

Traitements actuels du syndrome de Sjögren



15^{ème} Congrès Annuel
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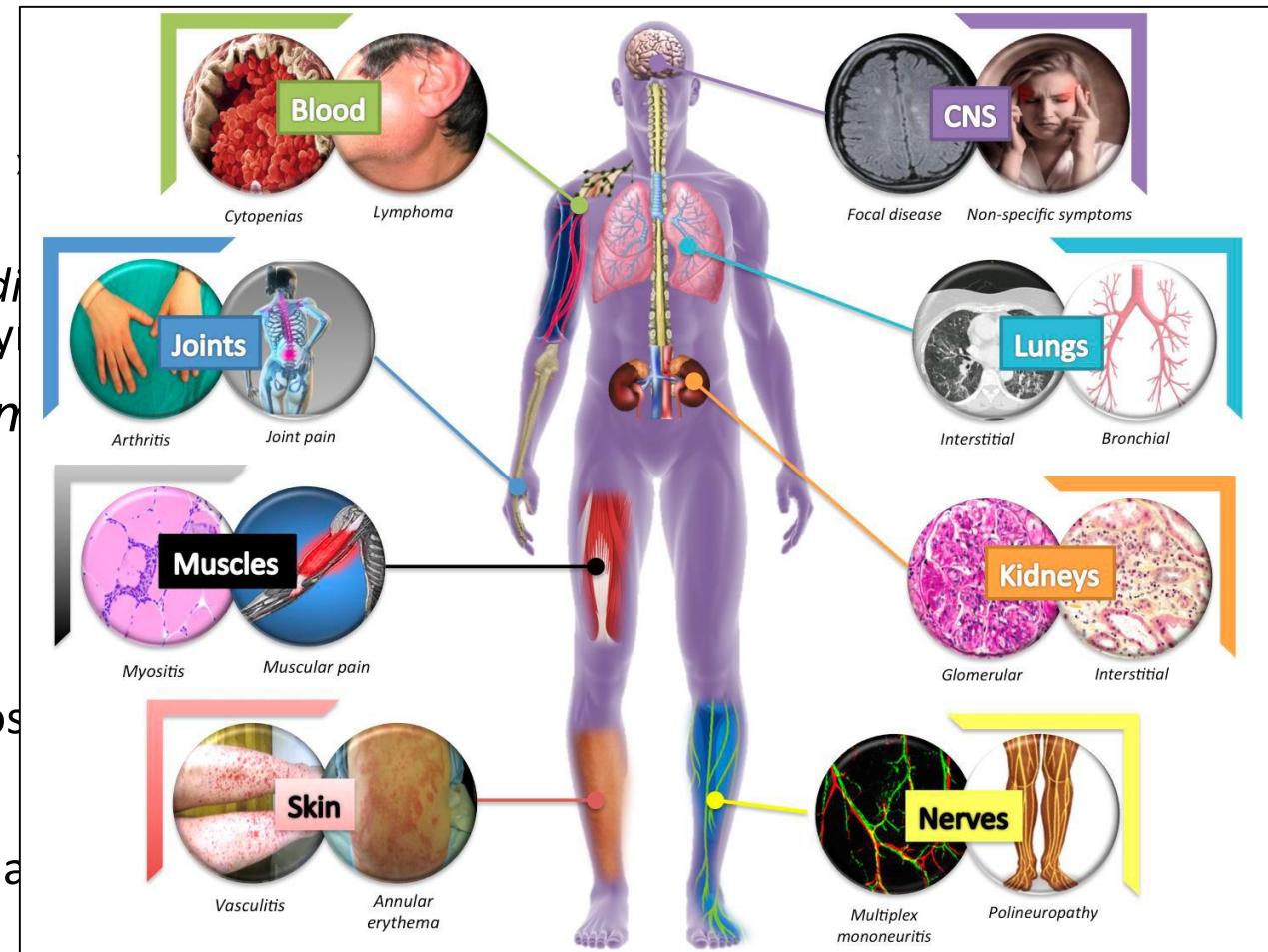
Présentation clinique : glandulaire/systémique

Formes évolutives

- Forme chronique « épithéliale » ou « glandulaire » : arthromyalgies
- Forme évolutive « extra épithéliale » (« Sjögren disease ») : complications (vascularite cryoglobulinémique, lymphome)

Facteurs de mauvais pronostic = FDR de forme évolutive

- Jeune âge (<35 ans)
- Tuméfactions parotidiennes
- Lymphopénie (CD4)
- Hypergammaglobulinémie, purpura d'hyperviscosité
- ANA (anti-SSA, SSB)
- Cryoglobulinémie, hypocomplémentémie, vasculite
- Gammapathie monoclonale
- ESSDAI élevée et Cryoglobuline (Brito-Zeron et al. Lancet 2023;61)
- Centres germinatifs dans la BGSA



Comment évaluer l'activité de la maladie de Sjögren ?

Manifestations systémiques cliniques et biologiques

Score ESSDAI = EULAR Sjogren Syndrome Disease Activity Index (score composite)

Item	Score min	Score max		Item	Score min	Score max	Biologie	Score min	Score max
Constitutionnels (fièvre, sueurs, poids)	0	6		Musculaire (myosite)	0	18	Biologique	0	6
Lymphadénopathies	0	12		Neurologique périphérique	0	15	Biologique (cytopénie)	0	6
Glandulaire (parotides, sous max)	0	4		Neurologique centrale	0	15	Immunologique (complément, cryo, gammaglobuline, pic mono)	0	2
Articulaire (arthralgies, synovites)	0	6							
Cutanée (érythème, vascularite, purpura)	0	9							
Pulmonaire (toux, dyspnée, PID, EFR)	0	15							
Rénale (prot, tubulopathie, I Rénale,)	0	15							

Score maximum = 123
Score ≥ 5 = maladie active

Comment évaluer l'activité de la maladie de Sjögren ?

Symptômes généraux

Score ESSPRI (EULAR Sjogren's Syndrome Patient Reported Index)

1) Comment évalueriez-vous l'intensité de votre **sécheresse** au cours de ces 2 dernières semaines ?

Pas de sécheresse	<input type="checkbox"/>	Sécheresse maximale imaginable									
	0	1	2	3	4	5	6	7	8	9	10

2) Comment évalueriez-vous l'intensité de votre **fatigue** au cours des 2 dernières semaines ?

Pas de fatigue	<input type="checkbox"/>	Fatigue maximale imaginable									
	0	1	2	3	4	5	6	7	8	9	10

3) Comment évalueriez-vous l'intensité de vos **douleurs** (articulaires et ou musculaires, des membres supérieurs et inférieurs) au cours des 2 dernières semaines ?

Pas de douleur	<input type="checkbox"/>	Douleur maximale imaginable									
	0	1	2	3	4	5	6	7	8	9	10

Score maximum = 10/10
Score ≥ 5 = maladie active

TRAITEMENTS ACTUELS DE LA MALADIE SYSTEMIQUE

- Hydroxychloroquine
- Corticoïdes
- Immunosuppresseurs/Ig IV
- Thérapies ciblées

Biothérapies

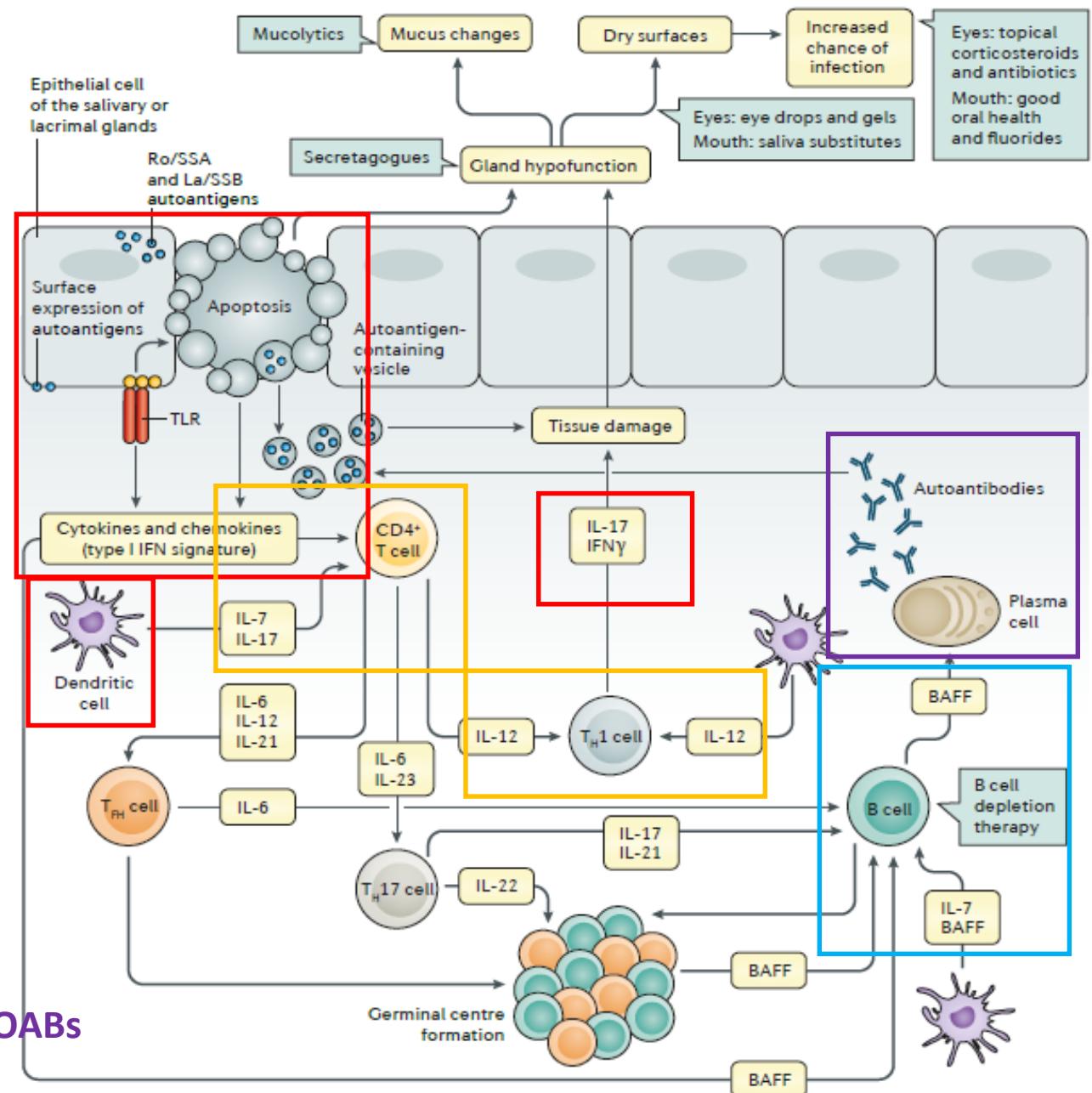
Physiopathologie : principales « voies »

INTERFERONS

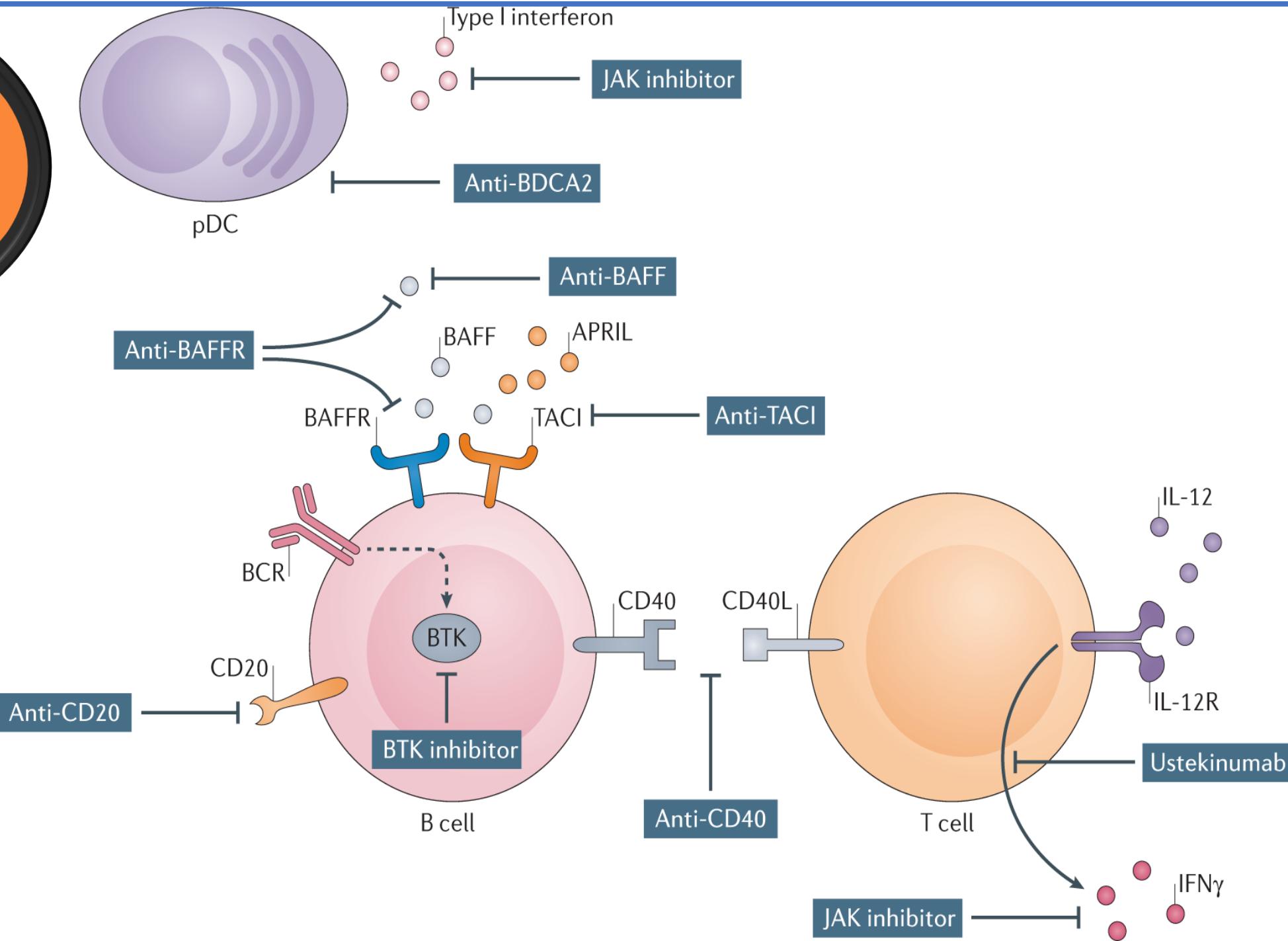
T CELLS

B CELLS

PLASMA CELLS & AUTOABS



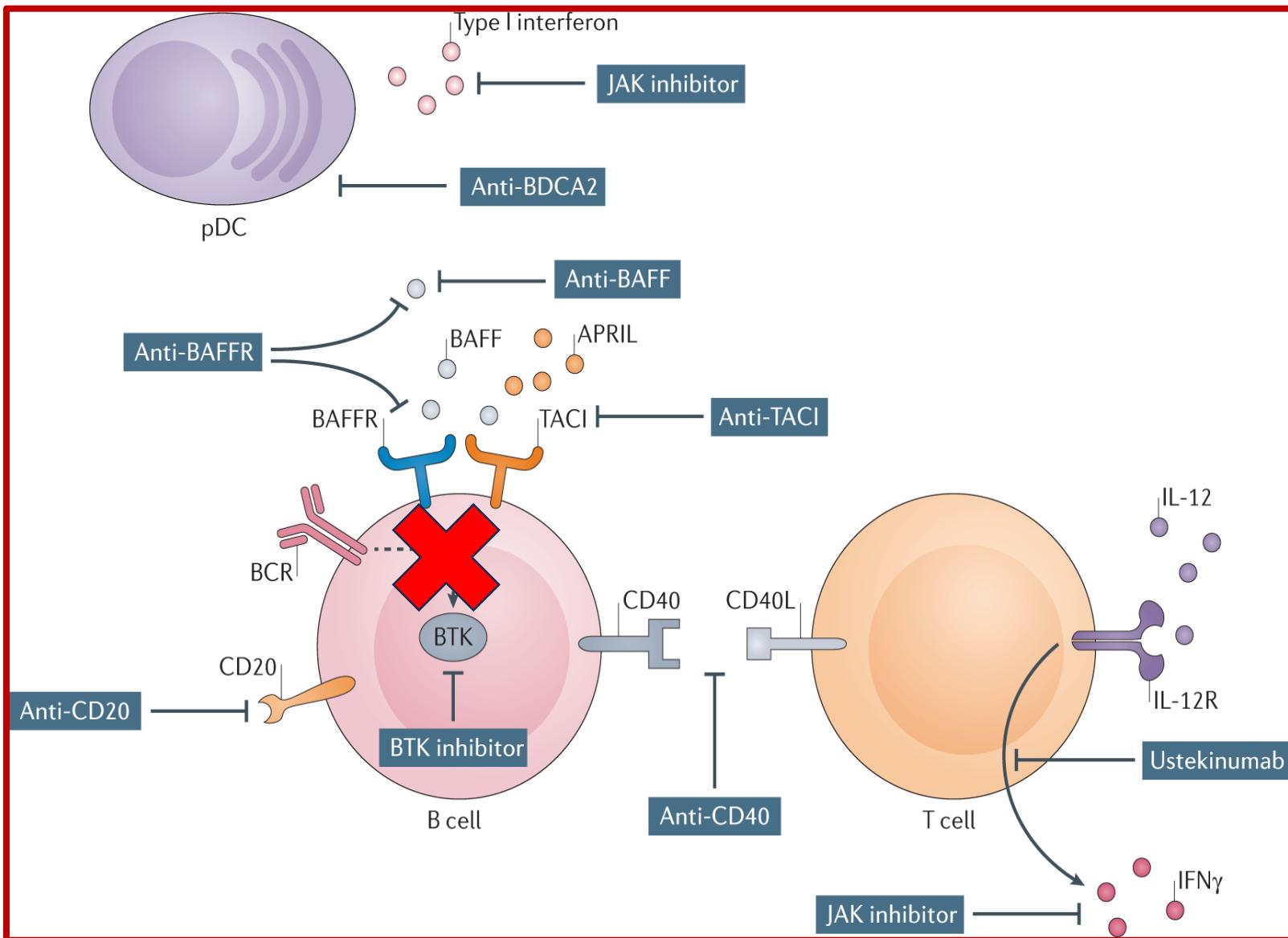
Biothérapies = cibles



BIOTHERAPIES DANS LE SYNDROME DE SJOGREN

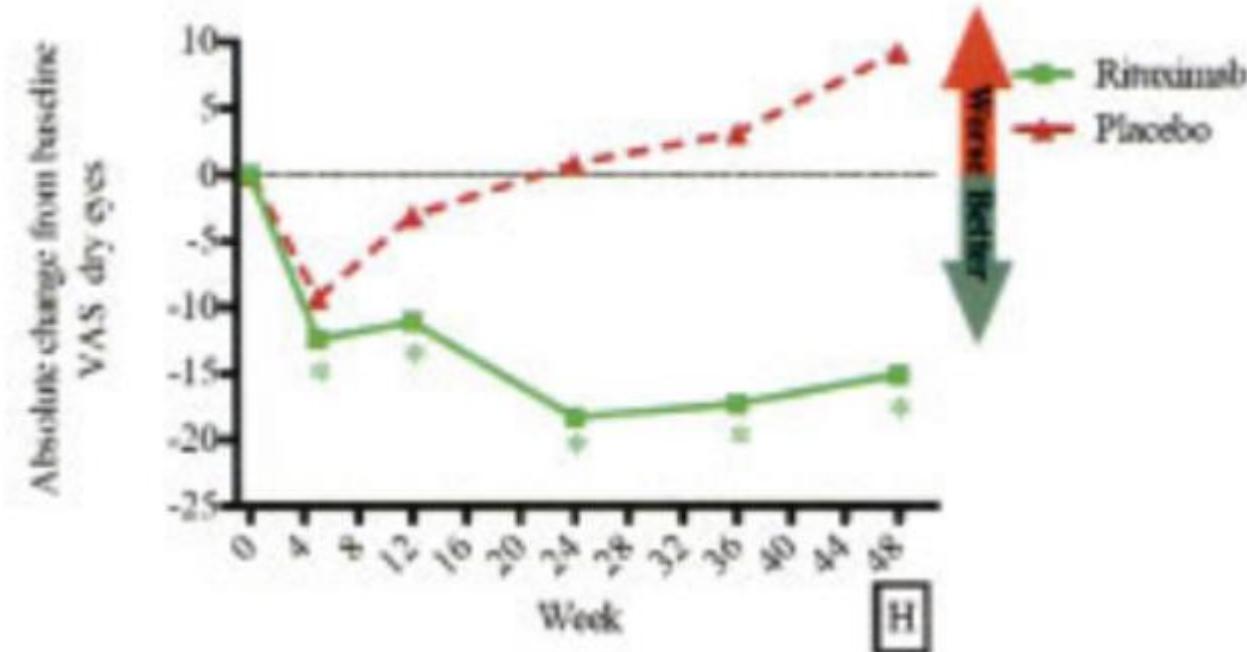
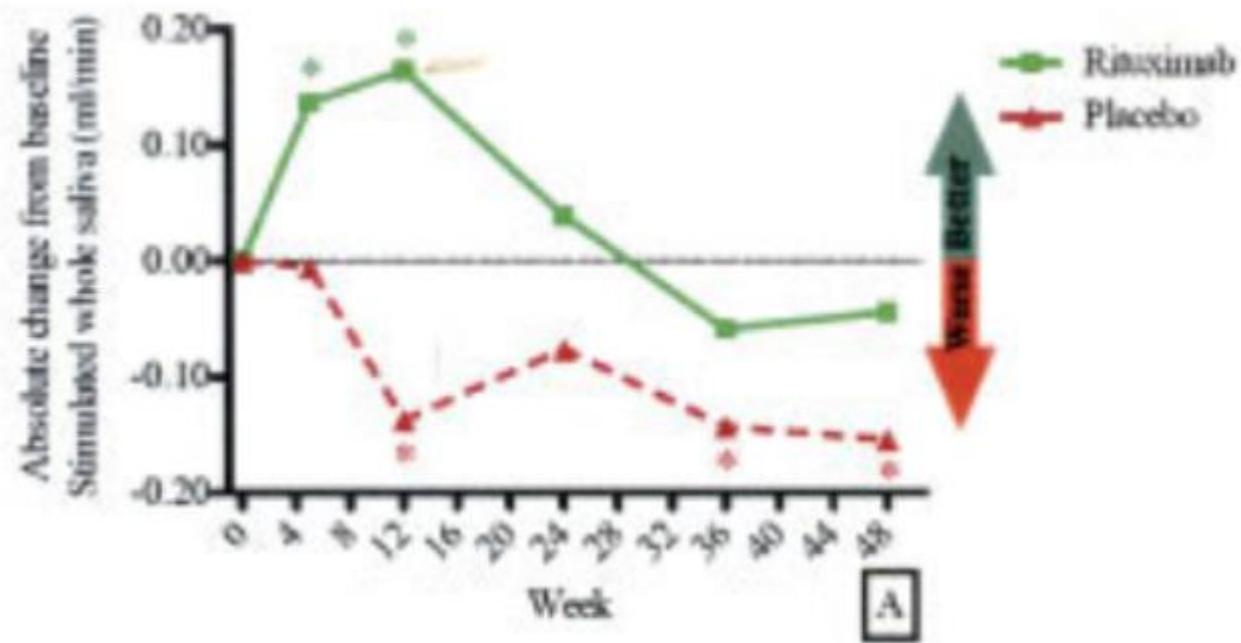
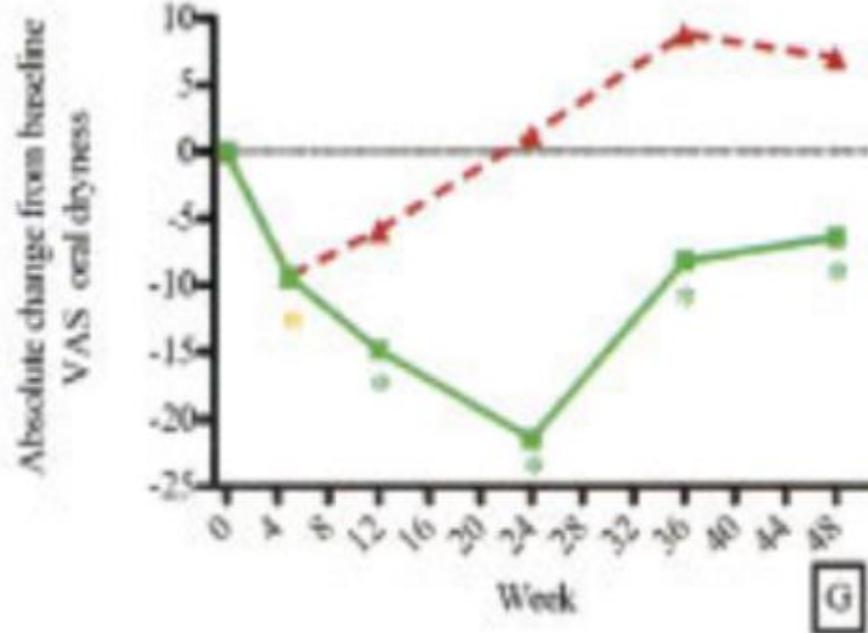
Beaucoup de déceptions, quelques lueurs
d'espoir

Déplétion lymphocytaire B



Rituximab

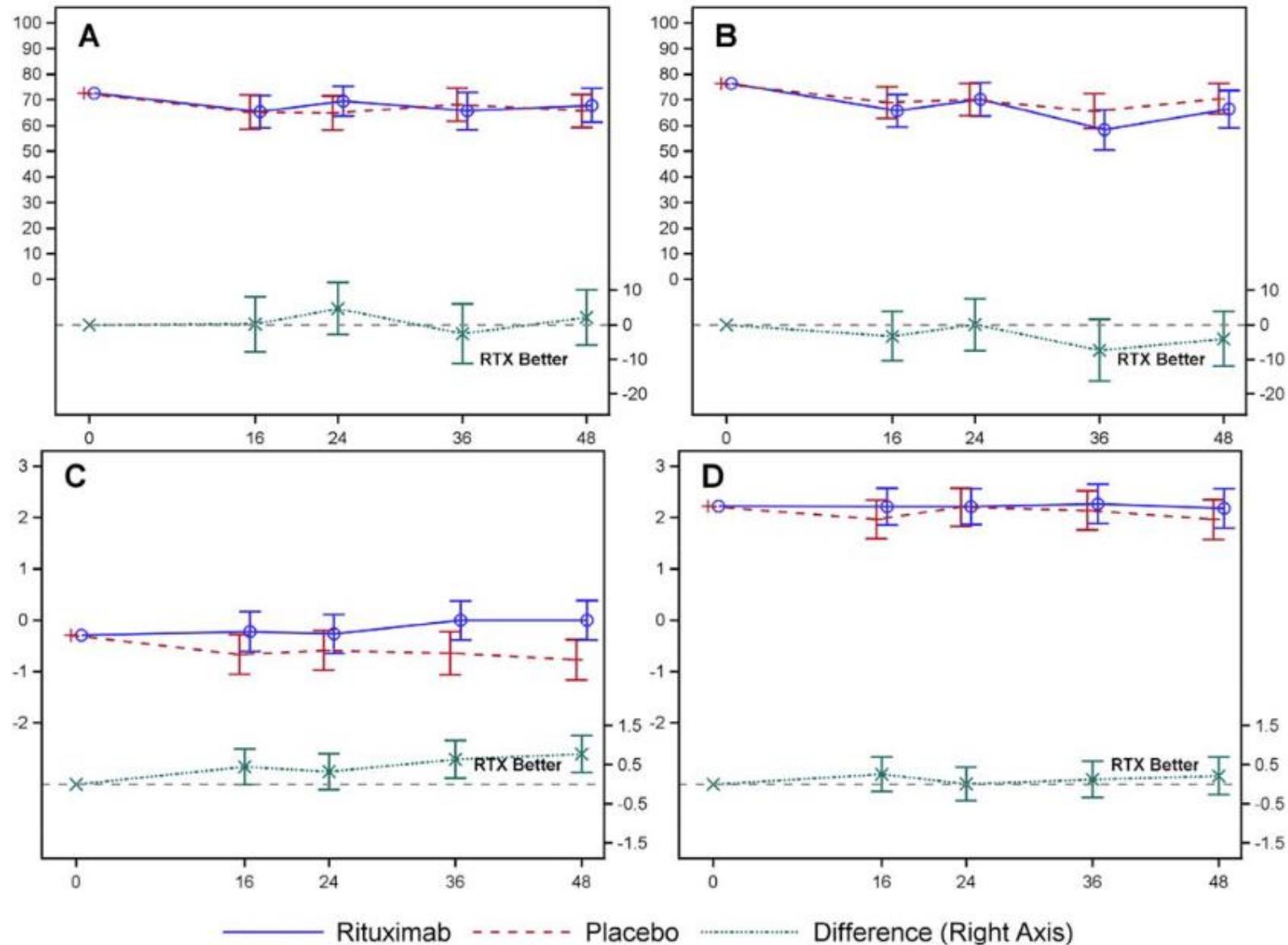
Meijer et al 2010



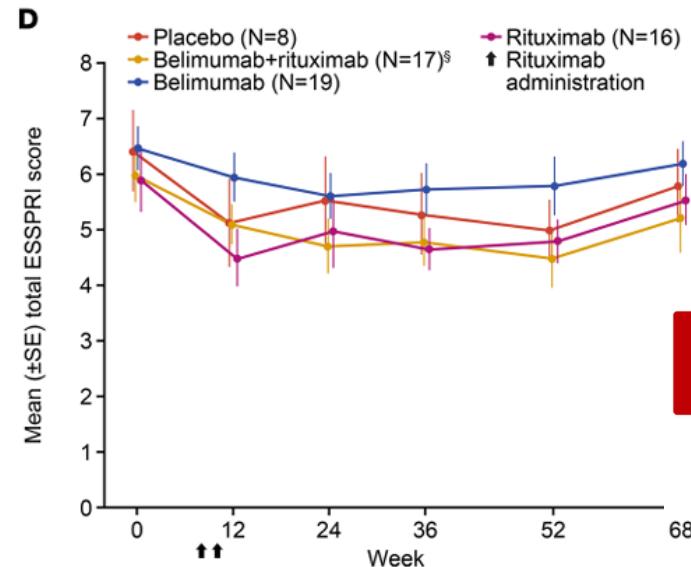
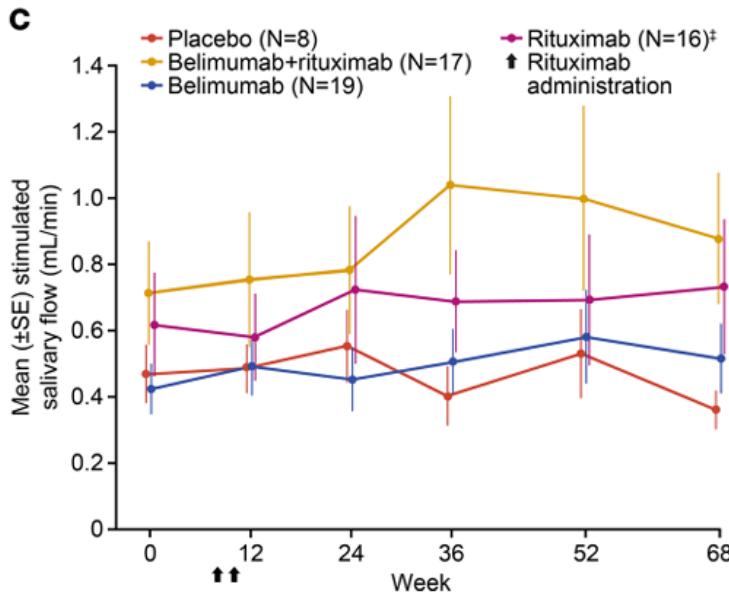
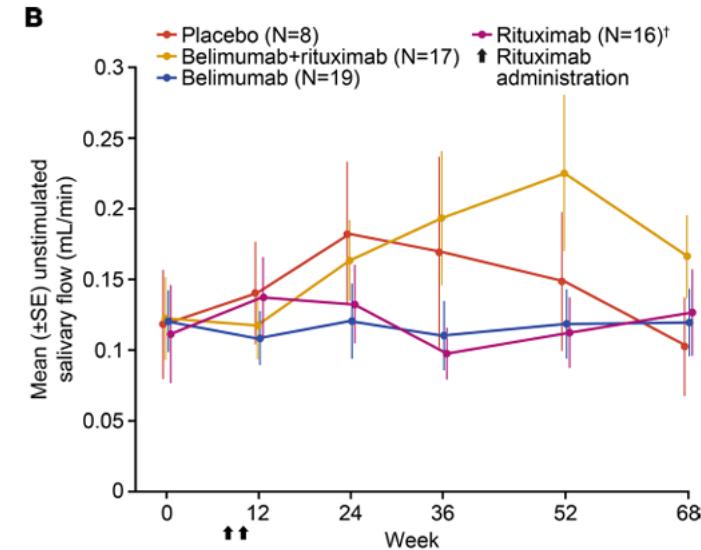
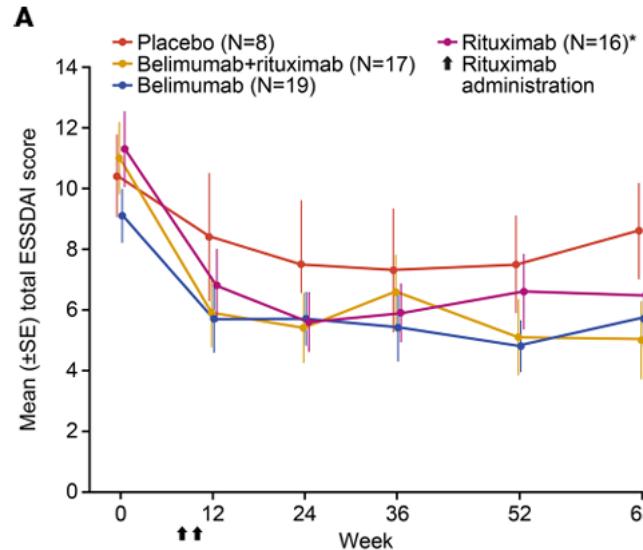
Rituximab: Bowman et al 2017



- A Fatigue
- B xerostomie
- C FS non stimulé (NS sur le flux salivaire stimulé)
- D Flux lacrymal (5 min)

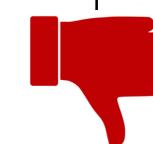
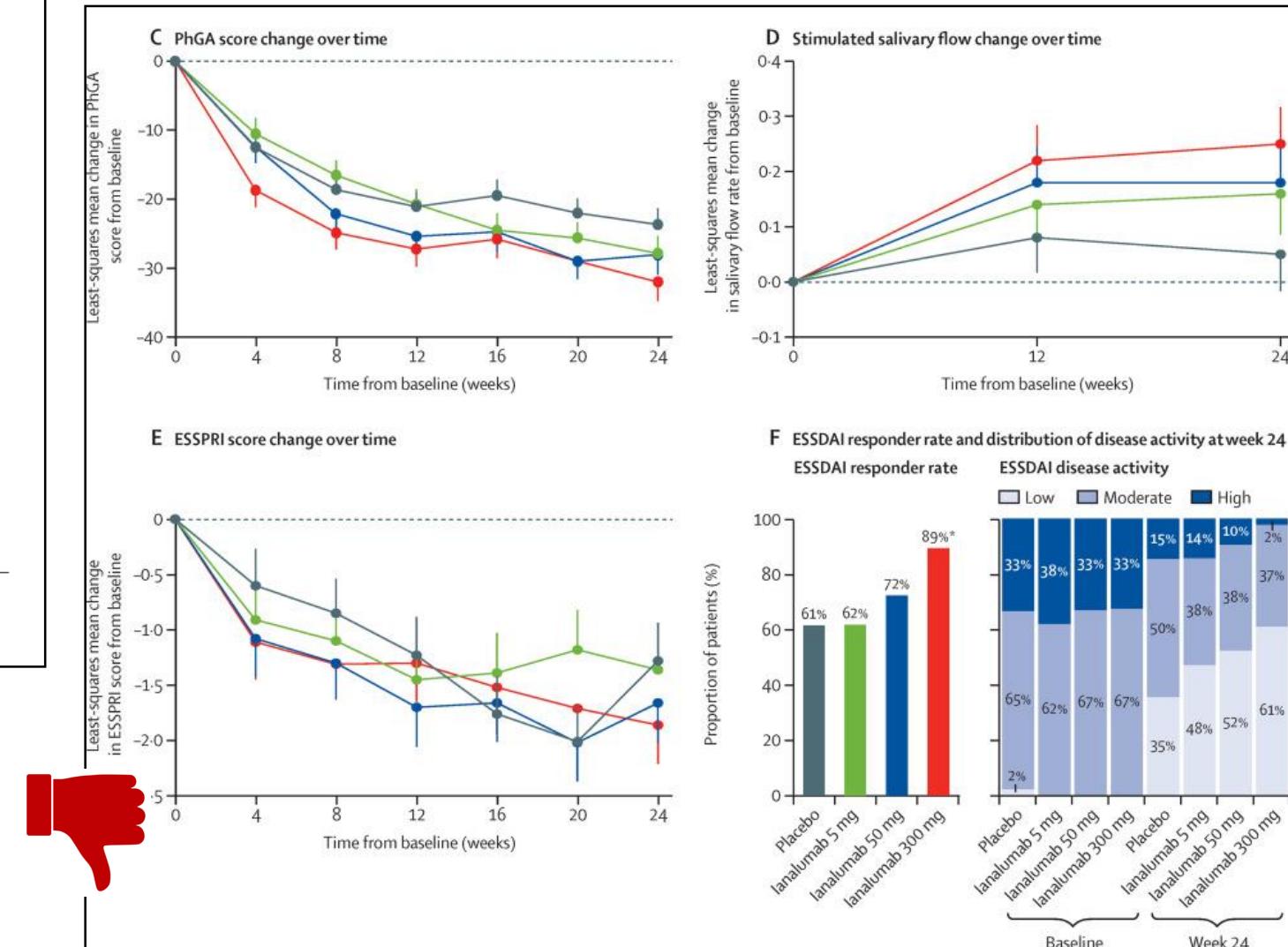
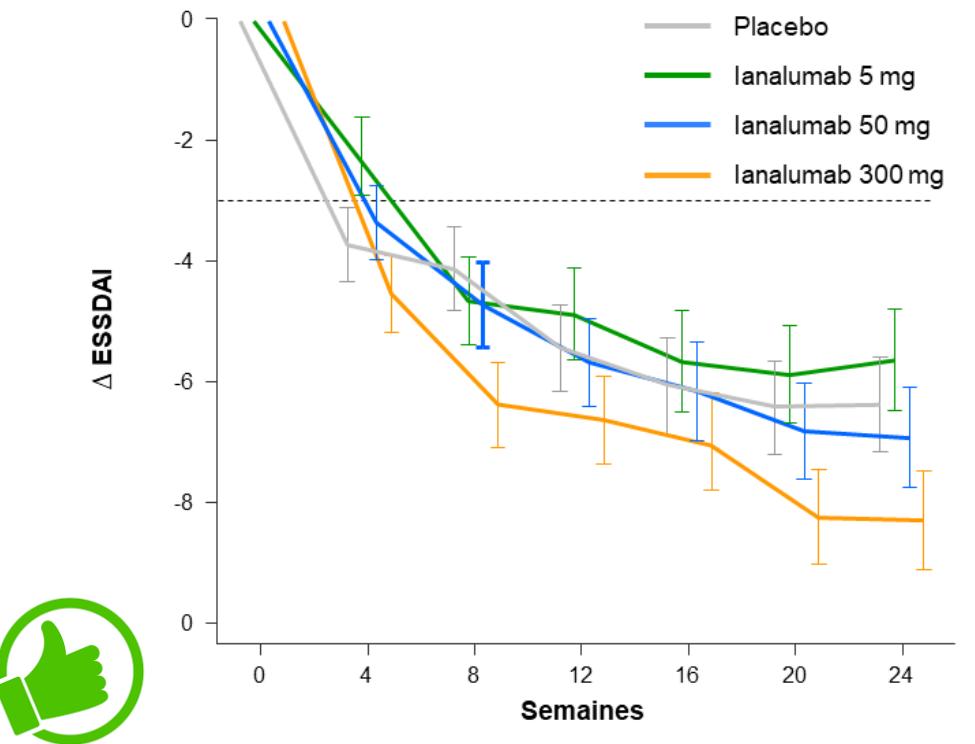


Rituximab/Belimumab: Mariette et al 2022



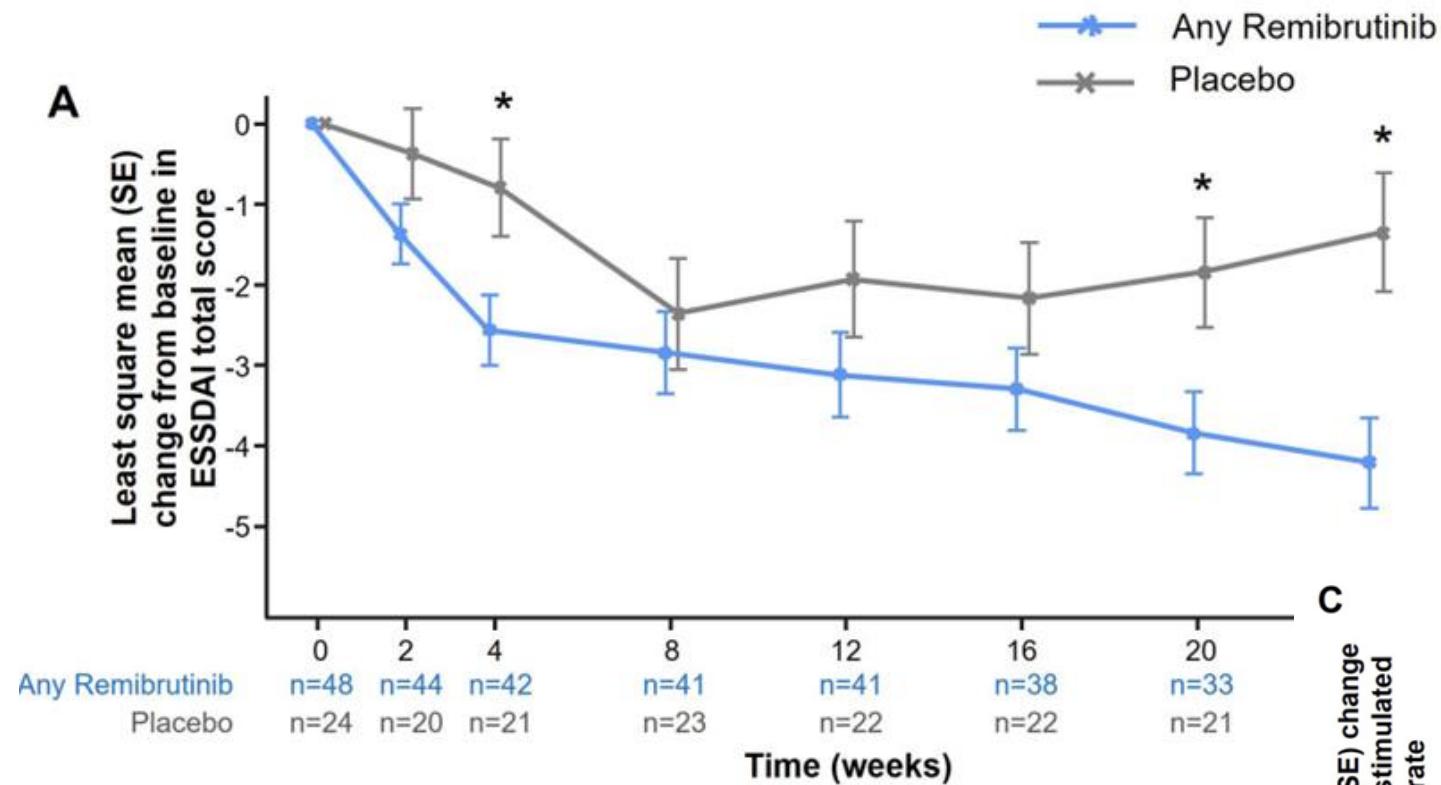
Ionalumab (anti-BAFF R): Bowman et al 2022

Évolution de l'ESSDAI entre l'inclusion et la semaine 24

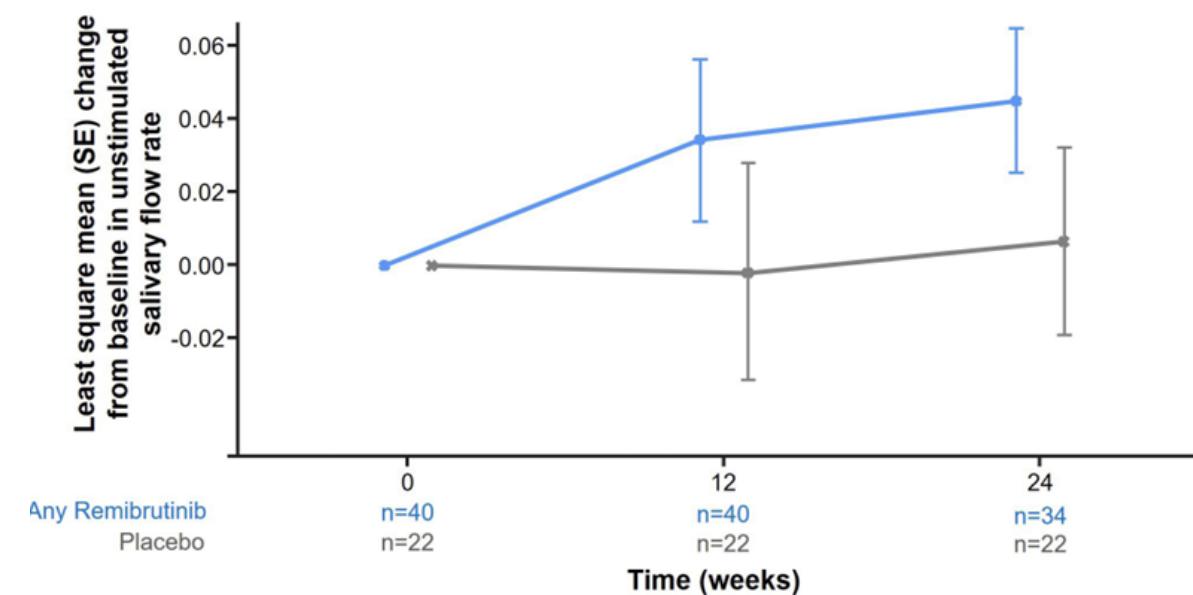


Remibrutinib (anti-BTK): Dorner et al 2024

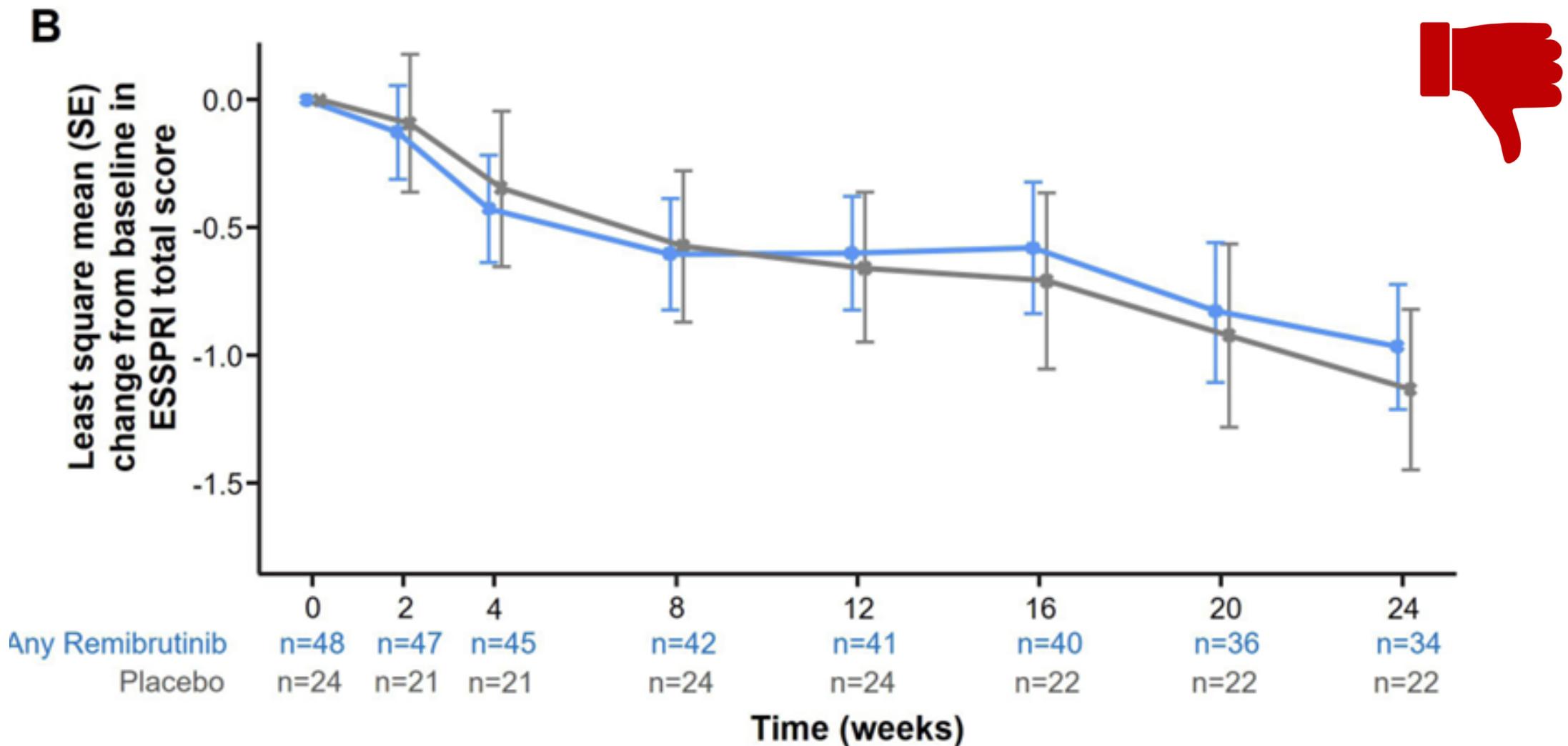
A



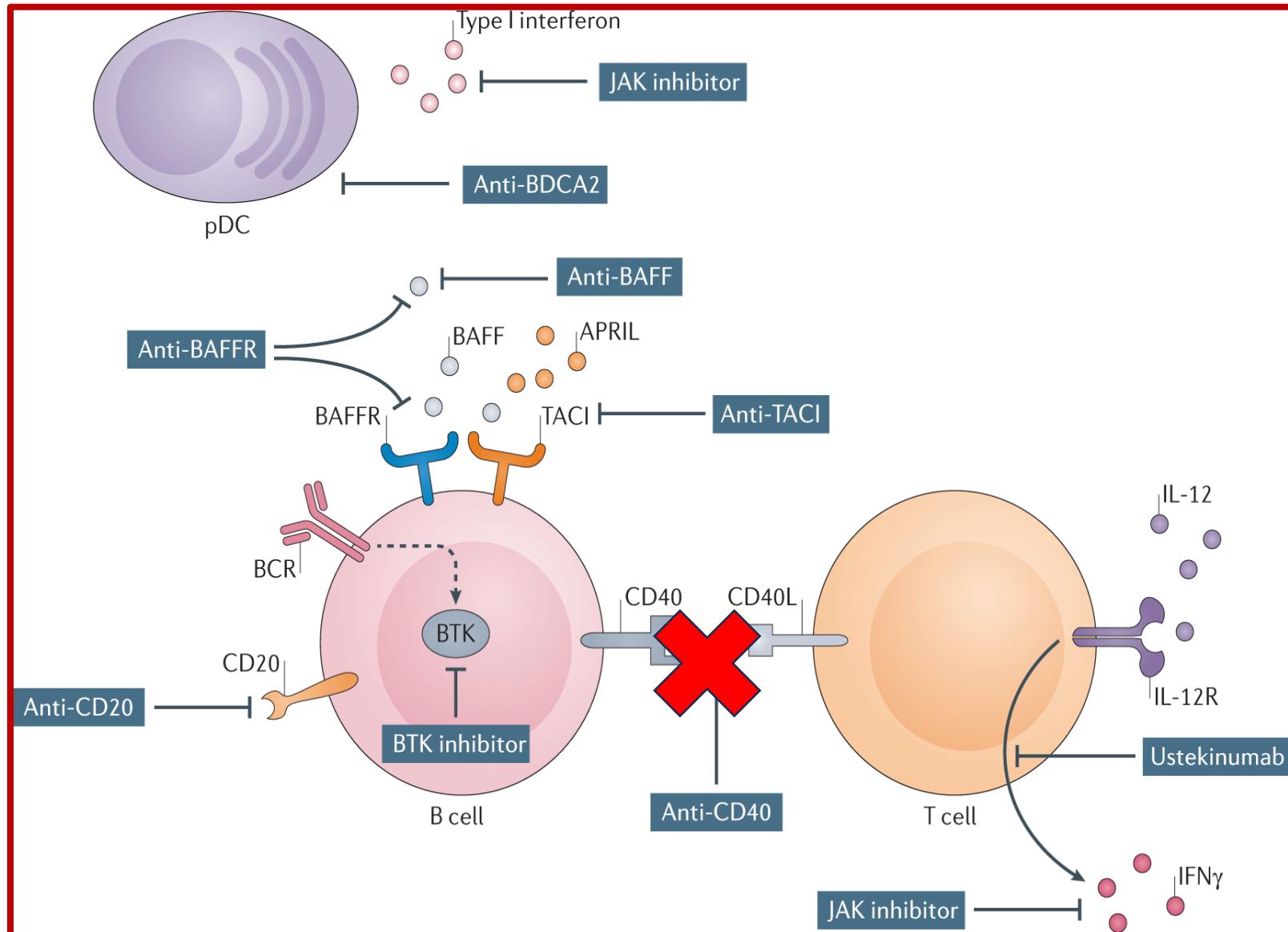
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Remibrutinib (anti-BTK): Dorner et al 2024

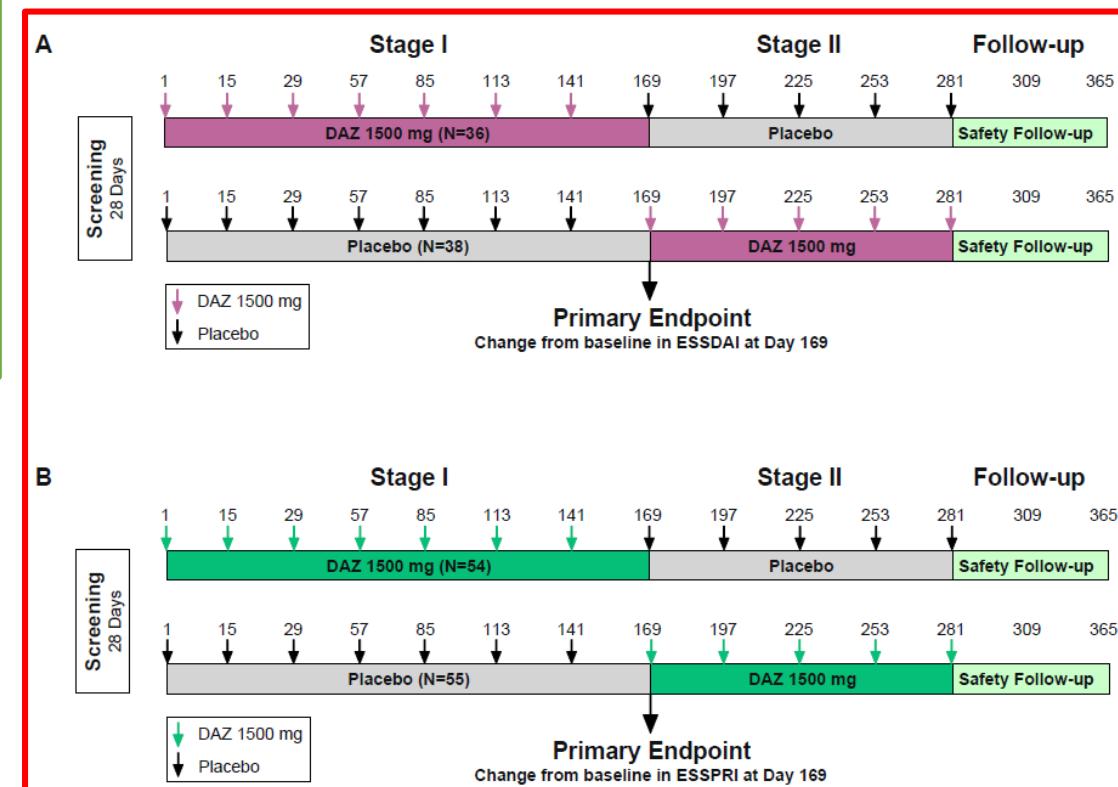
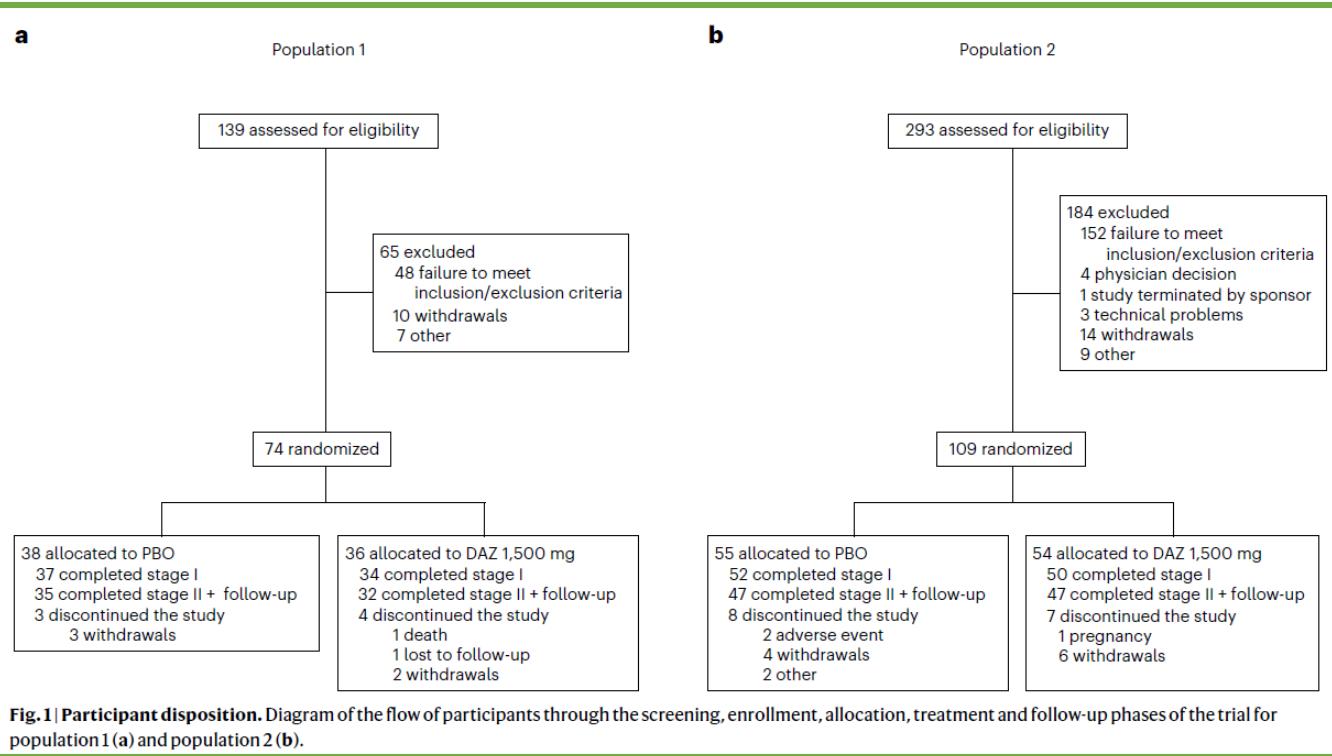


Inhibition de la co-stimulation lymphocytaire via CD40-CD40L



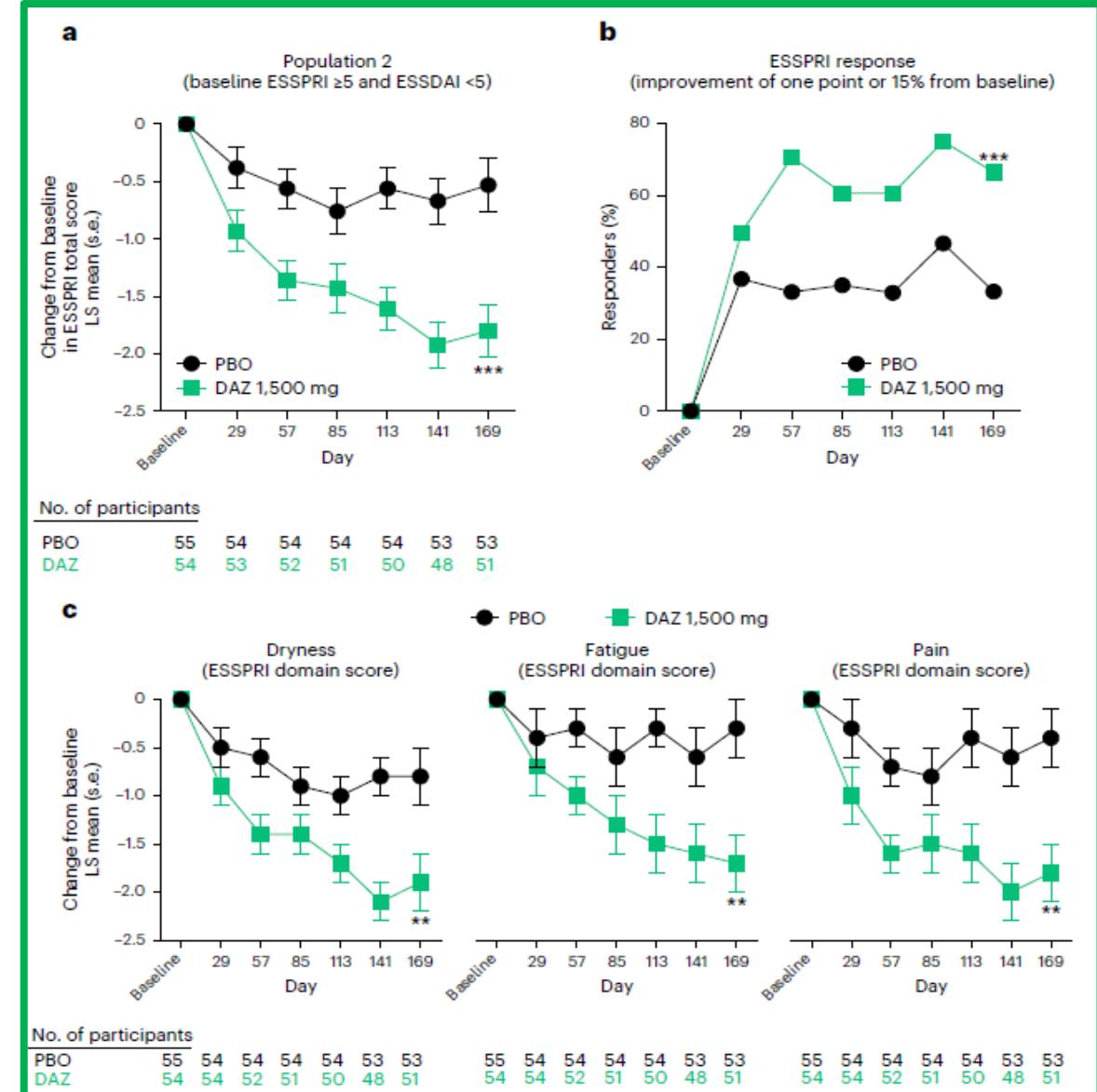
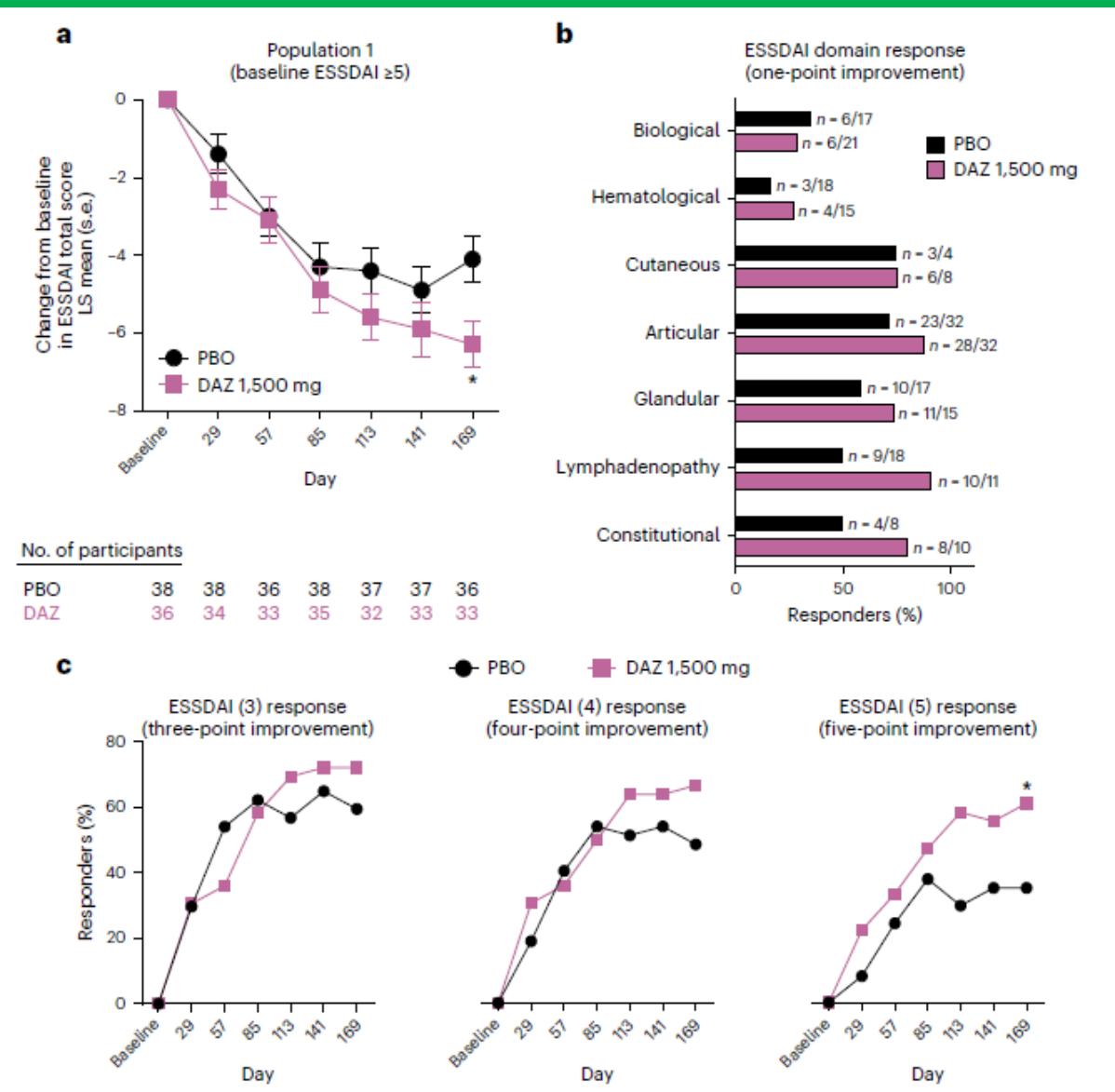
CD40 ligand antagonist dazodilibep in Sjögren's disease

A randomized, double-blinded, placebo-controlled, phase 2 trial (Nature Medicine 2024)



CD40 ligand antagonist dazodalibep in Sjögren's disease

A randomized, double-blinded, placebo-controlled, phase 2 trial (Nature Medicine 2024)

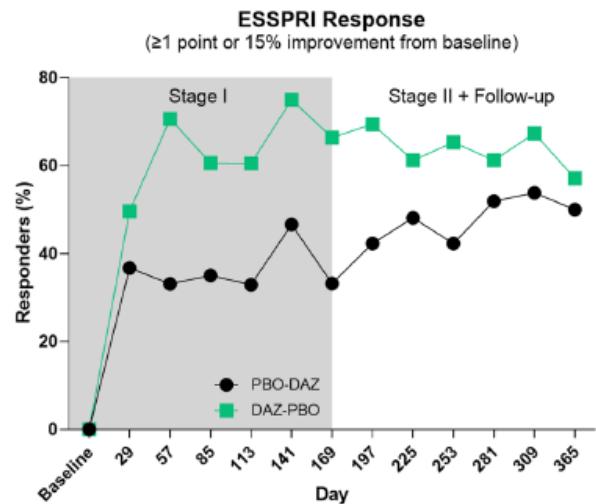


CD40 ligand antagonist dazodalibep in Sjögren's disease

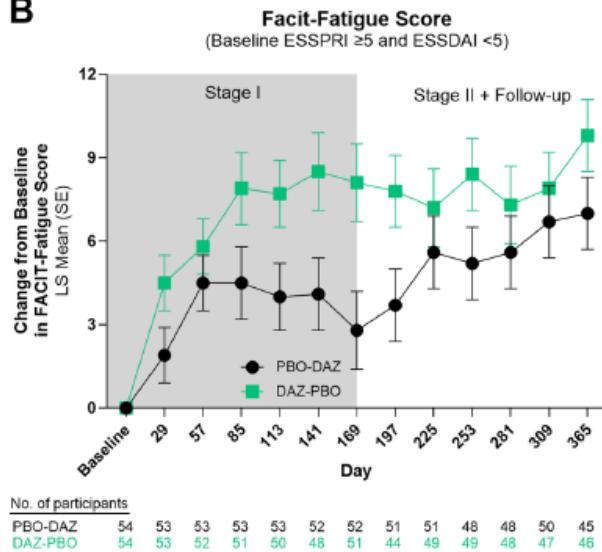
A randomized, double-blinded, placebo-controlled, phase 2 trial (Nature Medicine 2024)



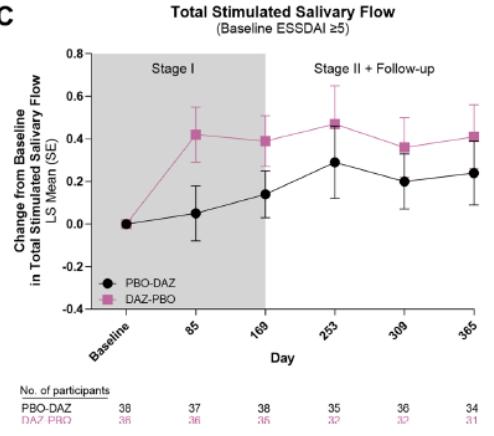
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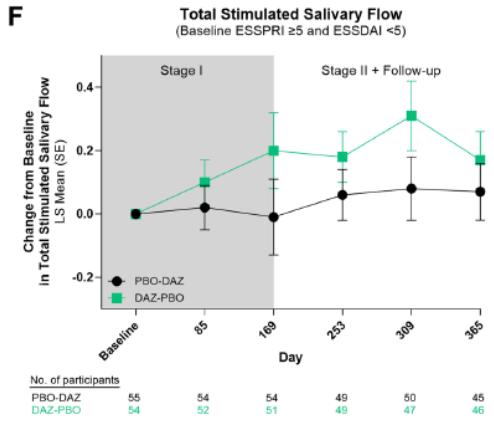
B



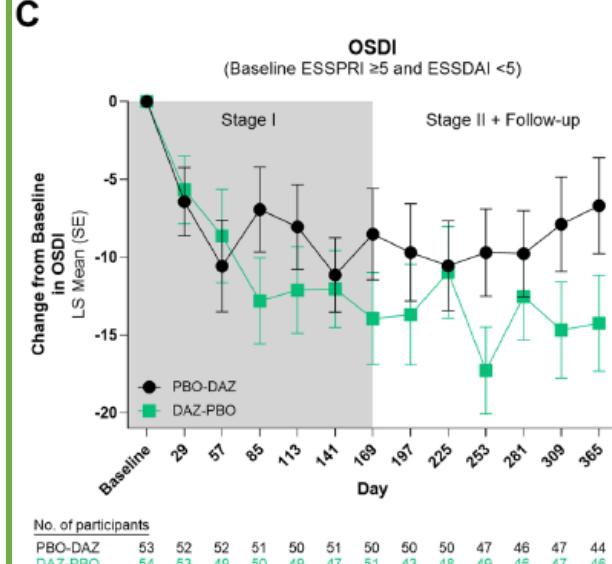
C



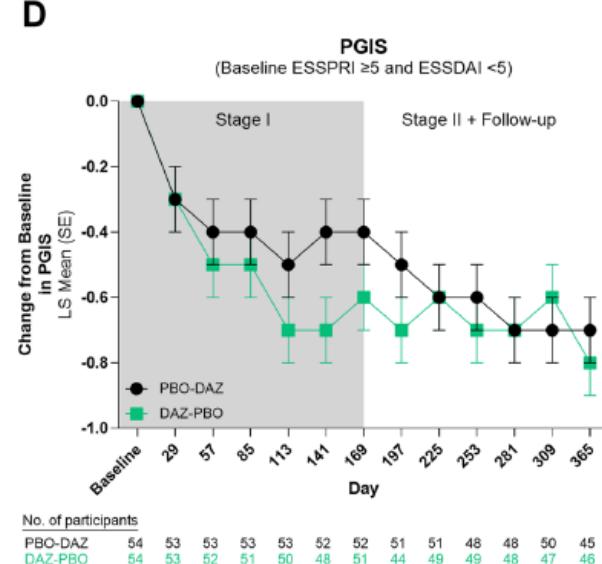
F



C



D



Anti-CD40, ISCALIMAB, in Sjögren's disease

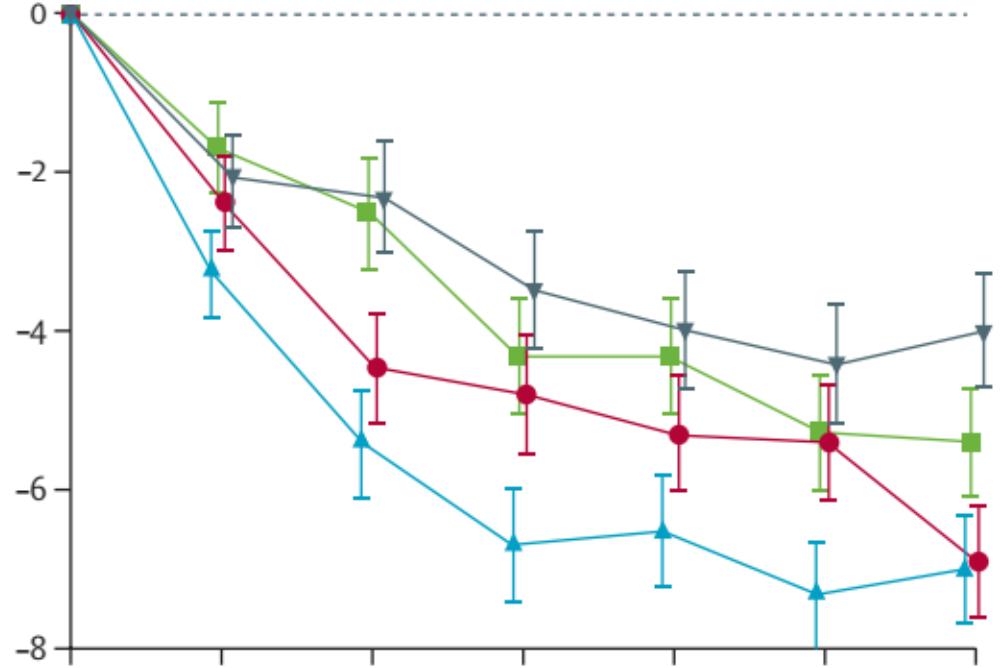
A randomised, double-blind, placebo-controlled, phase 2b (Lancet, 2024)



A Cohort 1: ESSDAI score change over 24 weeks

- Placebo
- Iscalimab 150 mg
- Iscalimab 300 mg
- Iscalimab 600 mg

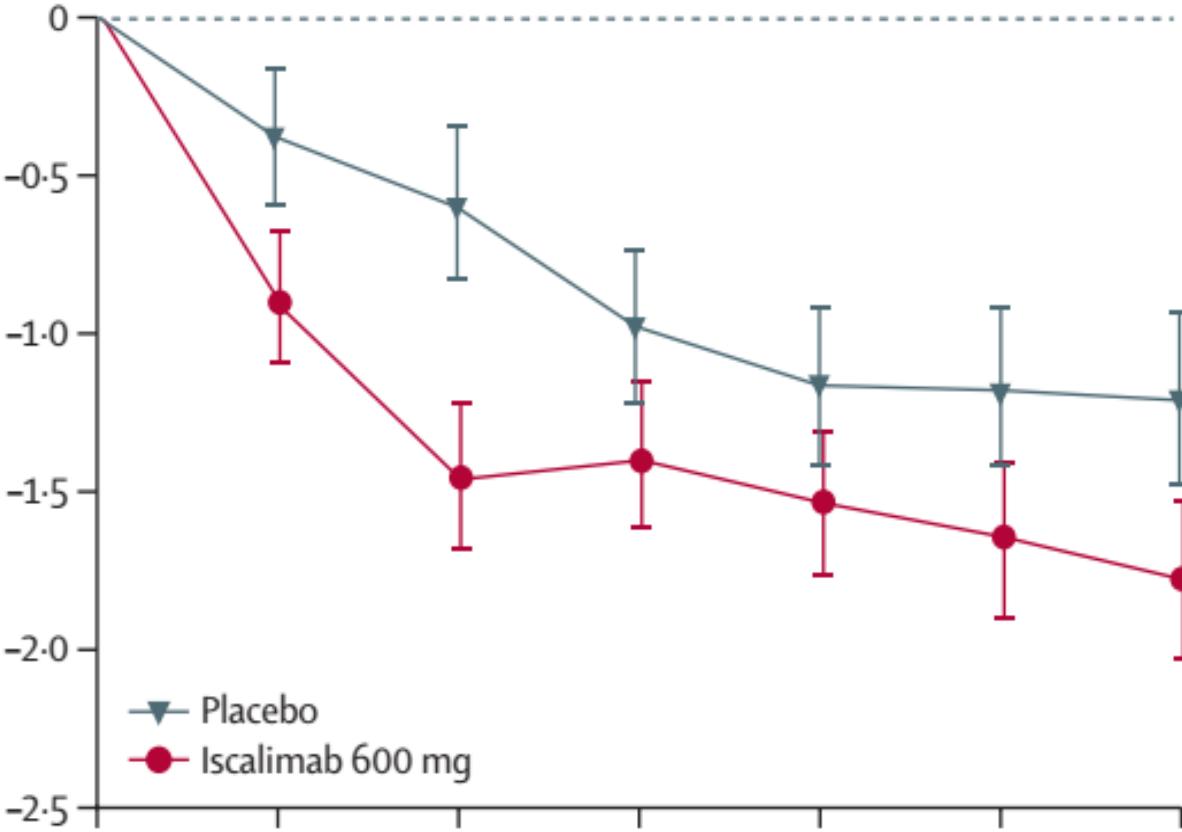
Least squares mean (\pm SE) change from baseline



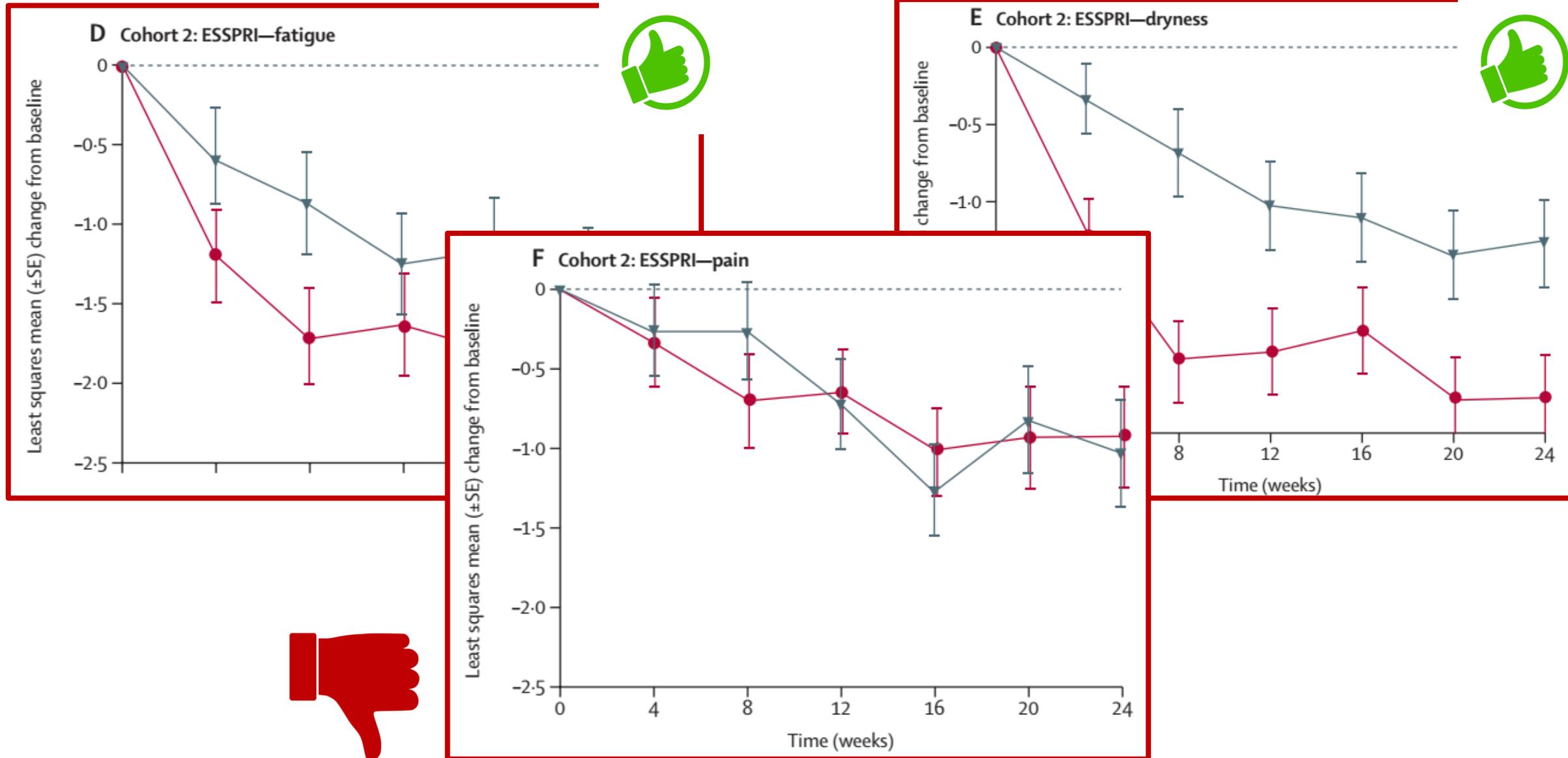
C Cohort 2: ESSPRI score change over 24 weeks

- Placebo
- Iscalimab 600 mg

Least squares mean (\pm SE) change from baseline



Anti-CD40, ISCALIMAB, in Sjögren's disease
A randomised, double-blind, placebo-controlled, phase 2b (Lancet, 2024)



Autres échecs : anti- TNF, CTLA-4, IL-1, IL6

ARTHRITIS & RHEUMATISM
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Inefficacy of Infliximab in Primary Sjögren's Syndrome

Results of the Randomized, Controlled Trial of Remicade In Primary Sjögren's Syndrome (TRIPSS)

Xavier Mariette,¹ Philippe Ravaud,² Serge Steinfeld,³ Gabriel Baron,² Joelle Goetz,⁴

OPEN ACCESS Freely available online



Interleukin-1 Inhibition and Fatigue in Primary Sjögren's Syndrome – A Double Blind, Randomised Clinical Trial

Katrine Brække Norheim^{1*}, Erna Harboe¹, Lasse G. Gøransson^{1,2}, Roald Omdal^{1,2}

Sjögren's syndrome



CLINICAL SCIENCE

Efficacy and safety of abatacept in active primary Sjögren's syndrome: results of a phase III, randomised, placebo-controlled trial

Alan N Baer ,¹ Jacques-Eric Gottenberg ,² William St Clair,³ Takayuki Sumida,⁴

Sjögren's syndrome

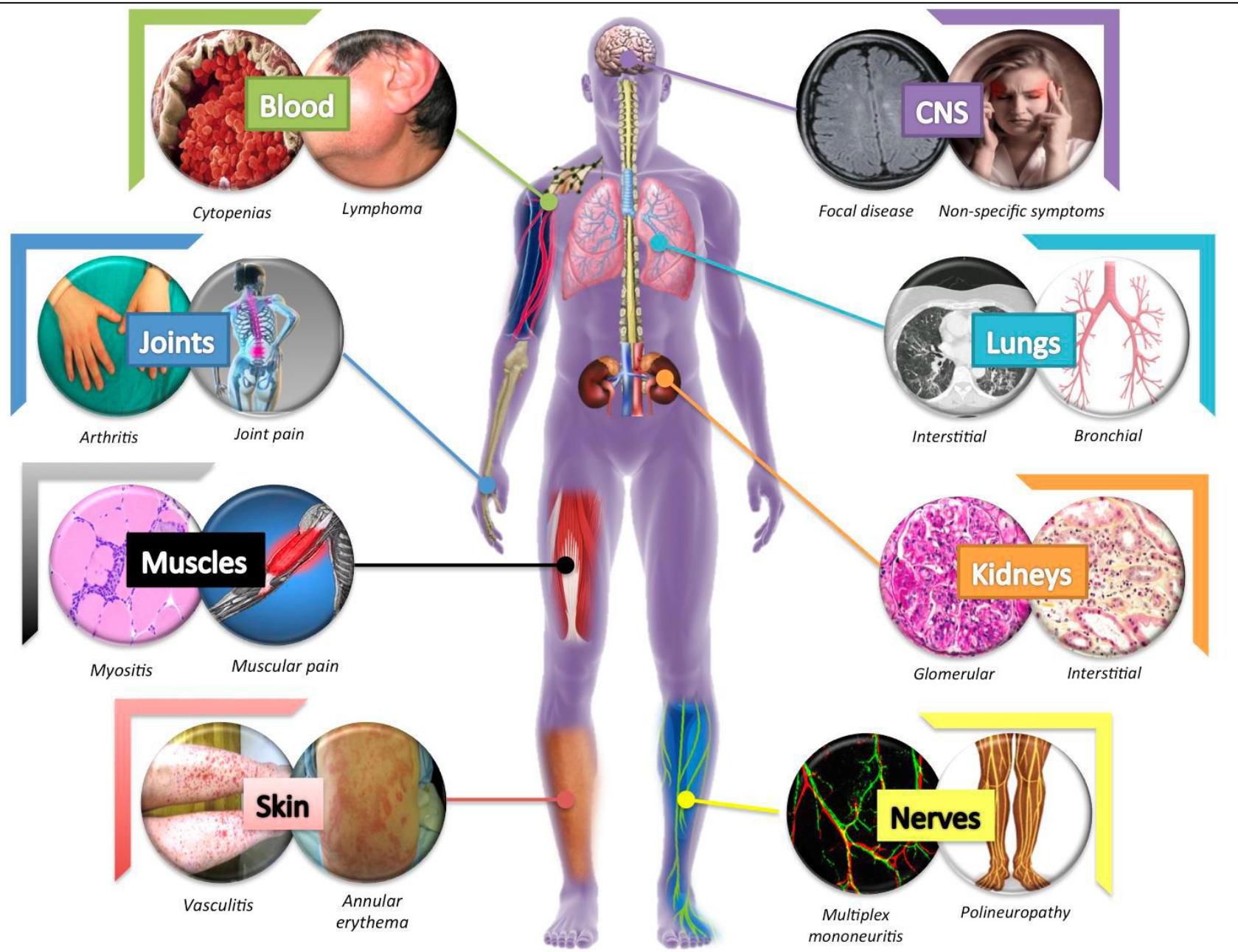
CLINICAL SCIENCE

Interleukin 6 receptor inhibition in primary Sjögren syndrome: a multicentre double-blind randomised placebo-controlled trial

Renaud Felten ,¹ Valérie Devauchelle-Pensec,² Raphaële Seror,³ Pierre Duffau,⁴

BIOTHERAPIES DANS LE SYNDROME DE SJOGREN

Beaucoup de déceptions, quelques lueurs
d'espoir



Traitements selon les organes atteints

EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies

Manuel Ramos-Casals ,^{1,2} Pilar Brito-Zerón,^{2,3} Stefano Bombardieri,⁴ Hendrika Bootsma,⁵ Salvatore De Vita,⁶ Thomas Dörner ,⁷ Benjamin A Fisher , Jacques-Eric Gottenberg,¹⁰ Gabriela Hernandez-Molina ,¹¹ Agnes Kocher ,^{12,1} Belchin Kostov,^{14,15} Aike A. Kruize,¹⁶ Thomas Mandl,¹⁷ Wan-Fai Ng,^{18,19} Soledad Retamozo,^{20,21} Raphaële Seror,^{22,23} Yehuda Shoenfeld,^{24,25} Antoni Sisó-Almirall ,^{14,26} Athanasios G. Tzioufas,²⁷ Claudio Vitali,²⁸ Simon Bowman,²⁹ Xavier Mariette,^{22,23} On behalf of the EULAR-Sjögren Syndrome Task Force Group



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Review article

French national diagnostic and care protocol for Sjögren's disease

Protocole national de diagnostic et de soins – Maladie de Sjögren

Valérie Devauchelle-Pensec ^{a,2,*}, Xavier Mariette ^{b,2}, Anas-Alexis Benyoussef^c, Sylvie Boisrame ^d, Béatrice Cochener^c, Divi Cornec^a, Gaëtane Nocturne^b, Jacques Eric Gottenberg^e, Eric Hachulla^f, Pierre Labalette^g, Véronique Le Guern^h, Ruth M'Bwang Seppohⁱ, Jacques Morel^j, Marie Orliaguet^d, Alain Saraux^a, Raphaële Seror^b, Nathalie Costedoat-Chalumeau^h, Collaborators¹

RHEUMATOLOGY

Guidelines



Rheumatology 2021;60:2122–2127
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Advance Access publication 2 February 2021

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AMERICAN COLLEGE
of RHEUMATOLOGY
Empowering Rheumatology Professionals

EXPERT PERSPECTIVES ON CLINICAL CHALLENGES

Expert Perspective: Challenges in Sjögren's Disease

Gaetane Nocturne  and Xavier Mariette 

The management of Sjögren's disease is challenging because of several factors. Indeed, the clinical presentations are heterogeneous, and one must be able to identify prognostic markers to adapt the follow-up. In addition, there is no validated treatment. Nevertheless, international experts have been working for several years to establish recommendations to guide management. Since research in this field is extremely active, we anticipate the development of effective treatments for our patients in the near future.

The management of Sjögren's syndrome: British Society for Rheumatology guideline scope

Elizabeth Price¹, Alexander Allen², Saaheha Rauz³, Anwar Tappuni⁴, Nurhan Sutcliffe ,⁵ Michele Bombardieri⁶, Sara Carty⁷, Coziana Ciurtin ,⁸ Bridget Crampton⁹, Lisa Duncalfe¹⁰, Benjamin Fisher ,¹¹ Peter Glennon¹², Katie L. Hackett ,¹³ Genevieve Larkin¹⁴, Wan-Fai Ng¹⁵, Athimalaipet V. Ramanan¹⁶, Saad Rassam¹⁷, Stephen B. Walsh¹⁸ and Simon Bowman¹⁹

TRAITEMENTS ACTUELS DES MANIFESTATIONS SYSTEMIQUES

- Hydroxychloroquine
- Corticoïdes
- Immunosuppresseurs/Ig IV
- Thérapies ciblées

Hydroxychloroquine



Méta-analyse (Wang SQ et al. BMC Musculoskeletal disorders. 2017;18:186.

Results: Four trials with totals of 215 SS patients, including two randomized controlled trials, one double blind crossover trial and one retrospective open-label study, were analyzed in this review. For dry mouth and dry eyes, the effectiveness of HCQ treatment was essentially the same as placebo treatment. For fatigue, the effectiveness of HCQ was lower than placebo. The efficacy of HCQ in treating pain associated with pSS was superior to that of the placebo. There was no significant difference between HCQ-treated groups and controls in terms of Schirmer test results, but HCQ could reduce the erythrocyte sedimentation rate compare with placebo. A descriptive safety assessment showed that gastrointestinal adverse effects were the most common adverse effects associated with HCQ.

- **Douleurs articulaires inflammatoires ou de polyarthrite**
- **Erythème annulaire limité ou de lésions de lupus cutané en cas d'échec d'un traitement topique (CS ou tacrolimus)**
- **Purpura isolé lié à une à une vascularite cryoglobulinémique**

Immunosuppresseurs/IgIV



Immunosuppresseurs	Indications
Corticoïdes	Traitemennt anti-inflammatoire de base des manifestations systémiques
Méthotrexate	Arthralgies inflammatoires ou polyarthrite R à l'HCQ Myosite

Immunosuppresseurs/IgIV



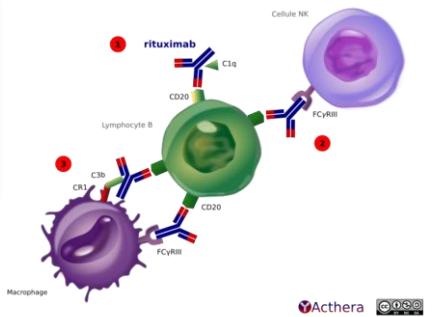
Immunosuppresseurs	Indications
Corticoïdes	Traitemennt anti-inflammatoire de base des manifestations systémiques
Méthotrexate	Arthralgies inflammatoires ou polyarthrite R à l'HCQ Myosite
Léflunomide	Arthralgies inflammatoires ou polyarthrite R à l'HCQ et au MTX (Cl à ces trts) Phase II, 15 patients, mauvaise tolérance et efficacité modeste

Immunosuppresseurs/IgIV



Immunosuppresseurs	Indications
Azathioprine Mycophénolate mofétil	Pneumopathies interstitielles diffuses Néphrite interstitielle Cytopénies Myosite Neuropathies sensitivo-motrices (vascularite)
Cyclophosphamide	Atteintes viscérales sévères = Méningo-encéphalite & myélite (attention à la SEP)
IGIV	Cytopénies Ganglionopathies Polyradiculonévrite chronique inflammatoire

Place du rituximab ?



- **Vascularites cryoglobulinémiques +++ / Schéma lymphome++**
- **Méningo-encéphalites/myélites**
- **Myosites/PRNC**
- **Pneumopathies interstitielles diffuses**
- **Cytopénies auto-immunes**
- **Néphropathies interstitielles**

CONCLUSION

- Biothérapie
 - Beau succès
 - Anti-angoisse
 - attente
 - Rituels
 - ...)
- Revenir
- Tenir compagnie



III en
bulinémie,
adapter le