

SUPPLEMENTARY MATERIAL**Supplementary Text. Working groups in areas of therapeutic interest in primary SS**

AREA 1. ORAL & DENTAL CARE: Aike Kruize (Coordination), Leila Khamashta, Jacques-Olivier Pers, Raphaèle Seror, Caroline H. Shiboski, Arjan Vissink (members).

AREA 2. OCULAR CARE & OTHER DRYNESS: Benjamin Fisher (Coordination), Saaeha Rauz, María-Teresa Sainz de la Maza, Jelle Vehof, Jenni Byrom, Helen Lewis, Hendrika Bootsma Elke Theander (members).

AREA 3. GENERAL SYMPTOMS (FATIGUE, PAIN...): Wan-Fai Ng (Coordination), Chiara Baldini, Ronald Omdal, Raphaèle Seror, Roser Solans Laqué, Elke Theander (members).

AREA 4. ORGAN-SPECIFIC SYSTEMIC TREATMENT: Raphaèle Seror (Coordination); Stefano Bombardieri, Jill P. Buyon*, Peter M. Izmirly*, Thomas Mandl, Sonja Praprotnik, Manuel Ramos-Casals*, Soledad Retamozo, Jorge Sánchez-Guerrero, Munther Khamashta*, Pilar Brito-Zerón*, Margit Zeher (members)
(*CHB subgroup).

AREA 5. TREATMENT OF LYMPHOMA; Xavier Mariette (Coordination), Hendrika Bootsma, Pilar Brito-Zerón, Salvatore De Vita, Michael Voulgarelis (members).

AREA 6. ENVIRONMENTAL FACTORS & VITAMINS: Yehuda Shoenfeld (Coordination), Chiara Baldini, Elena Bartoloni, Benjamin Fisher, Roberto Gerli, Valeria Valim, Gabriela Hernández-Molina (members)

AREA 7. NON-BIOLOGICAL THERAPIES: Jacques-Eric Gottenberg (Coordination), Roberto Caporali, José António P. Da Silva, Valerie Devauchelle, Marika Kvarnström, Roberta Priori, Valeria Valim, Cristina Vollenweider (members)

AREA 8. BIOLOGICAL AGENTS: Hendrika Bootsma (Coordination), Simon Bowman, Thomas Dörner, Roberto Giacomelli, Jacques-Enric Gottenberg, David Isenberg, Munther Khamashta, Alain Saraux, Roser Solans Laqué (members)

AREA 9. FUTURE THERAPIES: Gabriela Hernández-Molina (coordination), Fabiola Atzeni, Valerie Devauchelle, Marja Pertovaara (members).

Supplementary Table S1. Levels of evidence (LoE) and grades of recommendations (GoR) according to the Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009)

LoE	Design of studies	GoR	Evidence-based recommendations
1	Systematic review of RCTs (1a)	A	Consistent level 1 studies
	Individual RCT (1b)		
2	Systematic review of cohort studies (2a)	B	Consistent level 2 or 3 studies Extrapolations** from level 1 studies
	Individual cohort study (2b)		
	Low-quality* RCT (2b)		
	Outcomes research/ecological studies (2c)		
3	Systematic review of case-control studies (3a)	C	Consistent level 4 studies Extrapolations** from level 2 or 3 studies
	Individual case-control study (3b)		
4	Case-series/retrospective studies	D	Consistent level 5 evidence Troublingly inconsistent or inconclusive studies of any level
	Low-quality* cohort studies		
	Low-quality* case-control studies		
5	Expert opinion	D	

**Low quality defined according to the Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009)*

***Extrapolations were applied when target population do not meet the PICO criteria (primary SjS patients fulfilling the 2002/2016 criteria): associated SjS, former criteria, mixed populations*

Supplementary Table S2. Synthesis of evidence on organ-by-organ therapeutic management of systemic Sjögren (therapeutic algorithms)

First author	Year	ESSDAI domain	Study design (LoE)	Patients	Therapeutic intervention
Fauchais	2010	Articular	4	133	Multiple
Moerman	2017	Articular	2b	11	Rituximab
Moerman	2017	Articular	2b	11	Abatacept
Ramos-Casals	2004	Cutaneous	4	9	Multiple
Katayama	2010	Cutaneous	4	120	Multiple
Brito	2014	Cutaneous	4	43	Multiple
Deheinzelin	1996	Pulmonary	4	15	Multiple
Leone	1996	Pulmonary	4	8	Multiple
Ito	2005	Pulmonary	4	33	Multiple
Parambil	2006	Pulmonary	4	18	Multiple
Dalavanga	2006	Pulmonary	4	22	Multiple
Enomoto	2013	Pulmonary	4	33	Multiple
Chen	2016	Pulmonary	4	10	Rituximab
Roca	2017	Pulmonary	4	19	Multiple
Manfredi	2017	Pulmonary	4	13	Multiple
Ren	2008	Renal	4	130	Multiple
Maripuri	2009	Renal	4	24	Multiple
Goules	2013	Renal	4	10	Multiple
Jasiek	2017	Renal	4	95	Multiple
Shen	2017	Renal	4	70	GC + CYC
Carrillo-Pérez	2018	Renal	4	13	Multiple
Yang	2018	Renal	4	103	Multiple
Aoki	2003	Muscular	4	5	Multiple
Colafrancesco	2015	Muscular	4	17	Multiple
Espitia-Thibault	2017	Muscular	4	10	Multiple
Font	2003	Peripheral nerve system	4	15	Multiple
Delalande	2004	Peripheral nerve system	4	82	Multiple
Mori	2005	Peripheral nerve system	4	92	Multiple
Sene	2011	Peripheral nerve system	4	30	Multiple
Rist	2011	Peripheral nerve system	4	19	IVIg

Brito	2013	Peripheral nerve system	4	24	Multiple
Sivadasan	2017	Peripheral nerve system	4	42	Multiple
De Seze	2006	Central nervous system	4	14	CYC
Mekinian	2012	Central nervous system	4	11	Rituximab
Teixeira	2013	Central nervous system	4	26	Multiple
Jamilloux	2014	Central nervous system	4	93	Multiple
Jiang	2015	Hematological	4	6	Rituximab
Seror	2007	Systemic	4	16	Rituximab
Meijer	2010	Systemic	1b	30	Rituximab
Gottenberg	2013	Systemic	4	78	Rituximab
Devauchelle	2014	Systemic	1b	122	Rituximab
Gheitasi	2015	Systemic	4	1120	Multiple
De Vita	2015	Systemic	4	15	Belimumab
Sandhya	2015	Systemic	4	332	Multiple

Supplementary Table S3. Studies with available data on the efficacy of rituximab on systemic involvement in patients with primary SJS-2002

Author (year)	N	Study design (duration)	Drug, dose, regimen	Global systemic response (response/patients treated)	Organ-specific systemic response	Lymphoma (clinical response)	ESSDAI	Prednisone use
Gottenberg et al (2005)	6 (6)	Retrospective (8m)	Rituximab 375mg/m ² Weeks 0,1,2,3 (n=5)	Systemic features (4/4)	Vasculitis (2/2) Parotid + arthritis (2/2)	MALT (1/2)	NA	Reduced dose (4/5)
Seror et al (2007)	16 (16)	Retrospective (4.5 m)	Rituximab 375mg/m ²	Systemic features (9/11)	Vasculitis 4/5 Cytopenia 0/1 Pulmonary + arthritis 2/2 Arthritis 2/2 Renal 1/1 Parotid enlargement 3/3	Lymphoma (4/5)	NA	Reduced median daily dose of corticosteroids (10 to 5mg, p=0.003)
Ramos-Casals et al (2010)	24 (24)	Retrospective	Rituximab 375mg/m ² (n=20) Rituximab 1g /15d (n=4)	Systemic (12/16)	CNS 1/3 PN 5/5 Cytopenia 3/3 Renal 1/2 Arthritis 0/1 Muscular 1/1 PLE 1/1	Lymphoma (n=8): CR in 6, PR in 2	NA	NA
Gottenberg et al (2013)	78 (67)	Retrospective	Rituximab 375mg/m ² (n=11) Rituximab 1g /15d (n=67)	Systemic (44/74)	Articular 17/27 (63%) CNS 2/6 (33%) PN 6/12 (50%) Lung = 7/9 (78%) Vasculitis = 5/8 (63%) Renal = 5/6 (83%) Myositis = 0/3 (0%) Cytopenia = 2/2 (100%) Pancreatitis = 1/1 (100%) Parotid enlargement = 2/3 (67%) Sclera vasculitis 0/1 (0%)	NA	Total score 11 to 7.5 (p<0.00001)	Reduced median daily dose of corticosteroids mg/d (17.6 to 10.8, p=0.1)

Meiners et al (2012)	15	Prospective (24w)	Rituximab 1g/15 days	NA	NA	NA	Total score 9.0 to 2.5 (p=0.006)	NA
Mekinian et al (2012)	17	Retrospective	Rituximab 1g/15 days	NA	PN 11/17 (vasculitic 9/10 vs. non-vasculitic 2/7, p=0.03) CR of cryo-related skin and joint involvements	NA	Total score 18 to 12 (p<0.05)	NA
Carubbi et al (2013)	22	Case-control (120w)	Rituximab 1g/15 days	NA	NA	NA	Total score 20.3 to 5.2 (p<0.001)	NA
Meijer et al (2010)	30	RCT (48w)	Rituximab 1g/15d (n=20) Placebo (n=10)	NA	Vasculitis (p=0.03) Tendomyalgia (p=0.029) Arthritis (4/6) PN (1/1)	NA	NA	NA
Devauchelle-Pensec et al (2014)	122	RCT	Rituximab 1g/15d (n=63) Placebo (n=57)	NA	No differences in organ-by-organ ESSDAI domains	NA	Mean differences total score (-0.5, p>0.05)	NA
Jiang et al (2015)	6	Retrospective	Rituximab (100-500mg, weeks 0,1)	NA	Cytopenia (5CR, 1PR)	NA	NA	NA
Bowman et al (2017)	133	RCT (48 w)	Rituximab 1g/15d (n=67) Placebo (n=66)	NA	NA	NA	Log transformed total score (p=0.03 at 36w, p=0.07 at 48w)	NA

