

Supplementary Material on
Treating Spondyloarthropathies to Target –
A Systematic Literature Review Supporting Treatment Recommendations

including Supplementary Tables S1 (Search terms) and S2 (Studies, inclusion criteria at enrollment, patients baseline disease activity)

Table S1. Search terms

1	(treat\$ adj4 target\$).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]
2	(titrat\$ or adjust\$ or response-based).mp.
3	(optim\$ or adapt\$ or switch\$ or add\$ or chang\$ or expand\$ or step\$ or combin\$ or intensif\$ or escalat\$).ti.
4	((strateg\$ or aim\$ or goal\$ or target\$ or tight\$ or aggressiv\$ or control\$) adj2 (treat\$ or therap\$)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]
5	(lack\$ and effic\$).mp. or (insuffi\$ and respon\$).m_titl. [mp=ps, rs, ti, ot, ab, nm, hw, ui, an, sh, tn, dm, mf, dv, kw]
6	demand.m_titl. or demand.mp. or on-demand.mp.
7	((remission or ((low\$ or moderate or medium or high) and activity)) adj3 (strateg\$ or optimi\$ or adapt\$ or control\$ or frequency or dose\$ or dosing)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]
8	*Disease Progression/ or *Disease Management/ or *Disease Outbreaks/ or Disease/ or ((strateg\$ or proced\$ or consequ\$ or therap\$ or halt\$ or stop\$ or revers\$ or dela\$ or arrest\$ or detain\$ or slow\$ or preven\$ or retard\$ or avoid\$) adj3 (structural or functional or erosi\$ or progre\$ or disabilit\$ or invalidity or impediment or disablement or radiograph\$ or radiolog\$)).mp.
9	*Remission Induction/ or (strateg\$ or aim\$ or goal\$ or target\$ or tight\$ or aggressiv\$ or intens\$ or control\$).ti.
10	ankylosing spondylitis.mp. or ankylosing spondylitis/
11	psoriatic arthritis.mp. or psoriatic arthritis/
12	spondyl\$.m_titl.
13	seronegative.m_titl.
14	(psoriasis or (skin and psoriatic and arthritis) or pasi).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
15	(randomized controlled trial or clinical trial).pt. or Double-Blind Method/ or "double blind:".mp. or Placebos/ or placebo:.mp. or random:.mp. or single-blind method/ or exp Clinical Trials/ or clinical trial\$.mp. or ((singl\$ or doubl\$ or trebl\$) adj2 (blind\$ or mask\$)).mp. or placebo\$.mp. or exp Research Design/ or comparative study.pt. or exp Evaluation Studies/ or follow-up studies/ or prospective studies/ or (control\$ or prospectiv\$ or volunteer\$).mp. or clinical trial.mp. or Clinical Trial/ or meta-analysis.mp. or Meta-Analysis/

Table S2. Studies and their inclusion criteria at enrollment, patient baseline disease activity

STUDY / AUTHOR; PY	INCLUSION CRITERIA		BASELINE CHARACTERISTICS		
			DISEASE ACTIVITY	FUNCTION	
ANKYLOSING SPONDYLITIS	BASDAI	ADDITIONAL INCLUSION CRITERIA		BASDAI	BASFI
ATLAS 2006 ¹	≥ 4	at least 2 of 3 clinical criteria: • BASDAI ≥ 4 • MST ≥ 1 hour • VAS total back pain ≥ 4 (0-10)		6.3±1.7	5.2±2.2
ASSERT 2005 ²	≥ 4	BASDAI ≥ 4 and VAS spinal pain ≥ 4 (0-10)		6.6 (5.3-7.6)	5.7 (4.5-7.1)
Inman 2008 ³	≥ 4	BASDAI ≥ 4 and VAS total back pain ≥ 4 (0-10)		6.8 (5.7-7.7)	5.2 (3.2-5.9)
Haibel 2008 ⁴	≥ 4	-		6.5±1.2	5.4±2.0
CANDLE 2010 ⁵	≥ 4	-		not stated	not stated
Meric 2010 ⁶	≥ 4	-		36.6 (0.0-73.9)	not stated
Jois 2006 ⁷	≥ 4	-		6.6 (4.2-8.7)#	6.4 (4.7-8.2)#
Cherouvim 2004 ⁸	≥ 3	BASDAI ≥ 3 and pain >3 months with VAS pain ≥ 4 on 2 successive occasions		not stated	not stated
Collantes-Estevez 2005 ⁹	not stated	-		not stated	not stated
Van Denderen 2003 ¹⁰	not applicable	at least one of four clinical crit. • MST>30min • Peripheral synovitis • Enthesopathy • VAS pain>2	plus one laboratory criteria: • ESR>20mm/h or • CRP>20mg/l	4.4±4.4	4.5±4.1
Darmawan 2006 ¹¹				6.19±2.07	5.55±1.91
Cheung 2008 ¹²	not applicable	-		9.0 (8.3-9.6)* 8.5 (7.8-9.2)**p=n.sign.	7.0 (5.7-8.3)* 7.3 (6.2-8.5)**p=n.sign.
Breban 2008 ¹³	≥ 3	BASDAI ≥ 3 and VAS axial pain ≥ 3	and ≥ 1 of the following: • CRP more than twice ULN	6.2±1.5	5.4±2.0

			<ul style="list-style-type: none"> positive MRT of spine or SI joints enthesitis (power Doppler) 		
Braun 2008 ¹⁴	≥ 4	BASDAI ≥ 4 and VAS spinal pain ≥ 4		6.4±1.4 ¹⁵	5.2±1.9 ¹⁵
PSORIATIC ARTHRITIS	JOINT COUNTS	ADDITIONAL INCLUSION CRITERIA		SWOLLEN & TENDER JOINT COUNTS	HAQ
Cherouvim 2004 ⁸	≥ 3 SJC and ≥ 3 TJC			not stated	not stated
Collantes-Estevez 2005 ⁹	not stated	not stated		not stated	not stated
ADEPT 2009 ¹⁶	≥ 3 SJC and ≥ 3 TJC ¹⁷	-		SJC76: 14.3±12.2 TJC78:23.9±17.3 ¹⁷	1.0±0.6 ¹⁷
Kavanaugh 2009 ¹⁸	≥ 3 SJC and ≥ 3 TJC	SJC ≥ 3 and TJC ≥ 3 and negative RF	and at least 1 subset of PsA and plaque psoriasis with a lesion of ≥ 2cm Ø	SJC66: 12.0±8.4 TJC68: 22.5±5.7	not stated
IMPACT-2 2007 ¹⁹	≥ 5 SJC and ≥ 5 TJC	SJC ≥ 5 and TJC ≥ 5 and either <ul style="list-style-type: none"> CRP ≥ 15mg/l and/or MST ≥ 45 min 	active psoriasis, with at least one plaque ≥ 2cm Ø	SJC66: 13.9±7.9 TJC68: 24.6±14.1	1.1±0.6
Feletar 2004 ²⁰	≥ 6 SJC and / or ≥ 6 TJC	-		SJC66: 9.1±5.3	
Rahman 1998 ²¹	not stated	-		SJC: 15.4±9.1	
PSORIASIS	INCLUSION CRITERIA			PASI	Others
De Jong 2003 ²²	Stable psoriasis for ≥ 3 months			not stated	MPSS=2.5 [#]
Beissert 2009 ²³	PASI ≥ 10			22.4±9.2 24.6±11.1	-
Nevin 1995 ²⁴	not stated			21.7-54.2 ⁵	-

*Patients with spinal ankylosis; **patients without spinal ankylosis; Tender (TJC) and Swollen (SJC) are enlisted as specified in the respective manuscript. Where available, the applied number of joints (66 or 68 joint counts, etc) are specified. Mean±SD, median (Interquartilrange), #median (range), or \$range are given; Ø=diameter; SI joints=sacroiliac joints; RF=rheumatoid factor; PASI=, MPSS=modified psoriasis severity score

Bibliography

1. van der Heijde D, Kivitz A, Schiff MH, et al. for the ATLAS Study Group. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2006;54(7):2136-46.
2. van der Heijde D, Dijkmans B, Geusens P, et al. Efficacy and safety of infliximab in patients with ankylosing spondylitis: results of a randomized, placebo-controlled trial (ASSERT). *Arthritis Rheum* 2005;52:582-91.
3. Inman RD, Davis JC, van der Heijde D, et al. Efficacy and safety of golimumab in patients with ankylosing spondylitis: results of a randomized, double-blind, placebo-controlled, phase III trial. *Arthritis Rheum* 2008;58(11):3402-12.
4. Haibel H, Rudwaleit M, Listing J, et al. Efficacy of adalimumab in the treatment of axial spondylarthritis without radiographically defined sacroiliitis: Results of a twelve-week randomized, double-blind, placebo-controlled trial followed by an open-label extension up to week fifty-two. *Arthritis Rheum* 2008;58(7):1981-91.
5. Inman RD, Maksymowych WP for the CANDLE Study Group. A double-blind, placebo-controlled trial of low dose infliximab in ankylosing spondylitis. *J Rheumatol* 2010;37(6):1203-10.
6. Meric JC, Mulleman D, Ducourau E, et al. Therapeutic drug monitoring of infliximab in spondyloarthritis: an observational open-label study. *Ther Drug Monit* 2011;33(4):411-416.
7. Jois RN, Leeder J, Gibb A, et al. Low-dose infliximab treatment for ankylosing spondylitis--clinically- and cost-effective. *Rheumatol (Oxford)* 2006;45(12):1566-9.
8. Cherouvim EP, Zintzaras E, Boki KA, et al. Infliximab therapy for patients with active and refractory spondyloarthropathies at the dose of 3mg/kg: A 20-month open treatment. *J Clin Rheumatol* 2004;10:162-8.
9. Collantes-Estevez E, Munoz-Villanueva MC, Zarco P, et al. Effectiveness of reducing infliximab dose interval in non-responder patients with refractory spondyloarthropathies. An open extension of a multicenter study. *Rheumatology (Oxford)* 2005;44(11):1555-8.
10. Van Denderen JC, van der Horst-Bruinsma I, Bezemer PD, et al. Efficacy and safety of mesalazine (Salofalk) in an open study of 20 patients with ankylosing spondylitis. *J Rheumatol* 2003;30(7):1558-60.
11. Darmawan J, Nasution AR, Chen SL, et al. Excellent endpoints from step-down bridge combination therapy of 5 immunosuppressants in NSAID-refractory ankylosing spondylitis: 6 year international study in Asia - WHO-ILAR COPCORD stage II treatment of the autoimmune diseases. *J Rheumatol* 2006;33(12):2484-92.
12. Cheung PPM, Tymms KE, Wilson BJ, et al. Infliximab in severe active ankylosing spondylitis with spinal ankylosis. *Intern Med J* 2008;38(6):396-401.

13. Breban M, Ravaud P, Claudepierre P, et al. Maintenance of infliximab treatment in ankylosing spondylitis: results of a one-year randomized controlled trial comparing systematic versus on-demand treatment. *Arthritis Rheum* 2008;58(1):88-97.
14. Braun J, Baraliakos X, Listing J, et al. Persistent clinical efficacy and safety of anti-tumour necrosis factor alpha therapy with infliximab in patients with ankylosing spondylitis over 5 years: evidence for different types of response. *Ann Rheum Dis* 2008;67(3):340-345.
15. Braun J, Brandt J, Listing J, et al. Two year maintenance of efficacy and safety of infliximab in the treatment of ankylosing spondylitis. *Ann Rheum Dis* 2005;64:229–234.
16. Mease PJ, Ory P, Sharp JT, et al. Adalimumab for long-term treatment of psoriatic arthritis: 2-year data from the Adalimumab Effectiveness in Psoriatic Arthritis Trial (ADEPT). *Ann Rheum Dis* 2009;68(5):702-9.
17. Mease PJ, Gladman DD, Ritchlin CT et al. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2005;52:3279–89.
18. Kavanaugh A, McInnes I, Mease P, et al. Golimumab, a new human tumor necrosis factor alpha antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis: Twenty-four-week efficacy and safety results of a randomized, placebo-controlled study. *Arthritis Rheum* 2009;60(4):976-86.
19. Kavanaugh A, Krueger GG, Beutler A, et al. for the IMPACT 2 Study Group. Infliximab maintains a high degree of clinical response in patients with active psoriatic arthritis through 1 year of treatment: results from the IMPACT 2 trial. *Ann Rheum Dis* 2007;66(4):498-505.
20. Feletar M, Brockbank JE, Schentag CT, et al. Treatment of refractory psoriatic arthritis with infliximab: a 12 month observational study of 16 patients. *Ann Rheum Dis* 2004;63(2):156-61.
21. Rahman P, Gladman DD, Cook RJ, et al. The use of sulfasalazine in psoriatic arthritis: a clinical experience. *J Rheumatol* 1998;25(10):1957-61.
22. De Jong EMGJ, Mork NJ, Seijger MMB, et al. The combination of calcipotriol and methotrexate compared with methotrexate and vehicle in psoriasis: results of a multicentre placebo-controlled randomized trial. *British Journal of Dermatology* 2003;148:318-325.
23. Beissert S, Pauser S, Sticherling M, et al. A comparison of mycophenolate mofetil with ciclosporine for the treatment of chronic plaque-type psoriasis. *Dermatology* 2009;219:126-132.
24. Nevin RJ, Schulz EJ. Treatment of psoriasis with cyclosporine. *South African Medical Journal* 1995;85:1165-8.