Supplementary Table 4. Overview of clinical trials of biologic therapies using PROs as study endpoints

Reference	Therapy (assessment time frame) Patients (N)	Hierarchy of PRO(s) in endpoints	PRO(s)	Statistically significant improvement vs comparator
Norheim *et al*. (1)	Anakinra vs. placebo (4 weeks) N = 26	Primary (group-wise comparison of fatigue VAS scores at Week 4 adjusted for baseline)	Primary endpoint Fatigue Severity Scale (FSS) Fatigue VAS > 50% reduction Beck Depression Inventory (BDI)	NS NS *P* = 0.03 NS
Sankar *et al*. (2)	Etanercept vs. placebo (12 weeks) N = 28	Primary (improvement in 2 of the 3 Sjögren's disease domains: oral, ocular, and laboratory: ≥ 20% in dry mouth by VAS or ≥ 20% in total stimulated salivary flow, ≥ 20% improvement in either dry eyes VAS, van Bijsterveld score, or Schirmer I test; Laboratory: ≥ 20% in serum IgG level or ESR)	Primary endpoint Dry mouth VAS (0–100) Dry eye VAS (0–100)	36% etanercept group; 21% placebo group: NS NS NS
Mariette *et al*. (3)	Infliximab vs. placebo TRIPPS study (22 weeks) N = 103	Primary (≥ 30% improvement in 2 of the 3 VAS at Week 10)	Primary endpoint Joint Pain VAS (0–100) Fatigue VAS (0–100) Most disturbing buccal, ocular, skin, vaginal, bronchial dryness VAS (0–100) SF-36	27.8% infliximab group; 26.5% placebo group: NS NS NS NS NS NS

Reference	Therapy (assessment time frame) Patients (N)	Hierarchy of PRO(s) in endpoints	PRO(s)	Statistically significant improvement vs comparator
Dass *et al*. (4)	Rituximab vs. placebo (6 months) N = 17 pilot study	Primary (20% improvement in Fatigue VAS at 6 months)	Primary endpoint	87.5% rituximab group vs 55.6% placebo group: NS
			Fatigue VAS (6 months)	49.5% rituximab group vs 20.5% placebo group: NS
			FACIT-F	Not reported
			Pain VAS	Not reported
			PROFAD Somatic Fatigue Domain	NS
			SF-36 Social Functioning	12 rituximab group vs -25 placebo group: *P* = 0.01
Meijer *et al*. (5)	Rituximab vs. placebo (48 weeks) N = 30	Secondary	MFI	*P* = 0.023 for reduced activity at Week 36; *P* = 0.039 for reduced motivation at Week 12
			SF-36 Vitality	*P* = 0.013 at Week 36
			Oral sicca VAS (0–100)	Oral sicca and ocular sicca *P* < 0.05 for both at Week 48 and week 36
			Ocular sicca VAS (0–100)	

Reference	Therapy (assessment time frame) Patients (N)	Hierarchy of PRO(s) in endpoints	PRO(s)	Statistically significant improvement vs comparator
Carubbi *et al*. (6)	Rituximab vs. cDMARDs (120 weeks) N = 41	Secondary	Patient Global Disease Activity VAS	*P* < 0.01 at week 120
			Pain VAS	NS at week 120
			Fatigue VAS	*P* < 0.05 at week 120
			Dryness VAS	*P* < 0.01 at week 120
Devauchelle-Pensec *et al*. (7)	Rituximab vs. placebo TEARS study (6 months) N = 120	Primary (30 mm or greater improvement on 2 out of the 4 VAS scales at week 24)	Primary endpoint	23% rituximab group, 22% placebo group: NS
		Individual VAS scales secondary outcomes at Weeks 6 and 16	Global Disease VAS (0–100)	NS at Week 6 or 16
			Pain VAS (0–100)	NS at Week 6 or 16
			Fatigue VAS (0–100)	*P* < 0.001 at Week 6; *P* = 0.012 at Week 16
			Dryness VAS (0–100)	NS at Week 6 or 16

cDMARDS = conventional disease modifying anti-rheumatic drugs; ESR = erythrocyte sedimentation rate; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue; IgG = immunoglobulin G; MFI = Multidimensional Fatigue Inventory; NS = not significant; PRO = patient-reported outcome; PROFAD-SSI = Profile of Fatigue and Discomfort; SF-36 = 36-Item Short Form Survey; TEARS = Tolerance and Efficacy of Rituximab in Sjogren's Disease; TRIPPS = Trial of Remicade In Primary Sjögren's Syndrome; VAS = Visual Analog Scale.

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