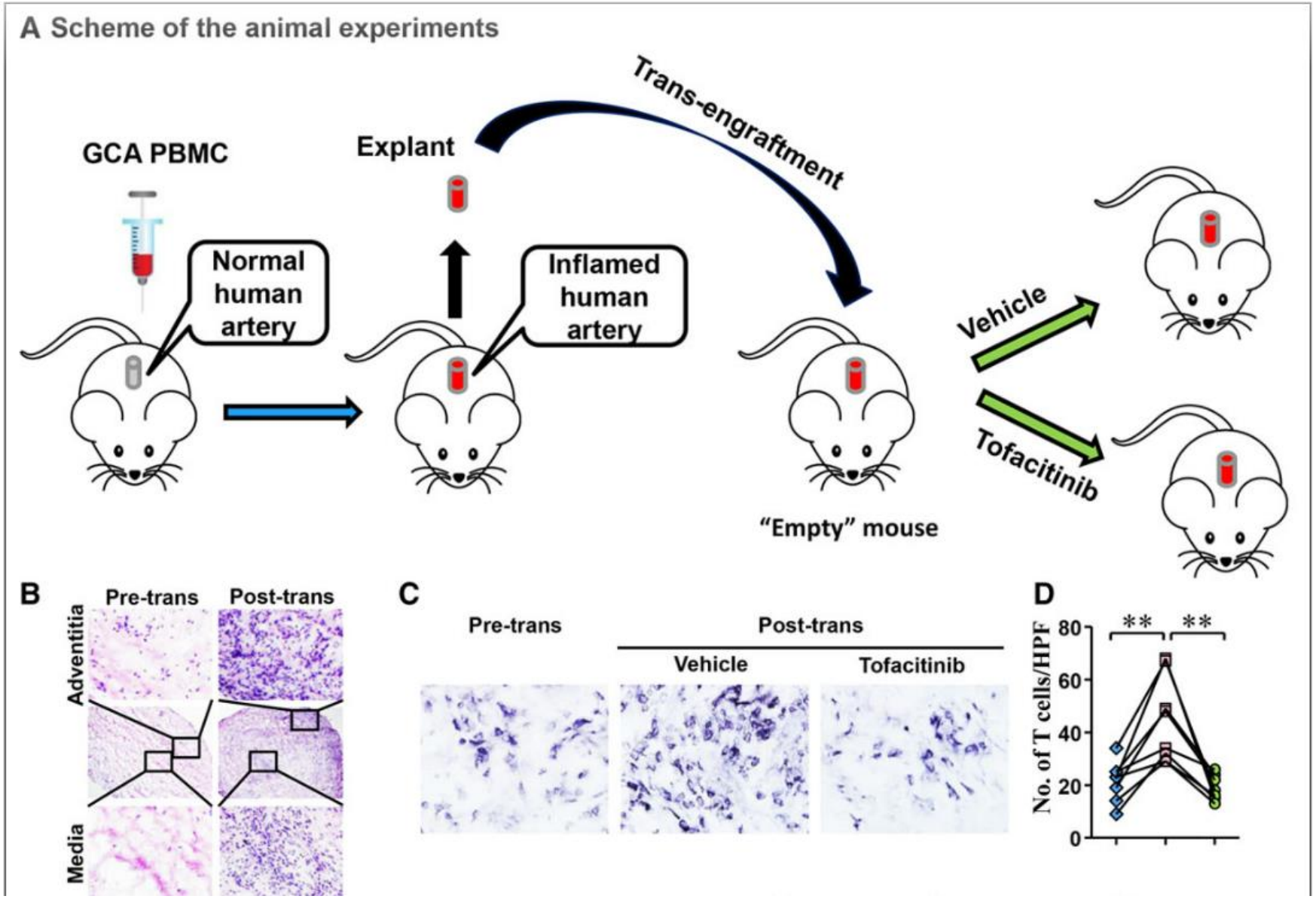
+

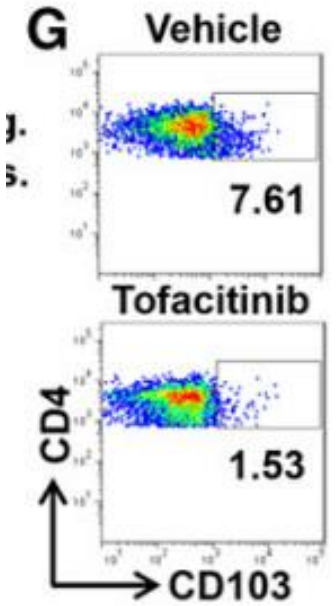
Εγχυση LPS
(TLR stimulation)

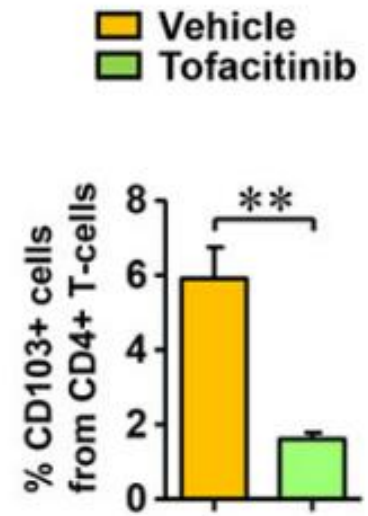
Εγχυση Τ λεμφοκυττάρων από ασθενή με GCA

Κροταφική αρτηρίτιδα



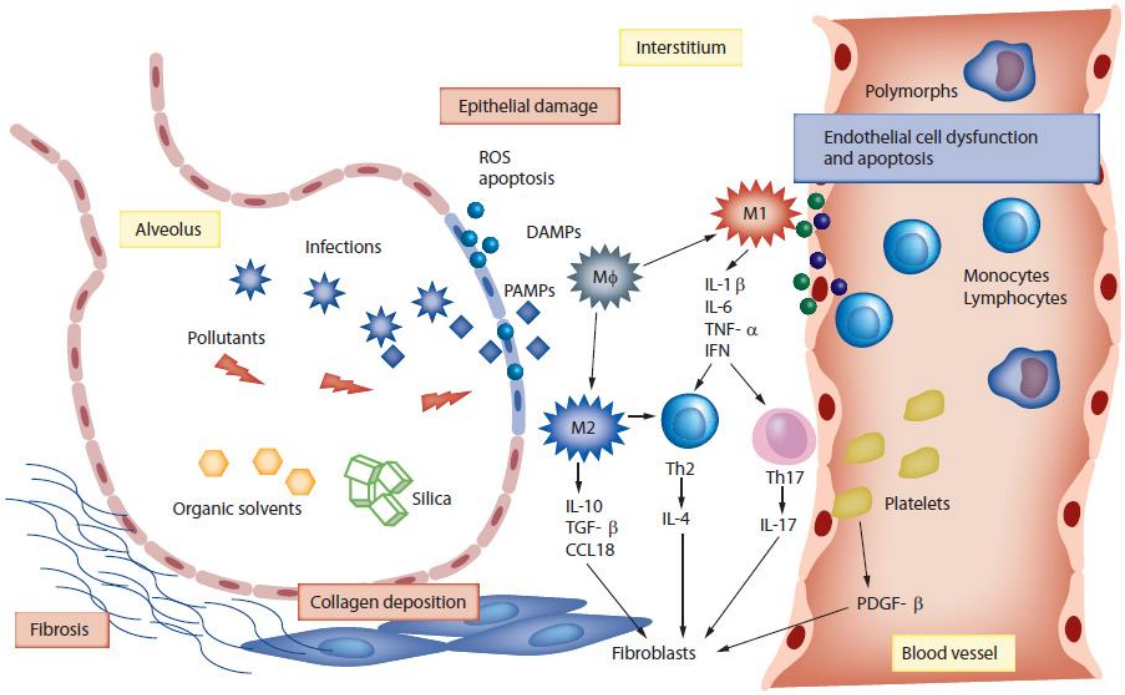

A Scheme of the animal experiments
GCA PBMC
Explant
Trans-engraftment
Normal human artery
Inflamed human artery
"Empty" mouse
Vehicle
Tofacitinib
B
Pre-trans
Post-trans
Adventitia
Media
C
Pre-trans
Post-trans
Vehicle
Tofacitinib
D
No. of T cells/HPF
**
**

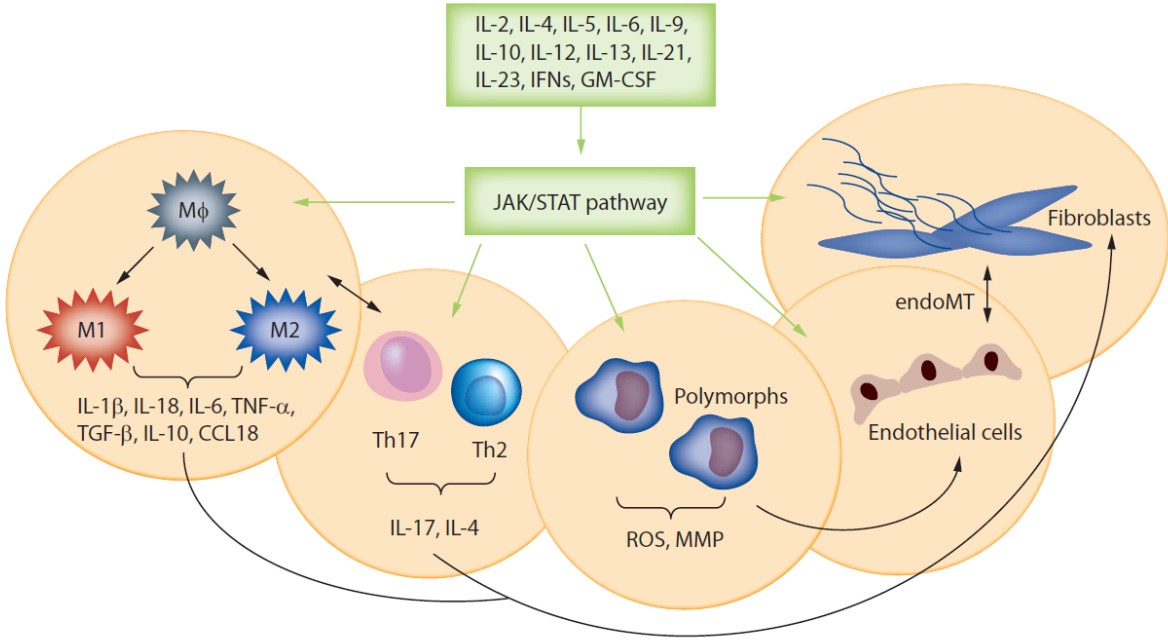

G
Vehicle
7.61
Tofacitinib
1.53
CD4
CD103


H
Vehicle
Tofacitinib
% CD103+ cells from CD4+ T-cells
**

The rationale for targeting the JAK/STAT pathway in scleroderma-associated interstitial lung disease

Rossella Talotta*,[1]

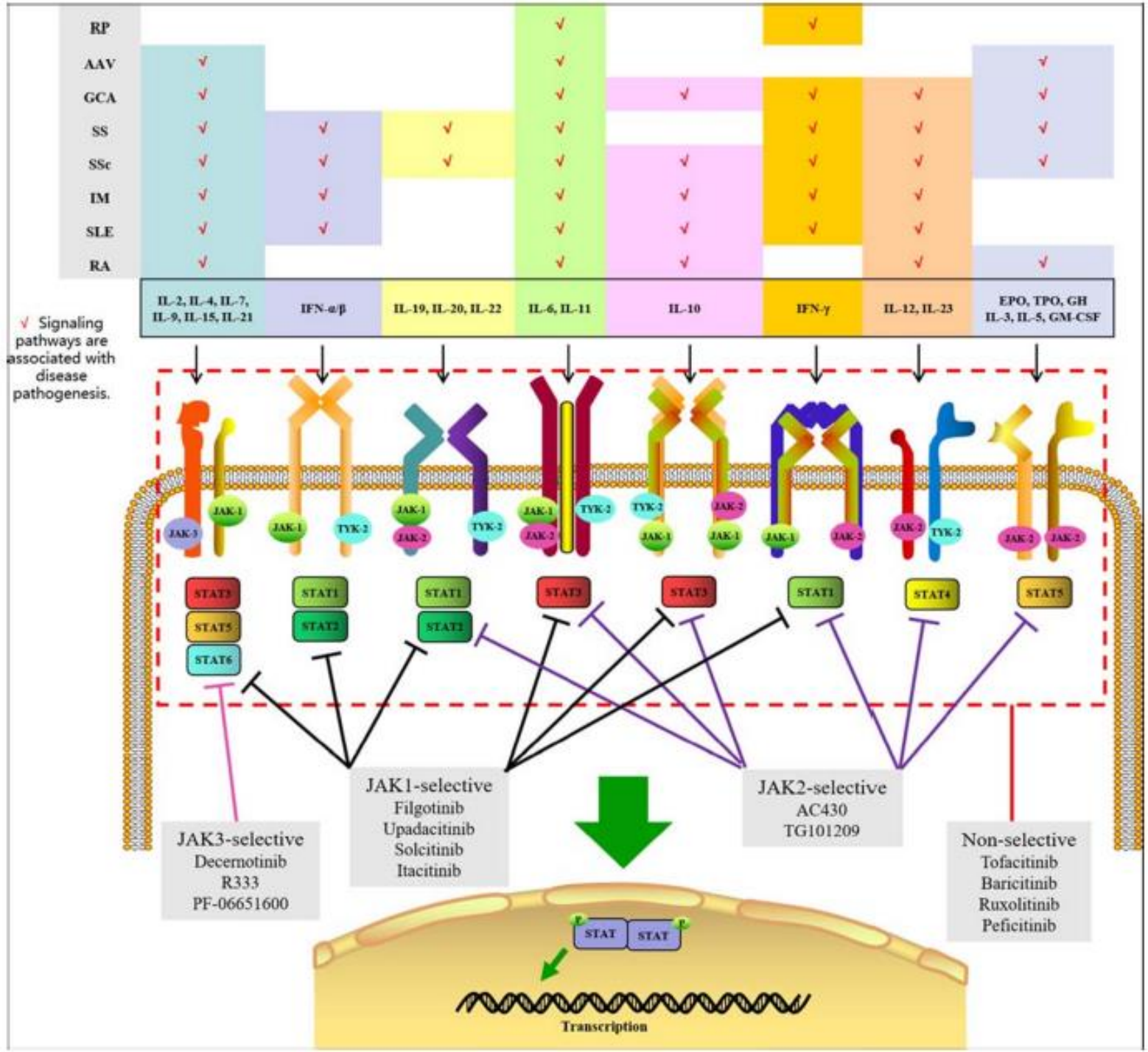


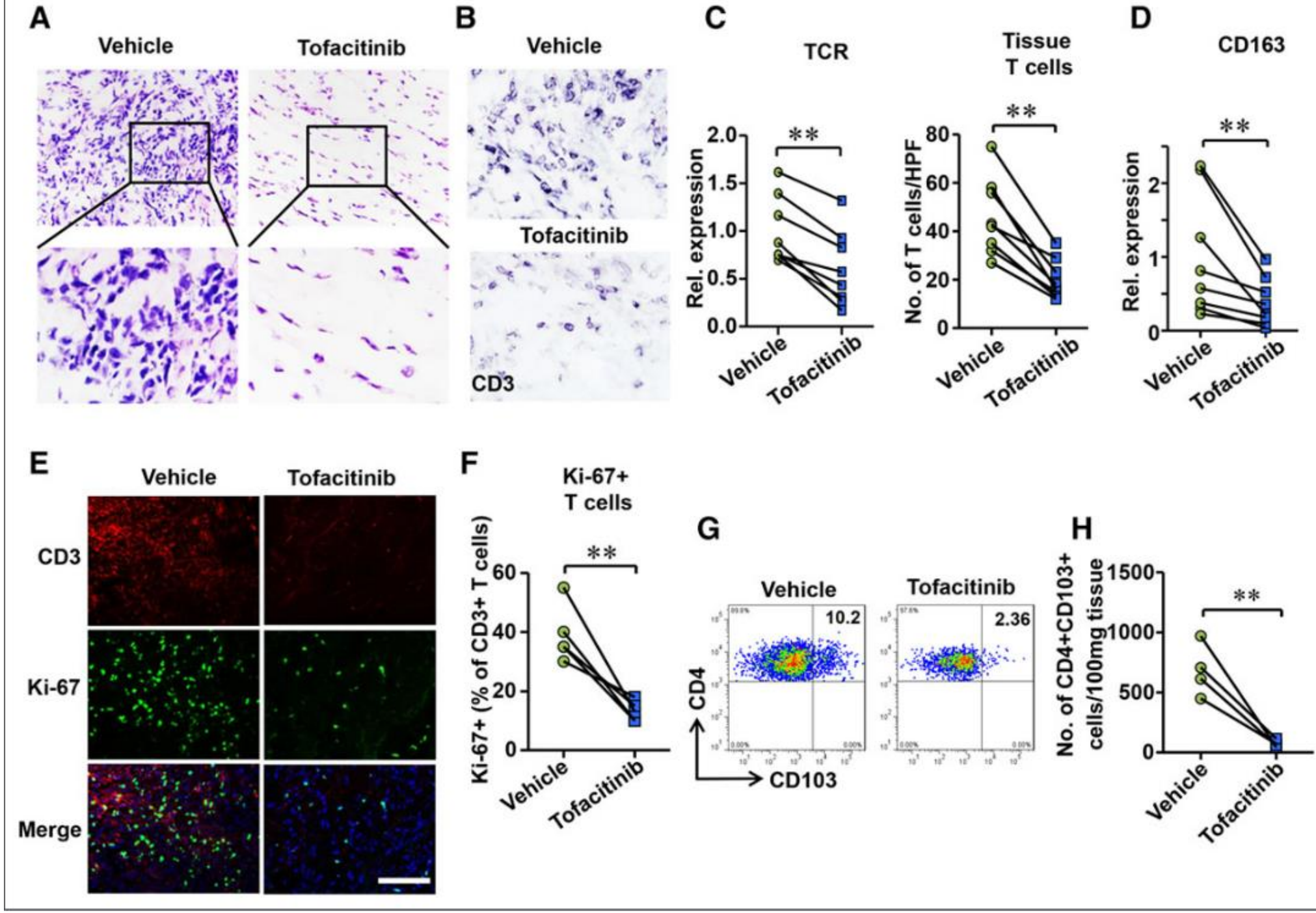


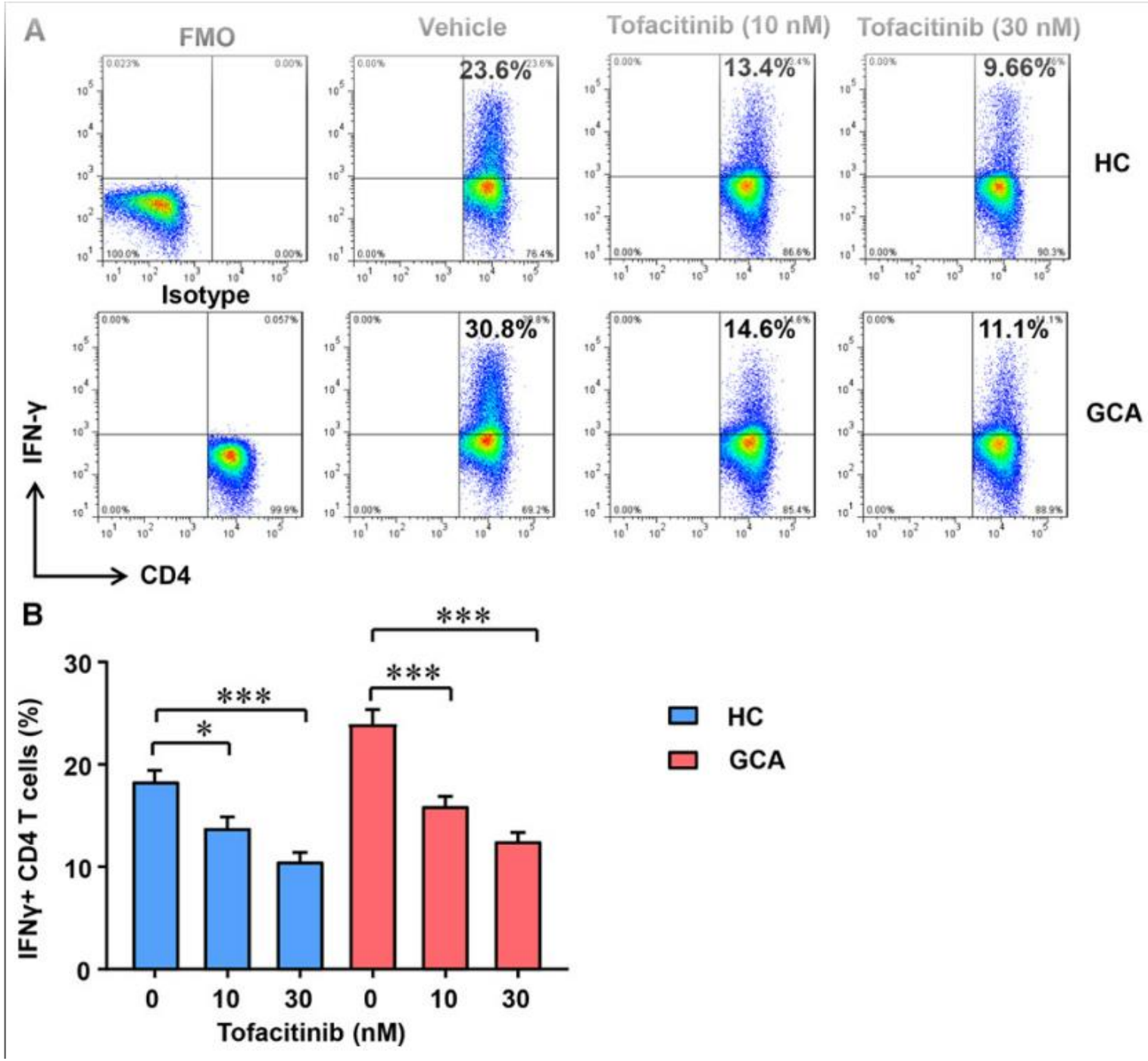
Clinical Reviews in Allergy & Immunology (2020) 59:334–351
https://doi.org/10.1007/s12016-020-08786-6

JAK Inhibitors: Prospects in Connective Tissue Diseases

Hanxiao You[1] · Dong Xu[1] · Jiuliang Zhao[1] · Jing Li[1] · Qian Wang[1] · Xinping Tian[1] · Mengtao Li[1] · Xiaofeng Zeng[1]




A
Vehicle
Tofacitinib
B
Vehicle
Tofacitinib
CD3
C
TCR
Rel. expression
2.0
1.5
1.0
0.5
0.0
**
Vehicle
Tofacitinib
Tissue
T cells
No. of T cells/HPF
80
60
40
20
0
**
Vehicle
Tofacitinib
D
CD163
Rel. expression
2
1
0
**
Vehicle
Tofacitinib
E
Vehicle
Tofacitinib
CD3
Ki-67
Merge
F
Ki-67+
T cells
Ki-67+ (% of CD3+ T cells)
60
40
20
0
**
Vehicle
Tofacitinib
G
Vehicle
Tofacitinib
10.2
2.36
CD4
CD103
H
No. of CD4+CD103+
cells/100mg tissue
1500
1000
500
0
**
Vehicle
Tofacitinib


A
FMO
Vehicle
Tofacitinib (10 nM)
Tofacitinib (30 nM)
HC
GCA
Isotype
23.6%
13.4%
9.66%
30.8%
14.6%
11.1%
IFN-γ
CD4
B
IFNγ+ CD4 T cells (%)
Tofacitinib (nM)
0
10
20
30
*
***
HC
GCA

Clinical Rheumatology (2022) 41:33–44
https://doi.org/10.1007/s10067-021-05973-4

REVIEW ARTICLE

A systematic review of clinical and preclinical evidences for Janus kinase inhibitors in large vessel vasculitis

Upendra Rathore[1] · Darpan Radheshyam Thakare[1] · Pallavi Patro[2] · Vikas Agarwal[1] · Aman Sharma[3] · Durga Prasanna Misra[1]

Table 2 Summary of outcomes of the cohort studies

Study [reference]/ disease	Drug	Clinical response	Normalization of inflammatory markers	Angiographic retardation (stabilization or improvement)	PET-CT	Relapses	Prednisolone dose before and after
Li et al. [34]/ TAK	Tofacitinib	↑ (4/5 patients)	↑ (4/5 patients)	↑ (3/5 patients)	NA	NA	↑ (2/5 patients)
Kong et al. [41]/ TAK	Tofacitinib (vs MTX)	↑ (CR vs MTX at 12 months; CR or PR vs MTX at 6 months)	NA	↑↓ (vs MTX)	NA	↑↓ (vs MTX)	↑↓ (vs MTX)
Régnier et al. [18]/ TAK	Baricitinib or Ruxolitinib	↑ (3/3 patients)	↑ (2/3 patients)	NA	NA	NA	↑ (2/3 patients)
Camellino et al. [39]/ LVV with/ without PMR, GCA	Baricitinib	↑ (improvement in the PMR-AS in those with PMR with or without LVV)	NA	↑ (One patient with PMR with LVV demonstrated angiographic retardation; not reported for others)	NA	NA	NA

Jakinibs in CTDs. Dermatomyositis

RHEUMATOLOGY

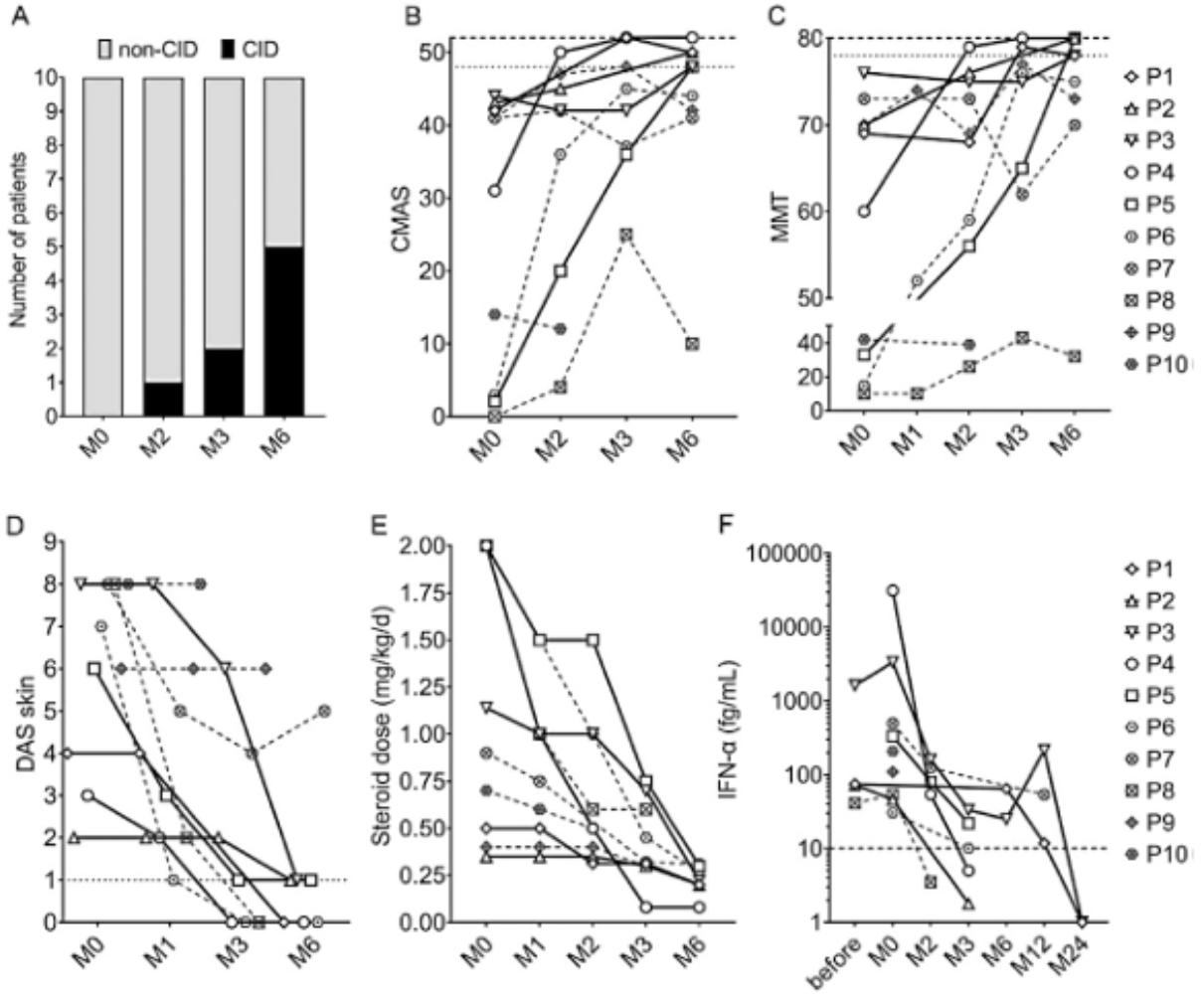
Rheumatology 2021;60:5801–5808
doi:10.1093/rheumatology/keab116
Advance Access publication 12 February 2021

Concise report

JAK inhibitors are effective in a subset of patients with juvenile dermatomyositis: a monocentric retrospective study

Tom Le Voyer[1,2], Cyril Gitiaux[3,4], François-Jérôme Authier[5,6], Christine Bodemer[7], Isabelle Melki [1,8,9], Pierre Quartier [1,10], Florence Aeschlimann[1,10], Arnaud Isapof[11], Jean Philippe Herbeuval[12], Vincent Bondet[13], Jean-Luc Charuel[14], Marie-Louise Frémond[8], Darragh Duffy[13], Mathieu P. Rodero[12] and Brigitte Bader-Meunier[1,10]

FIG. 1 Change in disease activity in 10 patients with JDM on JAKi treatment



Drug/JAK			Comparator (versus)								
			State of investigation	Rheumatoid arthritis	Psoriatic arthritis	Ankylosing spondylitis	Chronic plaque psoriasis	Ulcerative colitis	Crohn's disease	Atopic dermatitis	Systemic lupus erythm
Non-selective	Tofacitinib	JAK1-3	versus PLC							(topical)	
			versus TNF(R)i	ADA (NI)	ADA		ETN (NI)				
			State	Approved	Approved	Approved	Phase III[a]	Approved	Phase II	Phase II	Phase I[c]
	Peficitinib	JAK1-3	versus PLC								
			versus TNF(R)i								
			State	Appr. (JPN)			Phase II	Phase II			
	Baricitinib	JAK1,2	versus PLC				8/10 mg[b]				
			versus TNF(R)i	ADA (S)							
			State	Approved			Phase II			Approved	Phase III
Selective	Upadacitinib	JAK1,2	versus PLC								
			versus TNF(R)i	ADA (S)	ADA (NI/S)						
			State	Approved	Approved	Approved		Approved	Approved	Approved	Phase II[d]
	Filgotinib	JAK1	versus PLC								
			versus TNF(R)i	ADA (NI)							
			State	Appr. (EU)	Phase II	Phase II		Approved	Phase II		