

# Traitements actuels du syndrome de Sjögren



**15<sup>ème</sup> Congrès Annuel  
de l'A.I.L.A  
10 au 11 octobre 2024**



**Professeur Damien SENE**  
Département de Médecine interne  
Hôpital Lariboisière  
Université Paris Cité



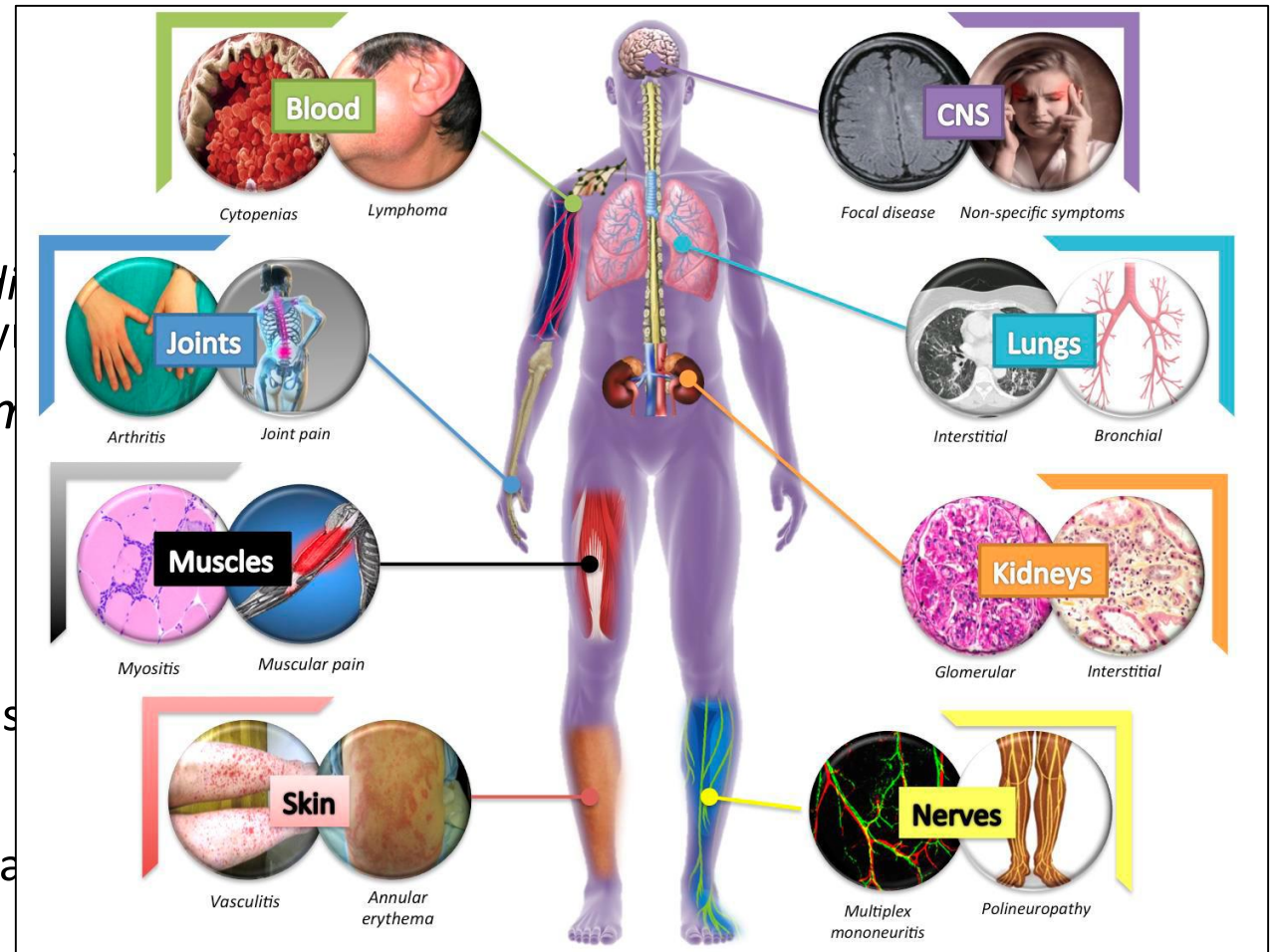
# Présentation clinique : glandulaire/systemique

## Formes évolutives

- Forme chronique « épithéliale » ou « glandulaire » arthromyalgies
- Forme évolutive « extra épithéliale » (« Sjögren dit complications (vascularite cryoglobulinémique, ly

## Facteurs de mauvais pronostic = FDR de form

- Jeune âge (<35 ans)
- Tuméfactions parotidiennes
- Lymphopénie (CD4)
- Hypergammaglobulinémie, purpura d'hyperviscosité
- ANA (anti-SSA, SSB)
- Cryoglobulinémie, hypocomplémentémie, vascularite
- 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
Constitutionnels (fièvre, sueurs, poids)	0	6		Musculaire (myosite)	0	18
Lymphadénopathies	0	12		Neurologique périphérique	0	15
Glandulaire (parotides, sous max)	0	4		Neurologique centrale	0	15
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				

Biologie	Score min	Score max
Biologique (cytopénie)	0	6
Immunologique (complément, cryo, gammaglobuline, pic mono)	0	2

**Score maximum = 123**  
**Score  $\geq 5$  = 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"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<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"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<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"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Douleur maximale imaginable
	0	1	2	3	4	5	6	7	8	9	10	

**Score maximum = 10/10**  
**Score  $\geq 5$  = maladie active**

# TRAITEMENTS ACTUELS DE LA MALADIE SYSTEMIQUE

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

# Biothérapies



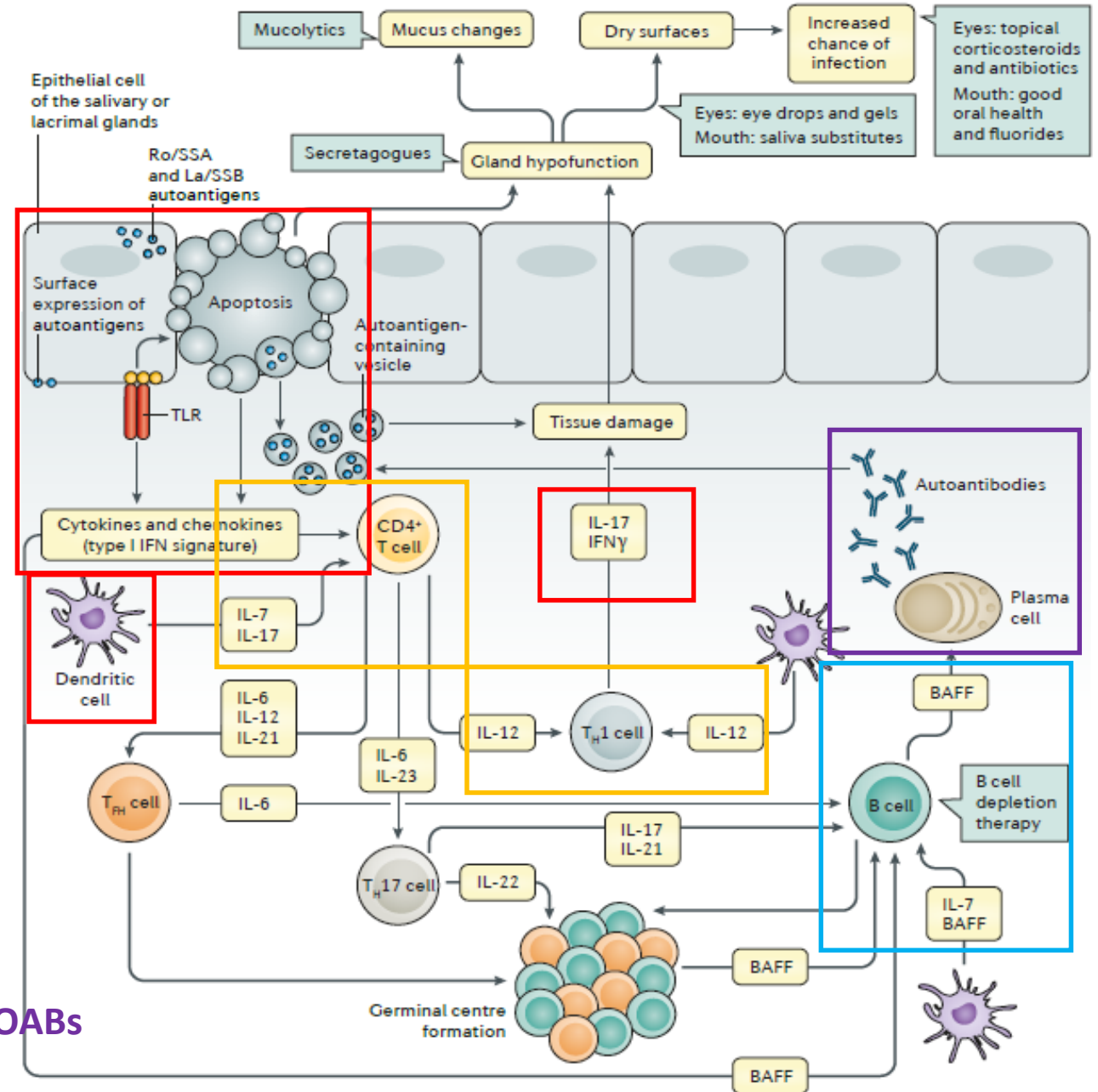
# Physiopathologie : principales « voies »

INTERFERONS

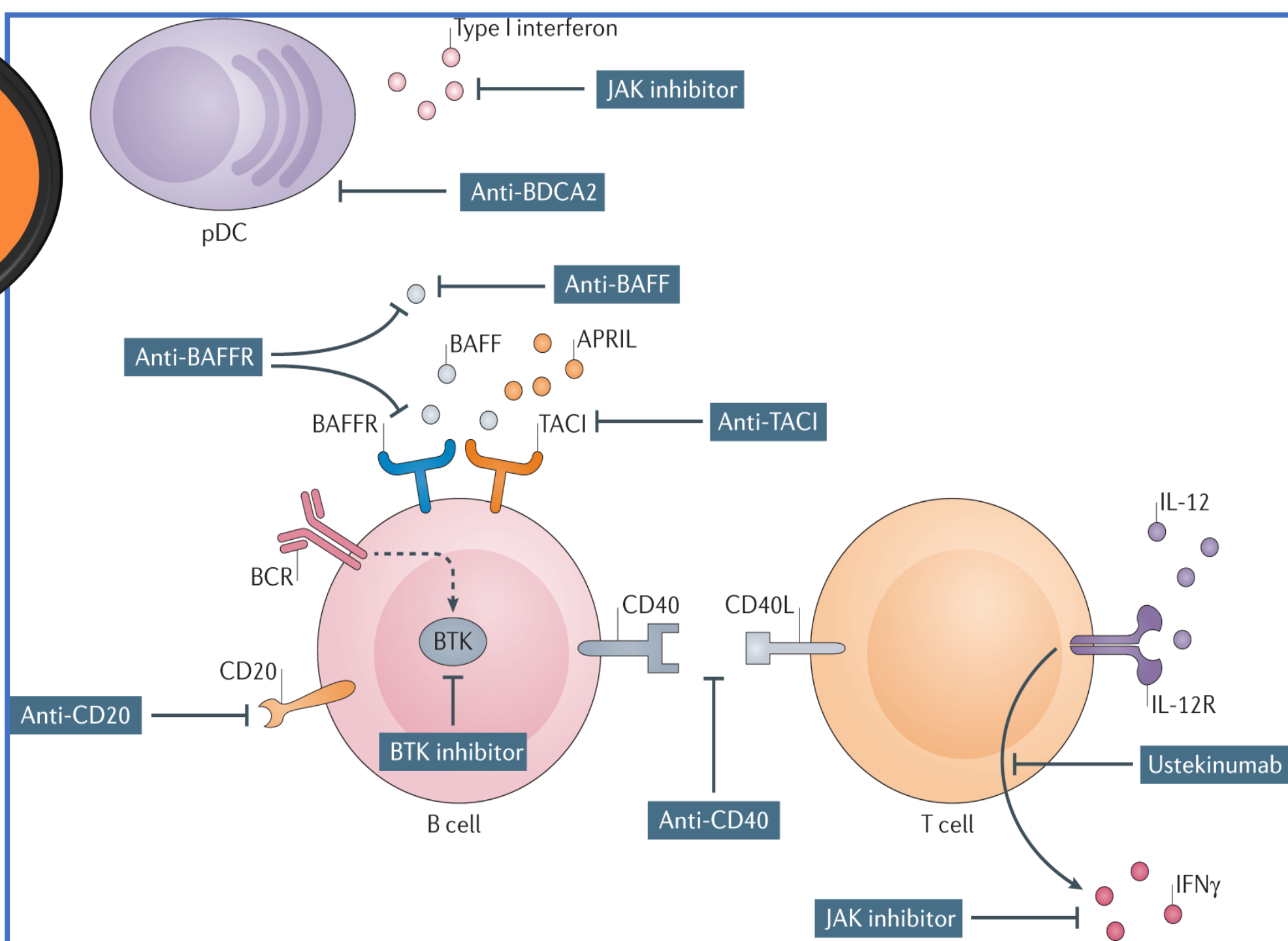
T CELLS

B CELLS

PLASMA CELLS & AUTOABs



Biothérapies  
= cibles

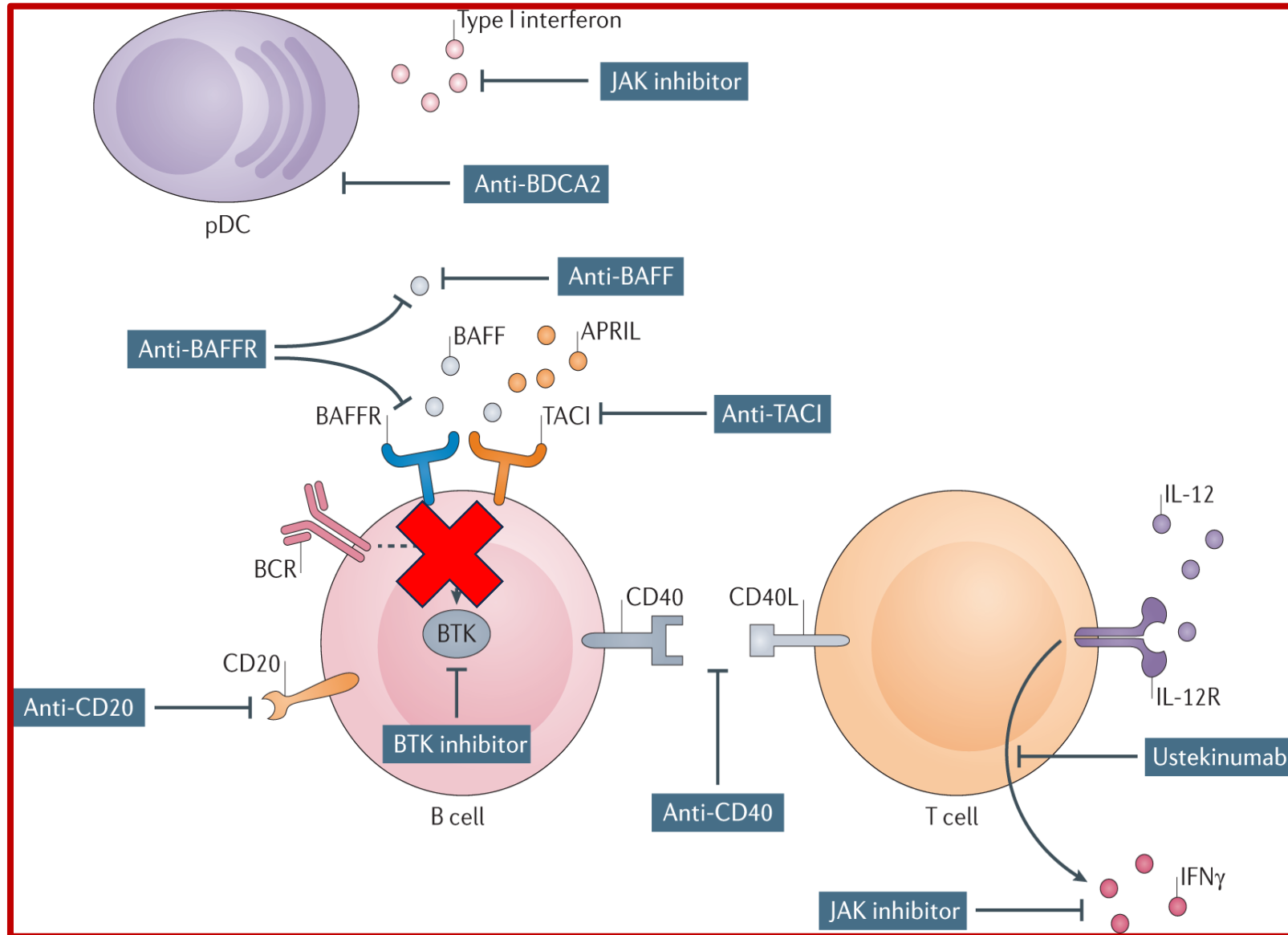




# BIOETHERAPIES DANS LE SYNDROME DE SJOGREN

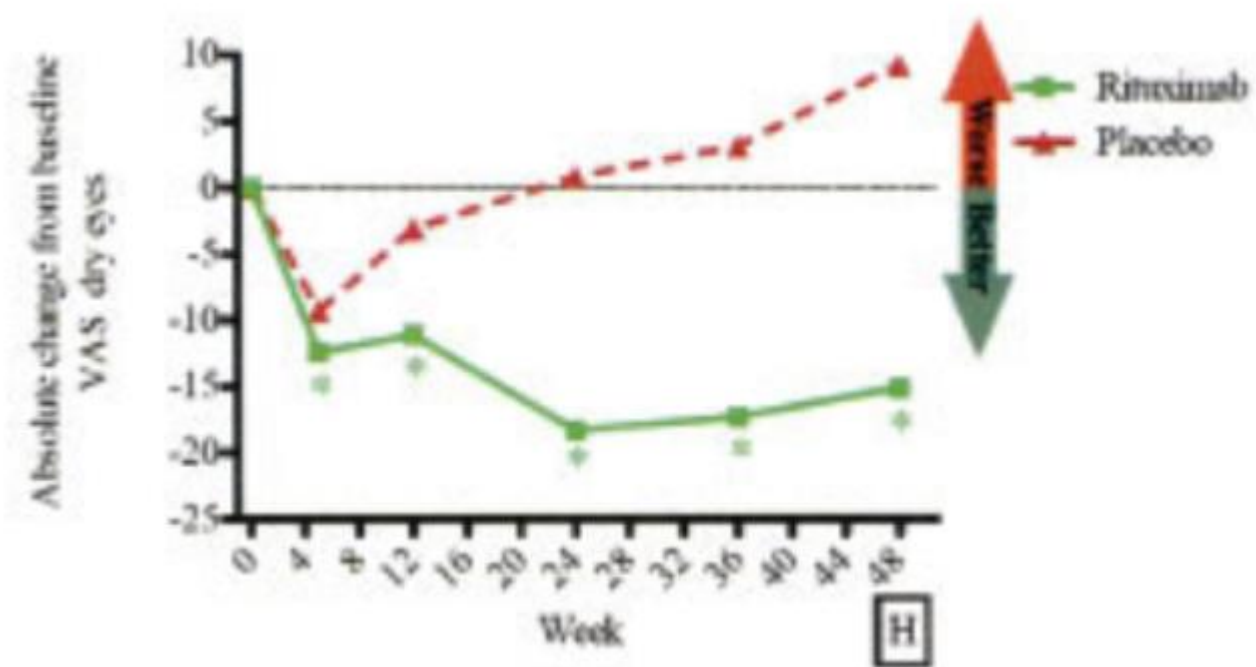
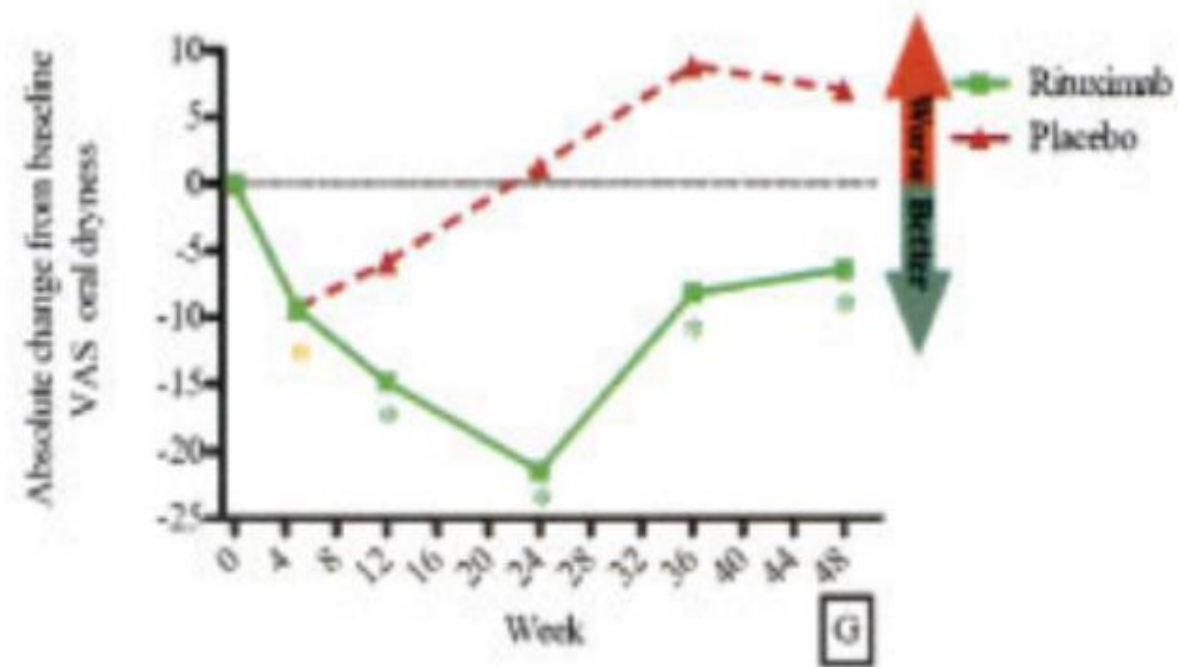
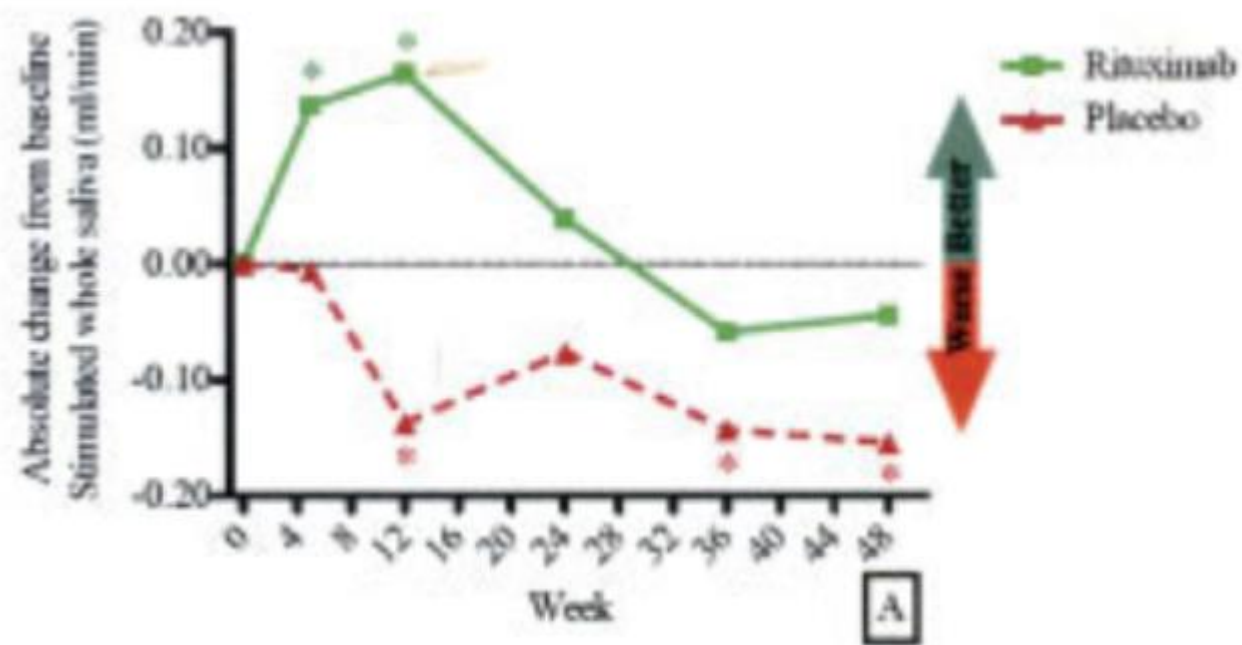
Beaucoup de déceptions, quelques lueurs  
d'espoir

# Déplétion lymphocytaire B



# Rituximab

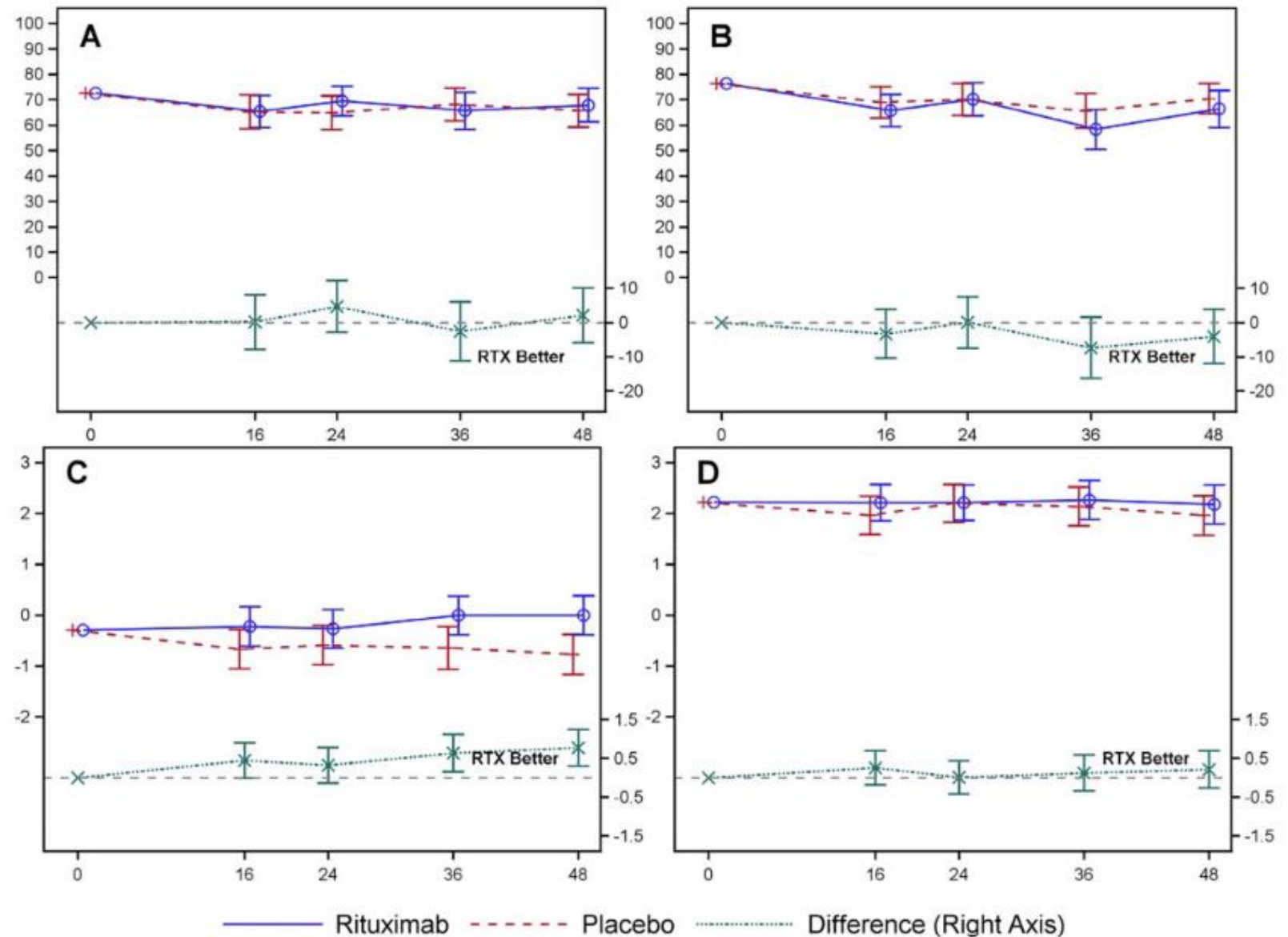
## Meijer et al 2010



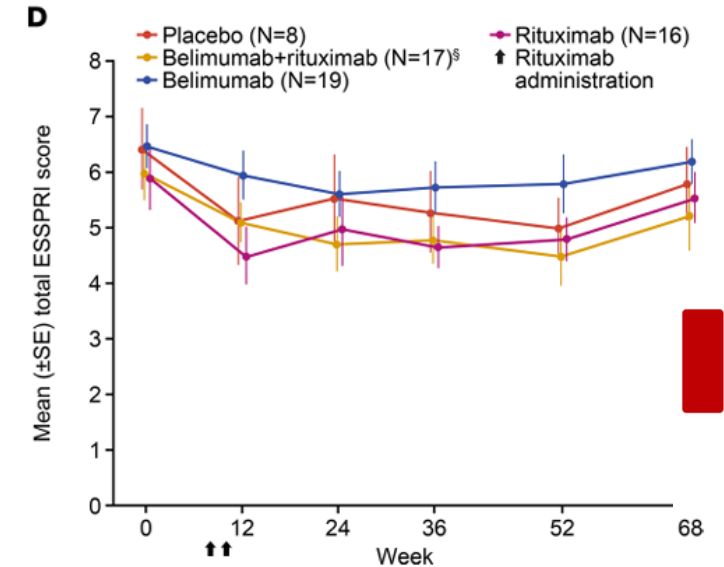
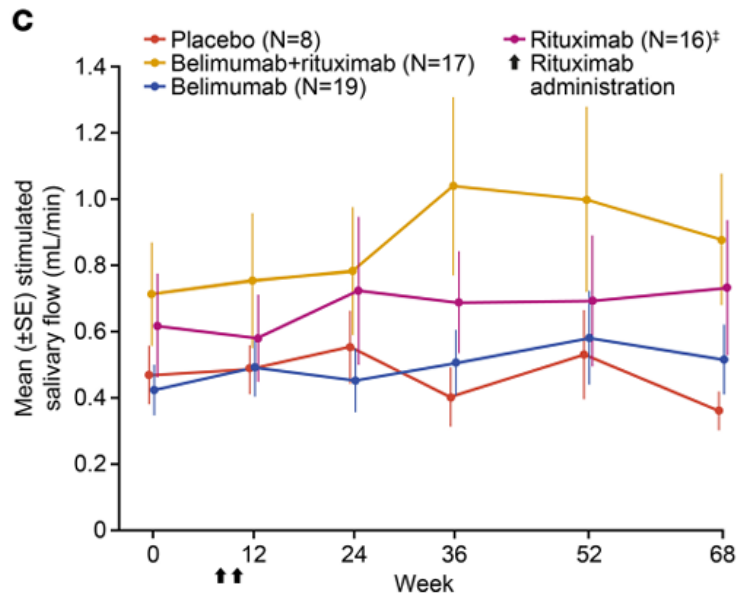
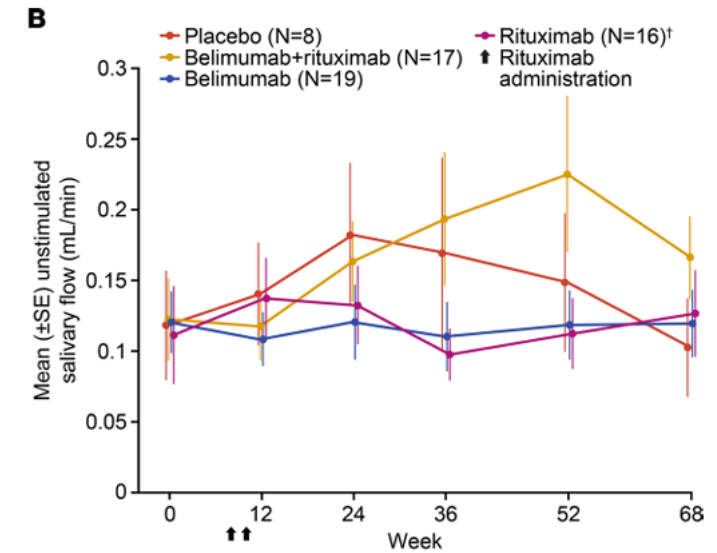
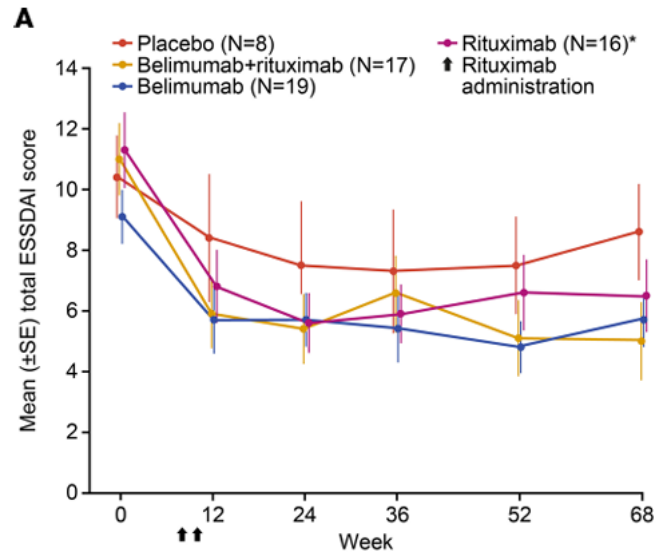
# Rituximab: Bowman et al 2017



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

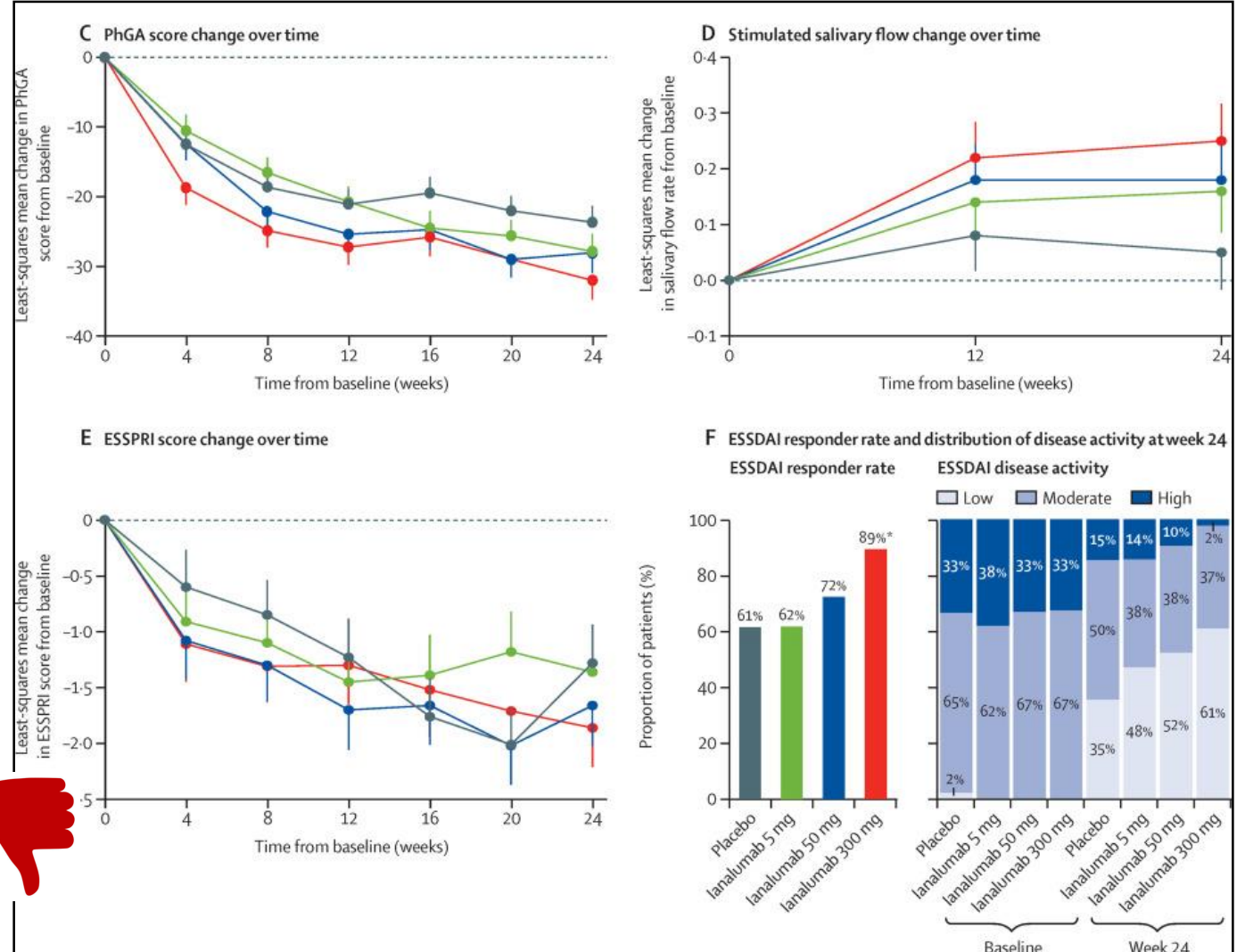
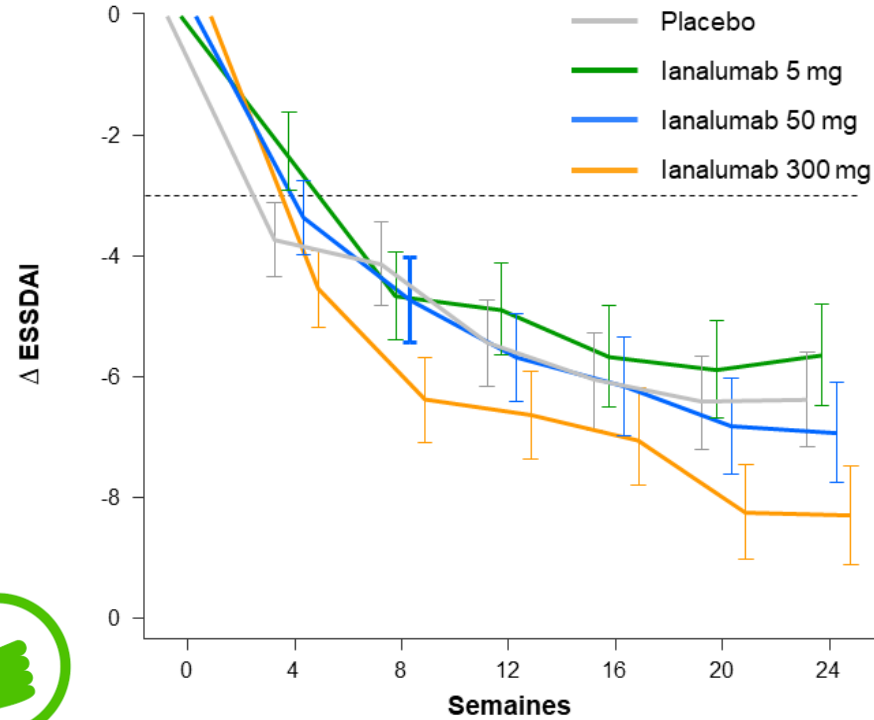


# Rituximab/Belimumab: Mariette et al 2022



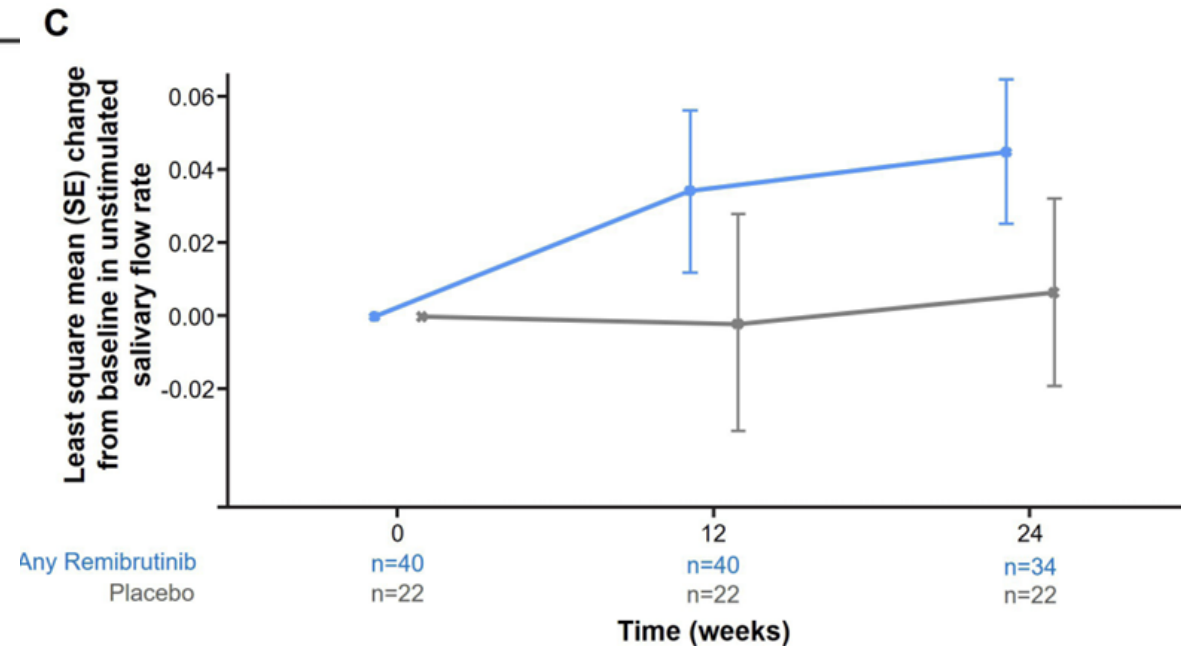
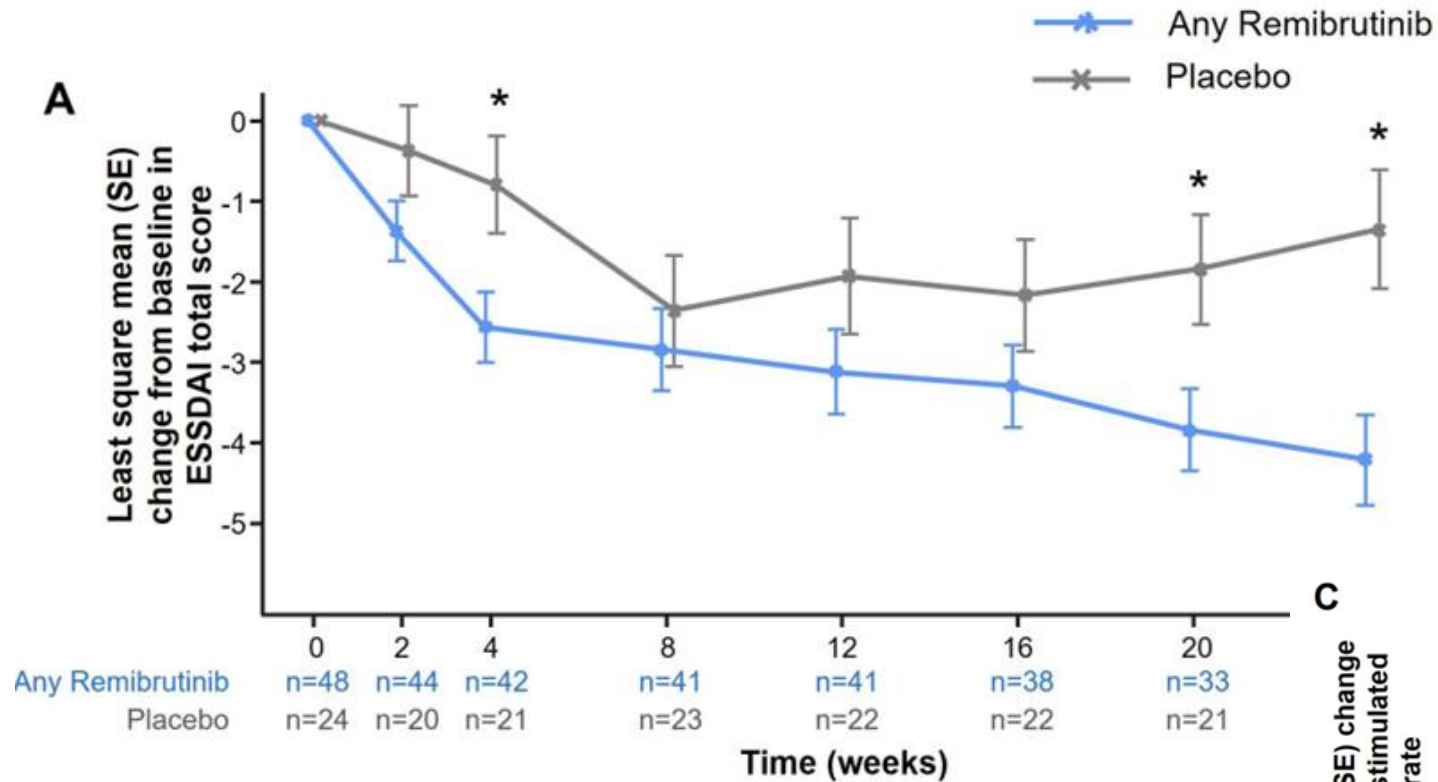
# Ianalumab (anti-BAFF R): Bowman et al 2022

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



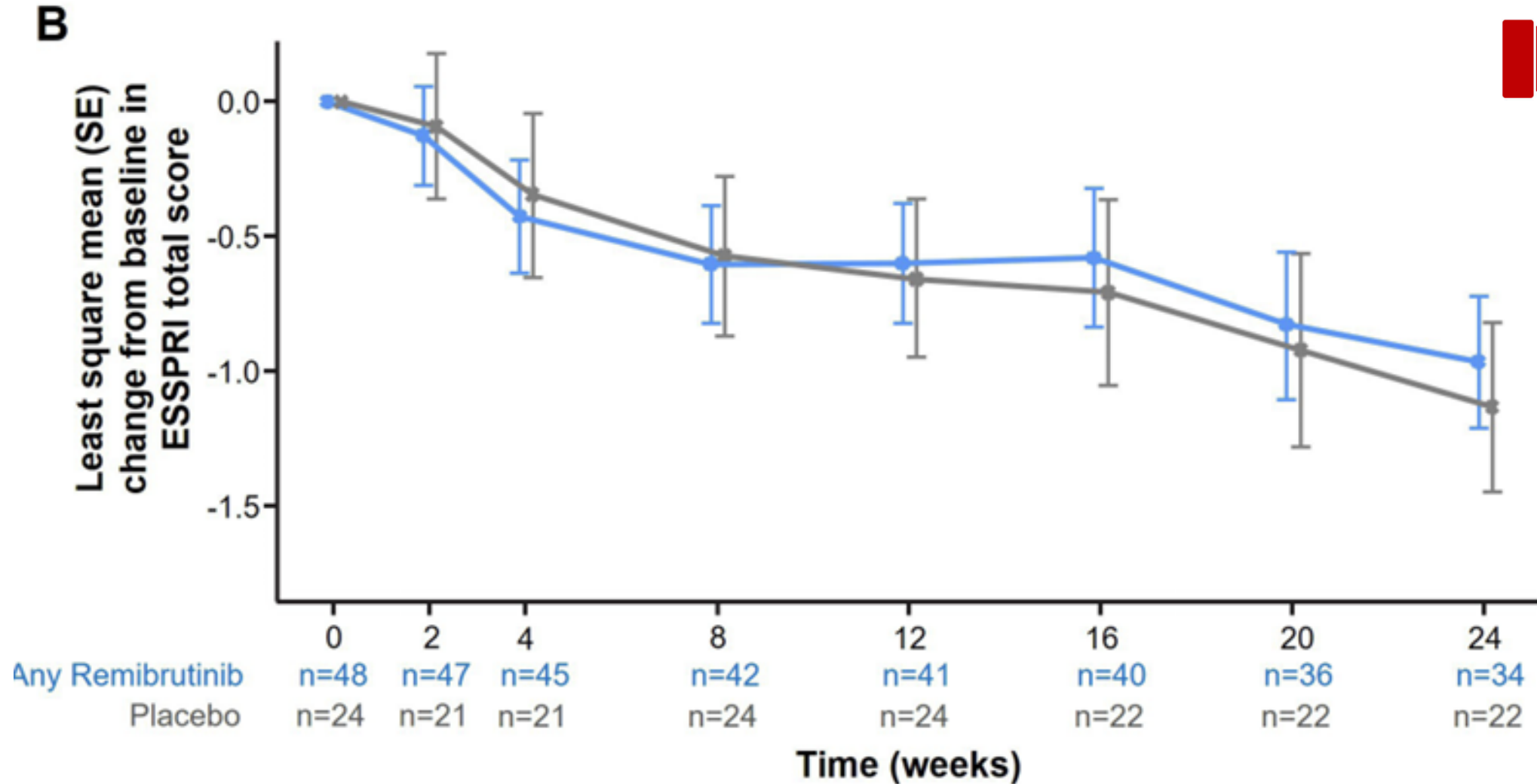
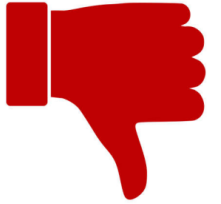


# Remibrutinib (anti-BTK): Dorner et al 2024

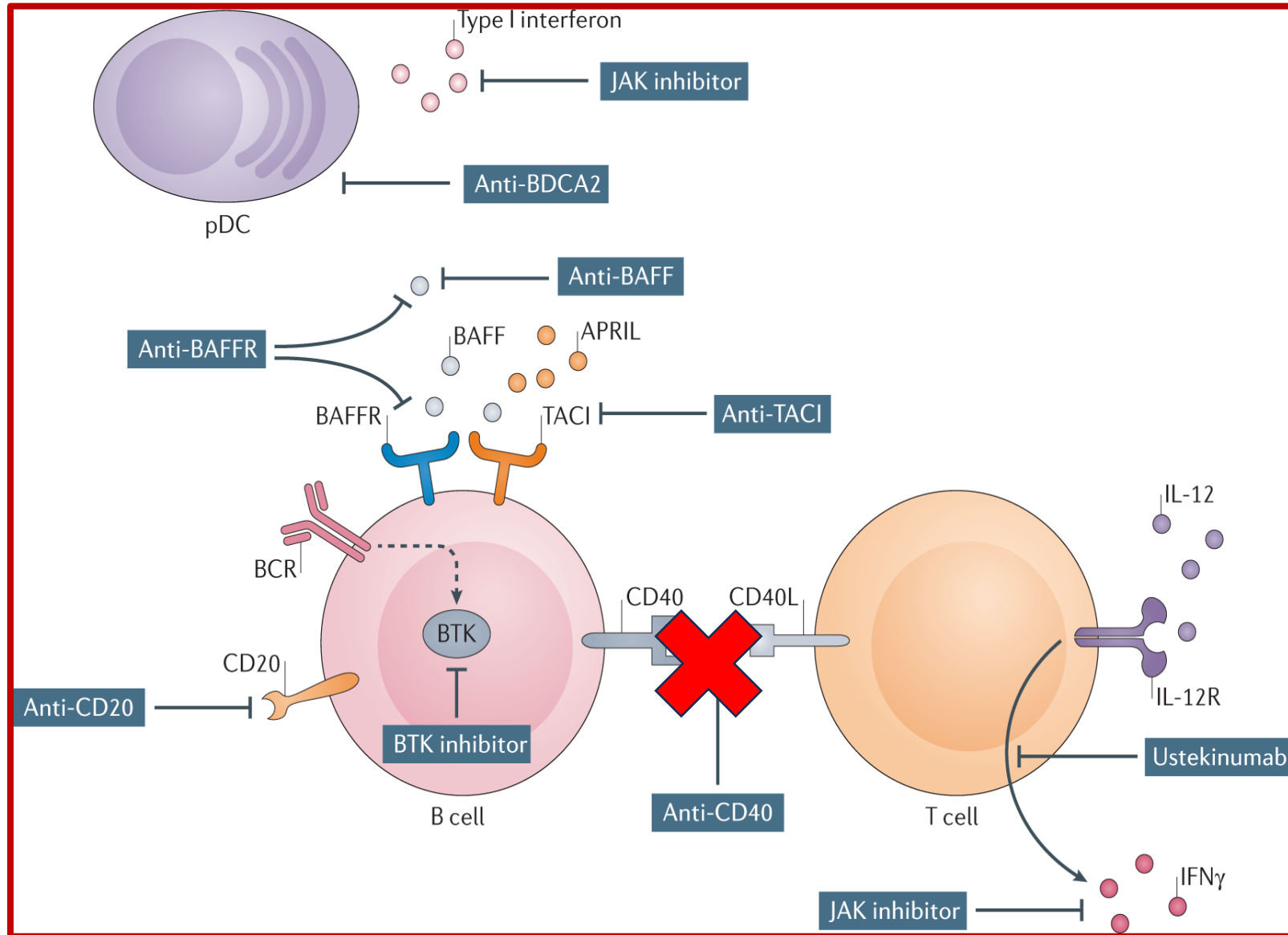




# Remibrutinib (anti-BTK): Dorner et al 2024

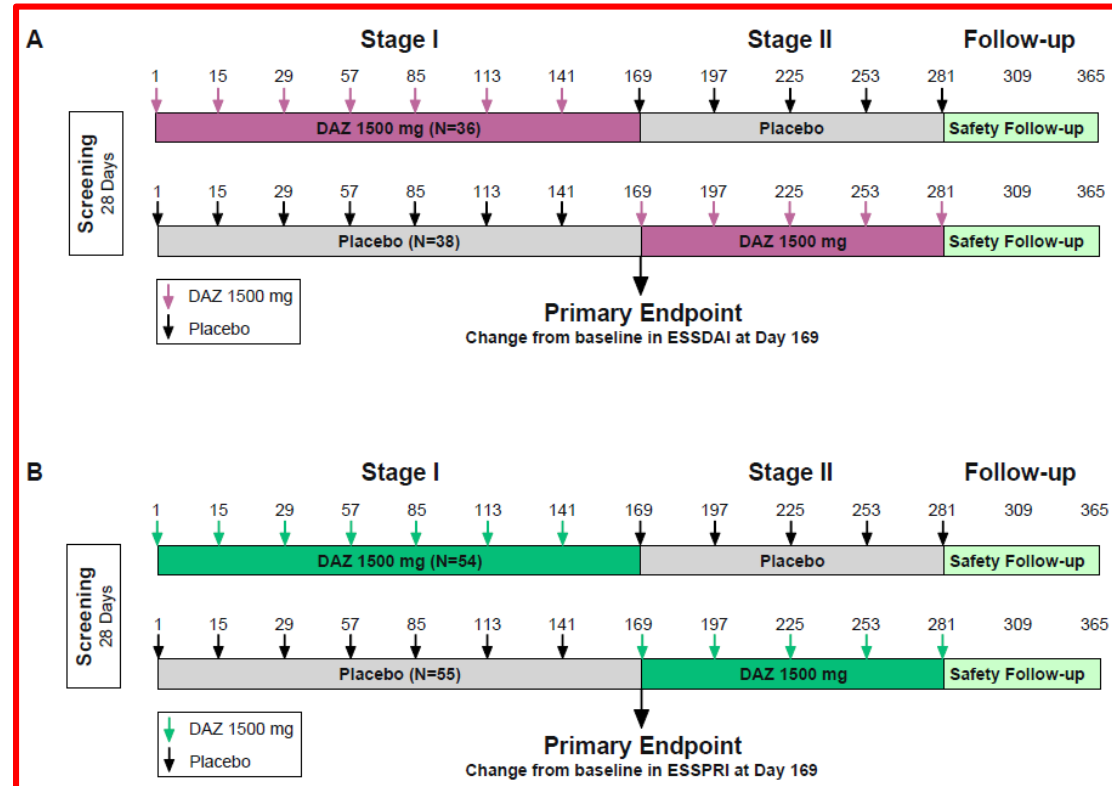
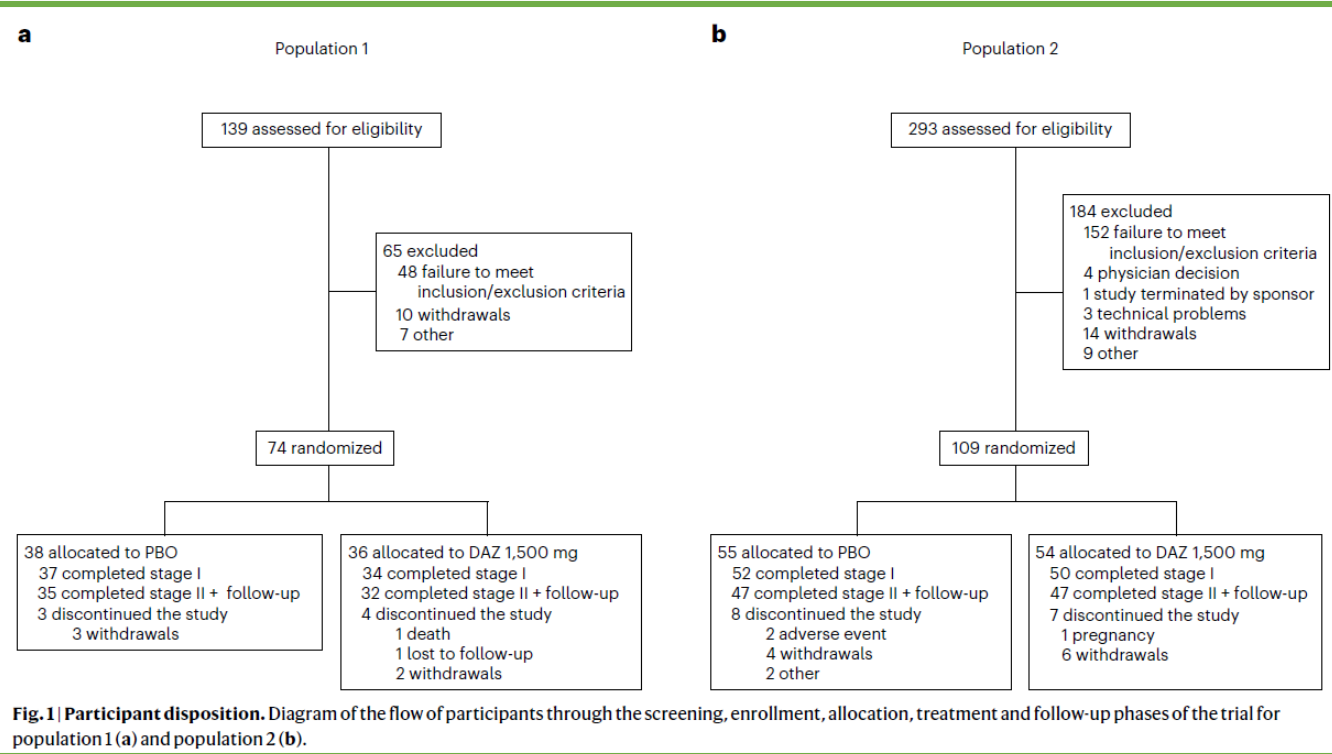


# Inhibition de la co-stimulation lymphocytaire via CD40-CD40L



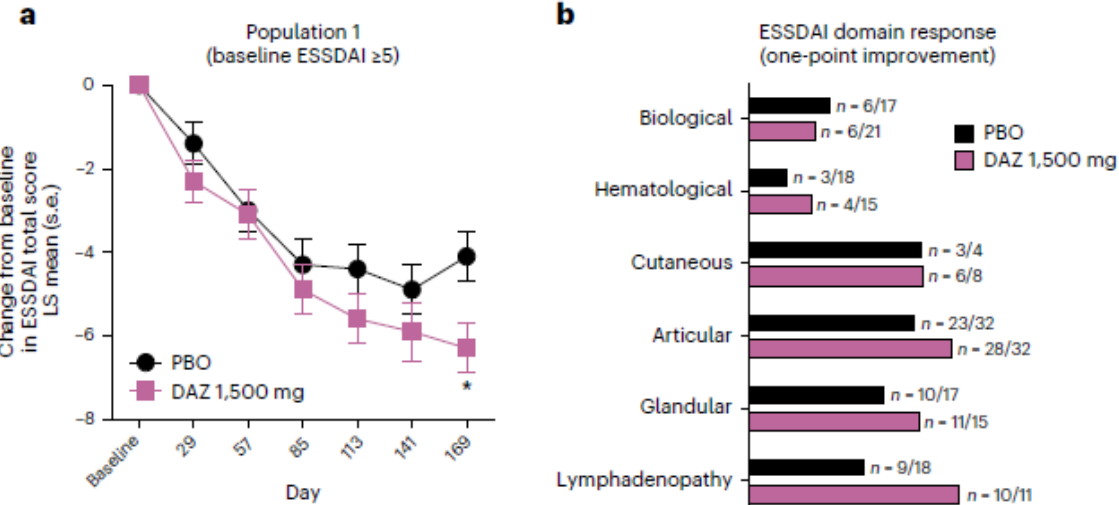
# CD40 ligand antagonist dazodalibep in Sjögren's disease

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



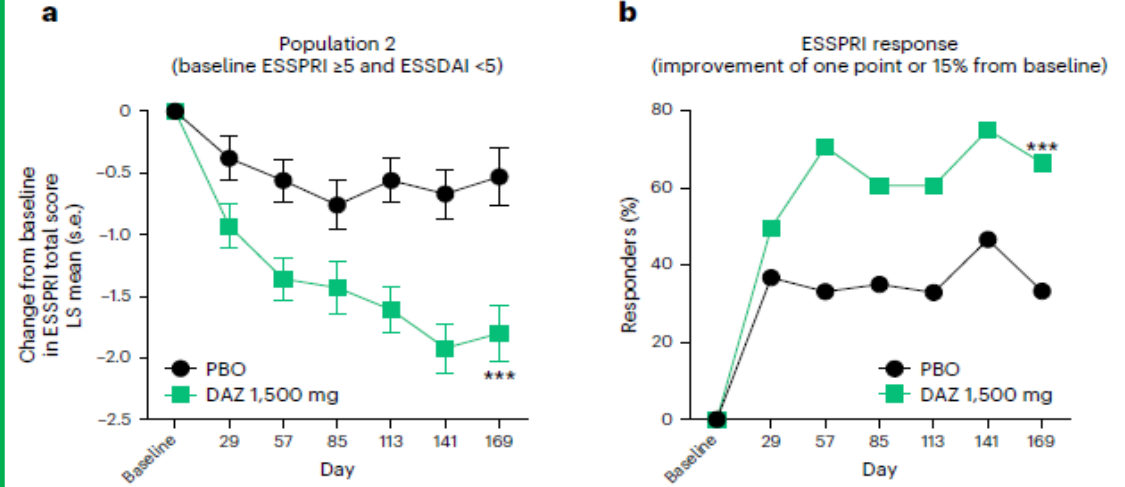
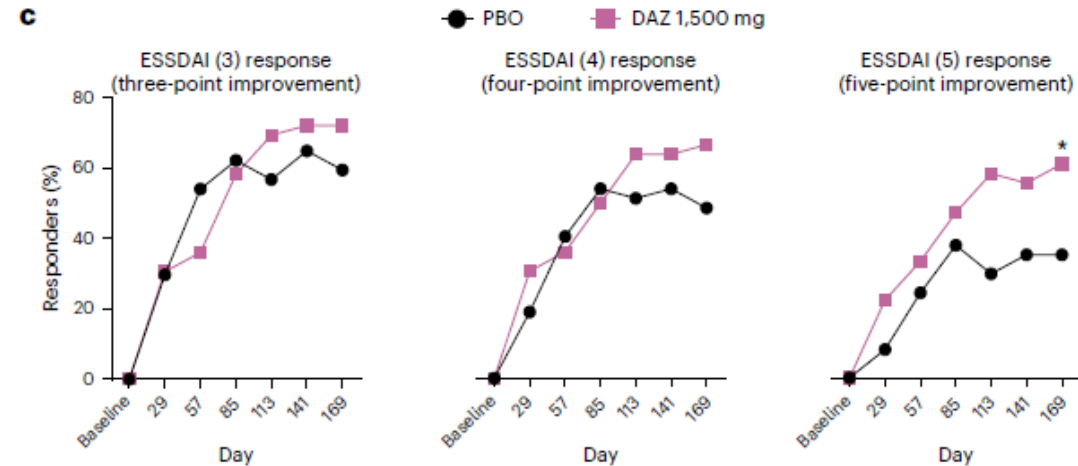
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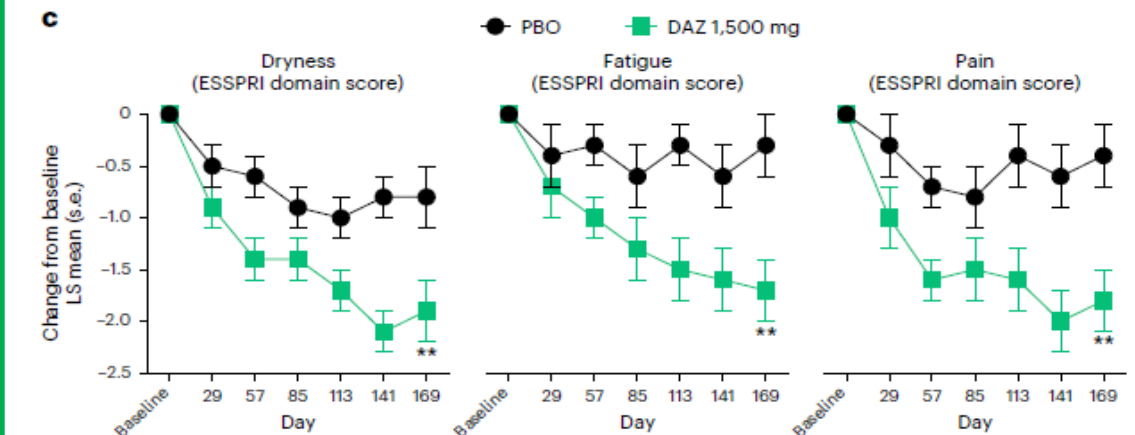
No. of participants

PBO	38	38	36	38	37	37	36
DAZ	36	34	33	35	32	33	33



No. of participants

PBO	55	54	54	54	54	53	53
DAZ	54	53	52	51	50	48	51

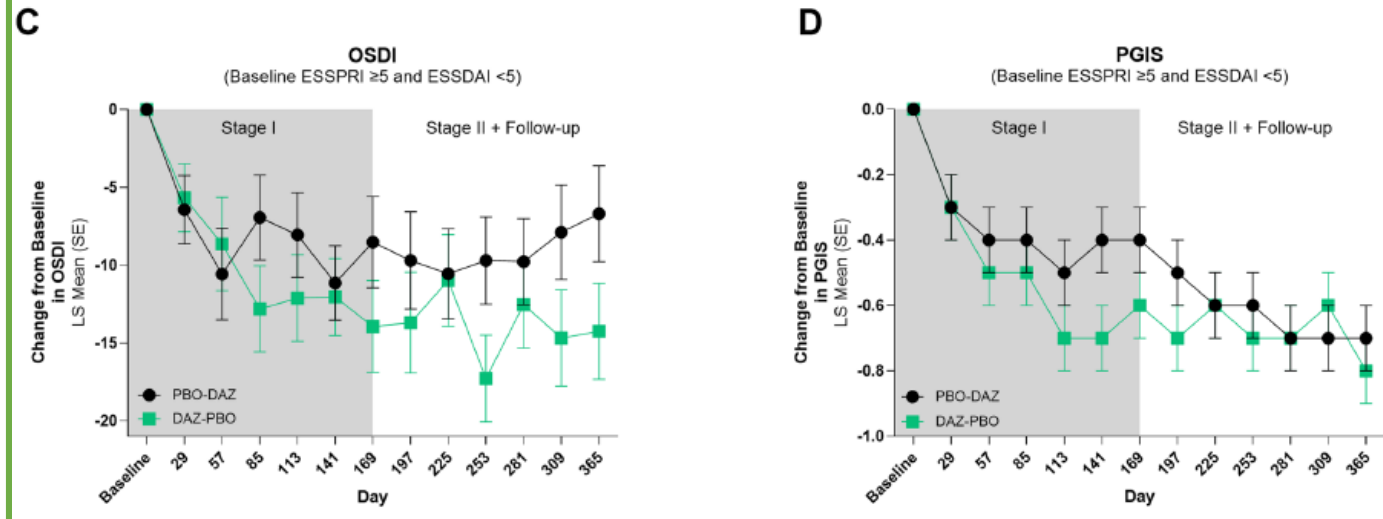
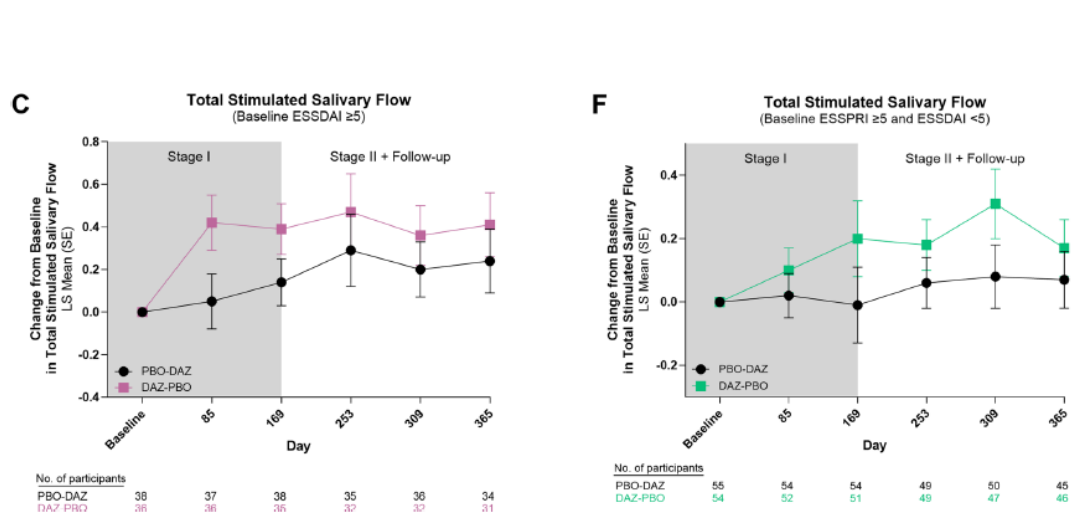
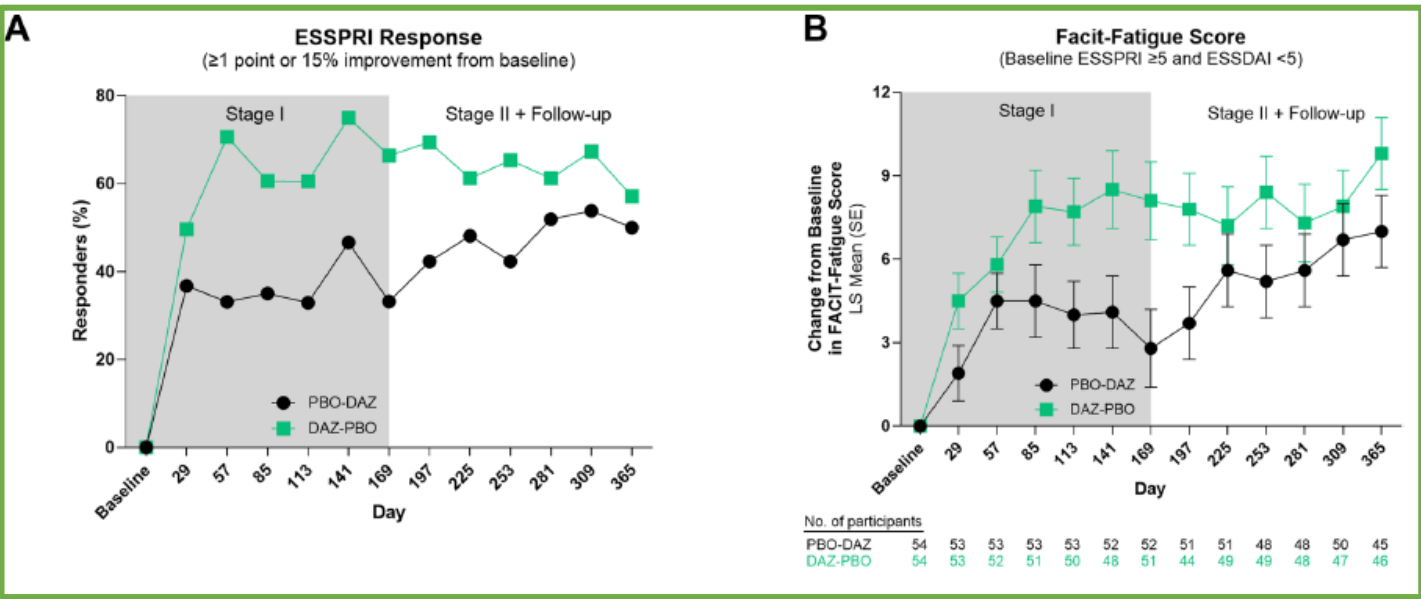


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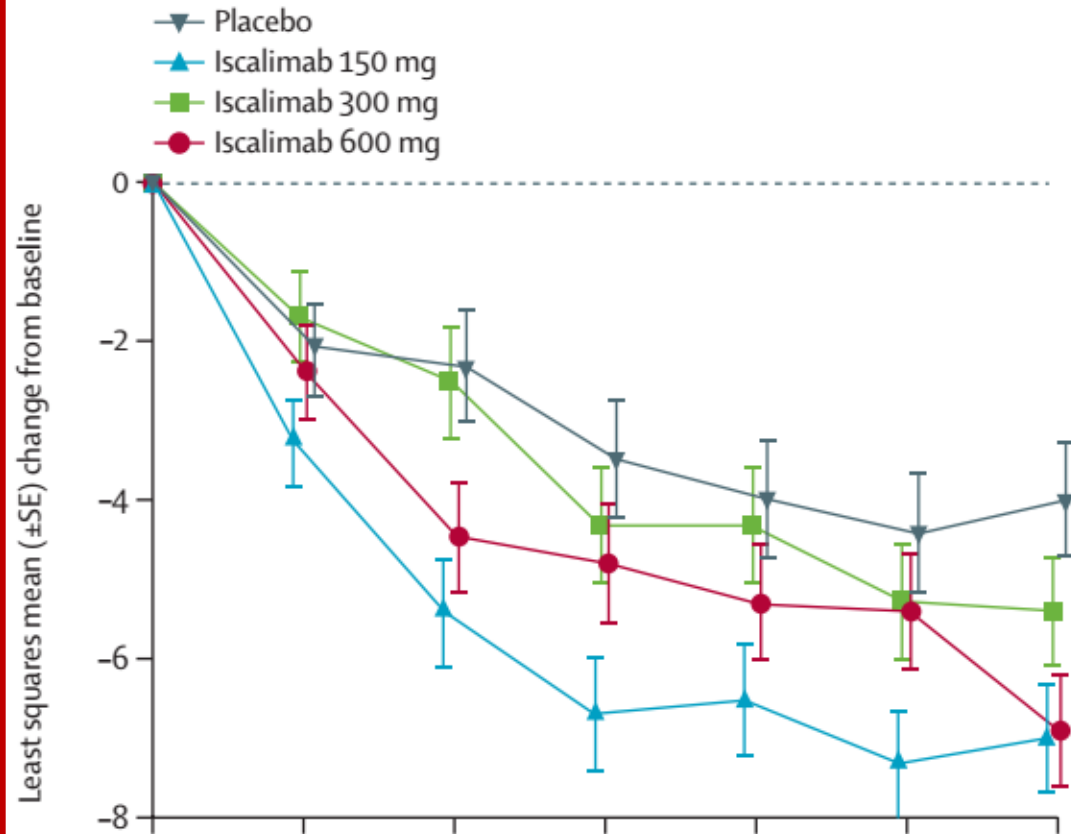


# Anti-CD40, ISCALIMAB, in Sjögren's disease

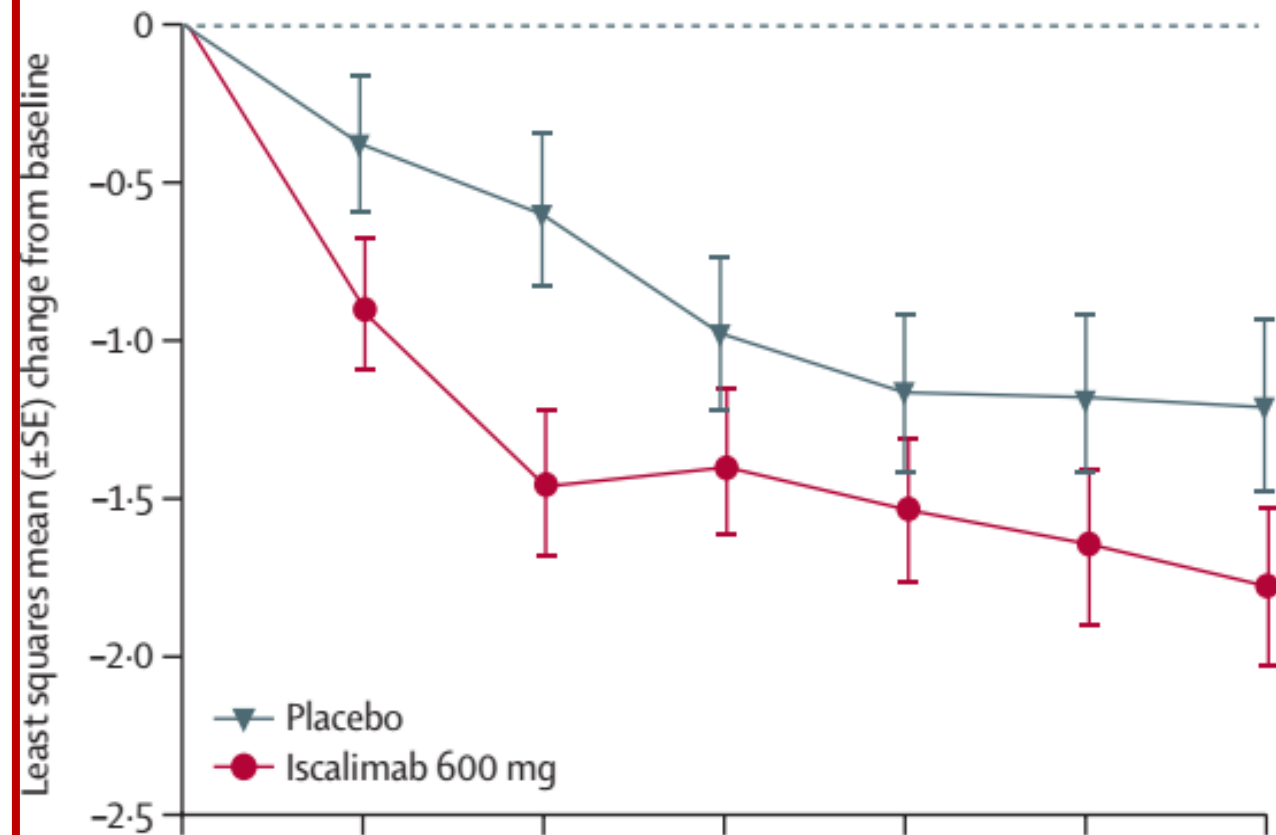
## A randomised, double-blind, placebo-controlled, phase 2b (Lancet, 2024)



**A** Cohort 1: ESSDAI score change over 24 weeks

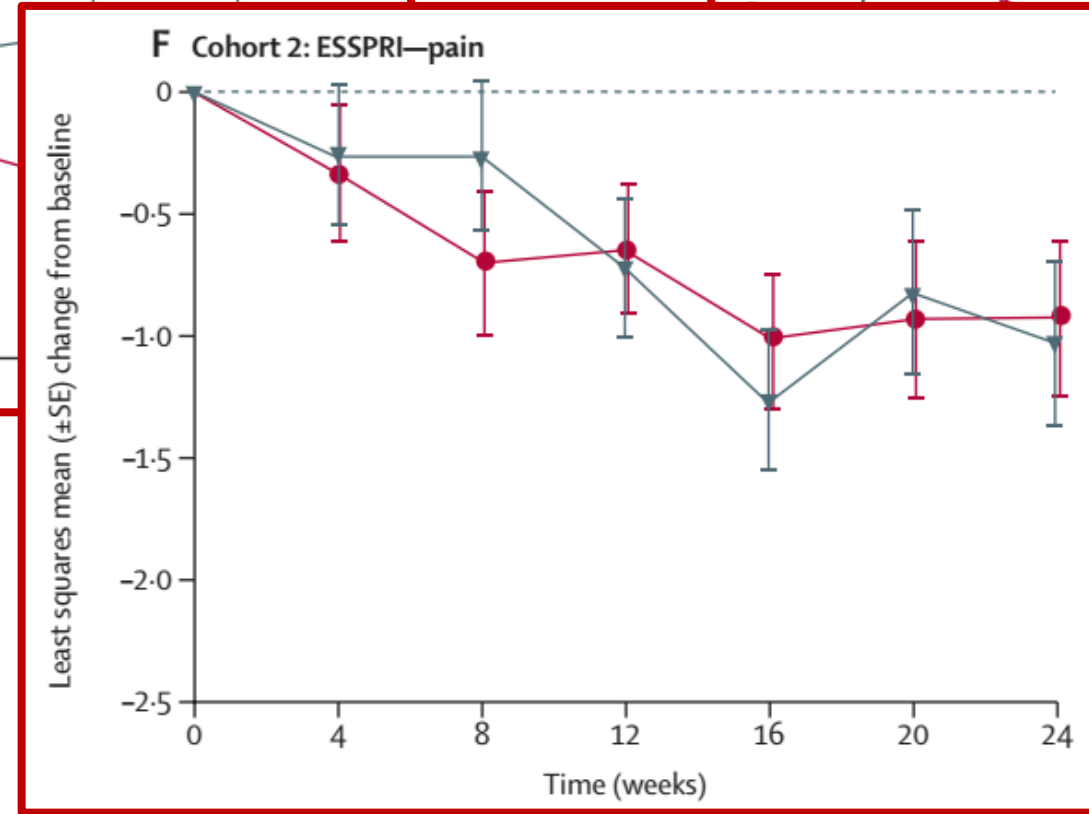
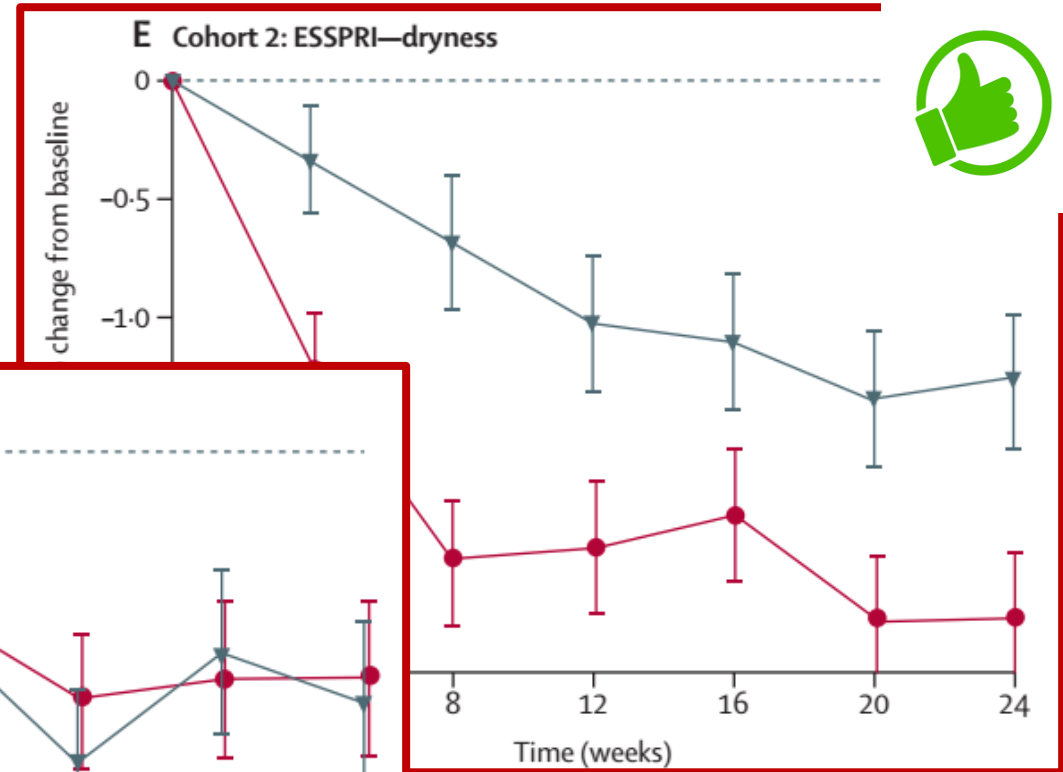
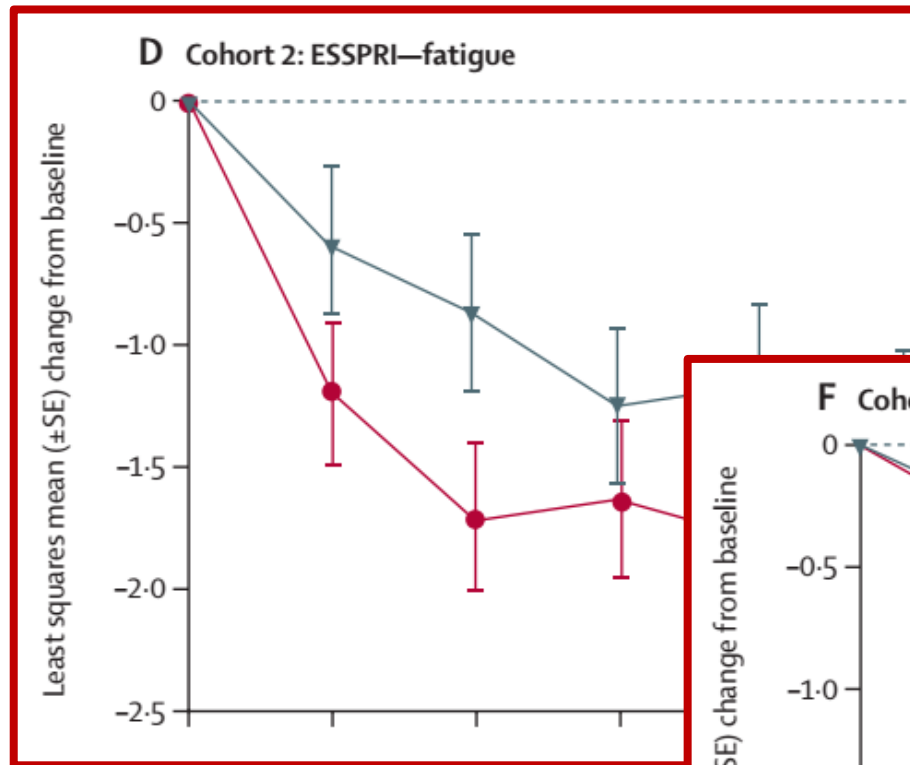


**C** Cohort 2: ESSPRI score change over 24 weeks



# 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  
Vol. 50, No. 4, April 2004, pp 1270–1276  
DOI 10.1002/art.20146  
© 2004, American College of Rheumatology

## Inefficacy of Infliximab in Primary Sjögren's Syndrome

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

Xavier Mariette,<sup>1</sup> Philippe Ravaud,<sup>2</sup> Serge Steinfeld,<sup>3</sup> Gabriel Baron,<sup>2</sup> Joelle Goetz,<sup>4</sup>

OPEN ACCESS Freely available online



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

Katrine Brække Norheim<sup>1\*</sup>, Erna Harboe<sup>1</sup>, Lasse G. Gøransson<sup>1,2</sup>, Roald Omdal<sup>1,2</sup>

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 ,<sup>1</sup> Jacques-Eric Gottenberg ,<sup>2</sup> E William St Clair,<sup>3</sup> Takayuki Sumida,<sup>4</sup>

Sjögren's syndrome

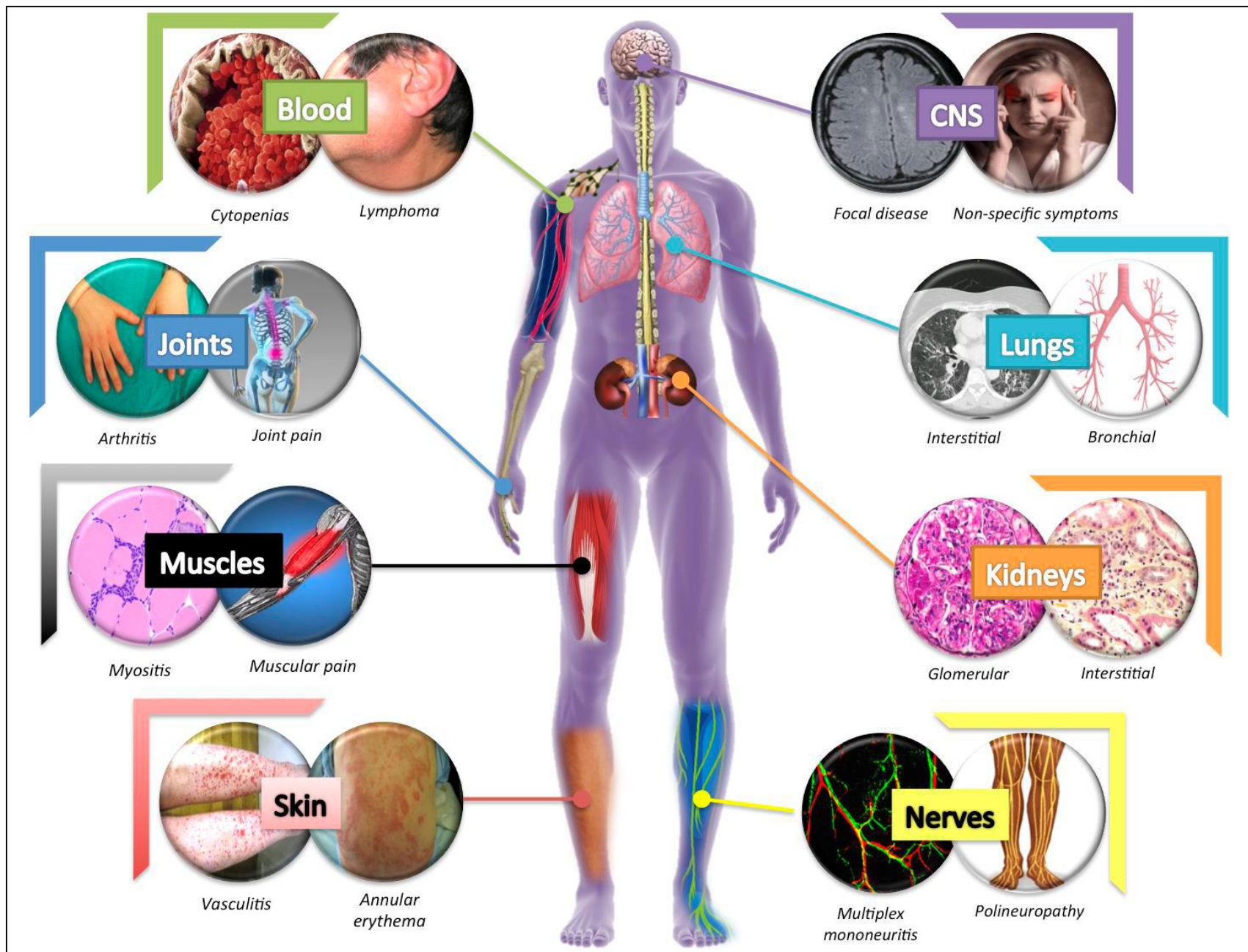
CLINICAL SCIENCE

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

Renaud Felten ,<sup>1</sup> Valérie Devauchelle-Pensec,<sup>2</sup> Raphaële Seror,<sup>3</sup> Pierre Duffau,<sup>4</sup>







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

RHEUMATOLOGY

## Guidelines



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

Elizabeth Price<sup>1</sup>, Alexander Allen<sup>2</sup>, Saaeha Rauz<sup>3</sup>, Anwar Tappuni<sup>4</sup>, Nurhan Sutcliffe <sup>5</sup>, Michele Bombardieri<sup>6</sup>, Sara Carty<sup>7</sup>, Coziana Ciurtin <sup>8</sup>, Bridget Crampton<sup>9</sup>, Lisa Duncalfe<sup>10</sup>, Benjamin Fisher <sup>11</sup>, Peter Glennon<sup>12</sup>, Katie L. Hackett <sup>13</sup>, Genevieve Larkin<sup>14</sup>, Wan-Fai Ng<sup>15</sup>, Athimalaipet V. Ramanan<sup>16</sup>, Saad Rassam<sup>17</sup>, Stephen B. Walsh<sup>18</sup> and Simon Bowman<sup>19</sup>

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doi:10.1093/rheumatology/keaa870  
Advance Access publication 2 February 2021



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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<sup>a,2,\*</sup>, Xavier Mariette<sup>b,2</sup>, Anas-Alexis Benyousséf<sup>c</sup>, Sylvie Boisrame<sup>d</sup>, Béatrice Cochener<sup>c</sup>, Divi Cornec<sup>a</sup>, Gaëtane Nocturne<sup>b</sup>, Jacques Eric Gottenberg<sup>e</sup>, Eric Hachulla<sup>f</sup>, Pierre Labalette<sup>g</sup>, Véronique Le Guern<sup>h</sup>, Ruth M'Bwang Seppoh<sup>i</sup>, Jacques Morel<sup>j</sup>, Marie Orliaguet<sup>d</sup>, Alain Saraux<sup>a</sup>, Raphaële Seror<sup>b</sup>, Nathalie Costedoat-Chalumeau<sup>h</sup>, Collaborators<sup>1</sup>



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### EXPERT PERSPECTIVES ON CLINICAL CHALLENGES

## Expert Perspective: Challenges in Sjögren's Disease

Gaëtane 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.

AMERICAN COLLEGE  
of RHEUMATOLOGY  
Empowering Rheumatology Professionals

# 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

fai2r

PNDS

Protocoles Nationaux de  
Diagnostic et de Soins

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



# Immunosuppresseurs/IgIV



PNDS

Protocoles Nationaux de  
Diagnostic et de Soins

Immunosuppresseurs	Indications
Corticoïdes	Traitement 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 (CI à ces trts) Phase II, 15 patients, mauvaise tolérance et efficacité modeste

# Immunosuppresseurs/IgIV

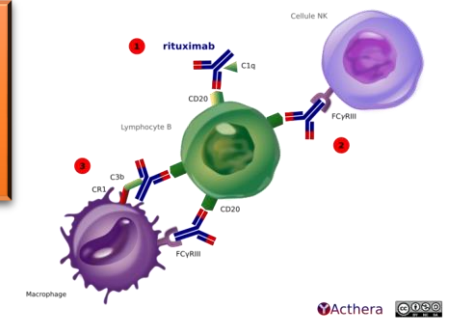
fai2r

PNDS

Protocoles Nationaux de  
Diagnostic et de Soins

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

# Place du rituximab ?



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

# CONCLUSION

- **Biothéra**

- Beau

- Anti-

- atter

- Ritux

- ...)

- **Revenir**

- **Tenir co**



III en

oulinémie,

adapter le

traitement symptomatique, en particulier le syndrome oculotut