Online supplementary material S4: Meta-analysis

Comparison 1. Adalimumab versus placebo

Analysis 1.1. Adalimumab 40mg versus placebo in Rheumatoid Arthritis at 52 weeks.

	Exp	erimen	tal	(Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD.	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Strand et al. , 2012	-12.7	14.29	265	-11	13.73	254	67.4%	-1.70 [-4.11, 0.71]	
Yount et al., 2007 (DE019)	-8.8	15.52	158	-5.4	14.78	136	32.6%	-3.40 [-6.87, 0.07]	
Total (95% CI)			423			390	100.0%	-2.25 [-4.23, -0.27]	-
Heterogeneity: Chi² = 0.62, o Test for overall effect: Z = 2.2			I² = 0%	•					-10 -5 0 5 10 Favours Adalimumab Favours Placebo

Analysis 1.2. Adalimumab 40mg versus placebo in Rheumatoid Arthritis at 12 weeks.

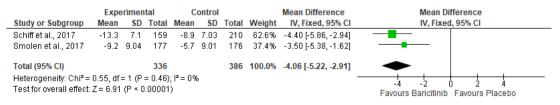
	Exp	eriment	tal	C	Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Strand et al. , 2012	-10.8	14.34	265	-8.5	14.1	254	22.6%	-2.30 [-4.75, 0.15]	
Strand et al., 2016	-5.04	7.95	188	-1.57	7.74	96	36.7%	-3.47 [-5.39, -1.55]	_ _
Yount et al., 2007 (ARMADA)	-8.2	15.22	66	-4	14.11	52	4.8%	-4.20 [-9.51, 1.11]	
Yount et al., 2007 (DE019)	-7	14.15	183	-4.6	14.96	160	14.1%	-2.40 [-5.49, 0.69]	
Yount et al., 2007 (STAR)	-6.8	15.3	301	-3.6	15.77	294	21.7%	-3.20 [-5.70, -0.70]	
Total (95% CI)			1003			856	100.0%	-3.03 [-4.19, -1.87]	◆
Heterogeneity: Chi ² = 0.91, df=	= 4 (P = 1	0.92); I ^z	= 0%						
Test for overall effect: Z = 5.10	(P < 0.0	0001)							-10 -5 0 5 10 Favours Adalimumab Favours Placebo

Analysis 1.3. Adalimumab 40mg versus placebo in Psoriatic Arthritis at 12 weeks.

	Experimental Control							Mean Difference	Mean Difference
Study or Subgroup	Mean	Total	Mean SD Total		Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Genovese et al., 2007	-2.6	7.1	49	-2.3	6.7	46	49.0%	-0.30 [-3.08, 2.48]	
Gladman et al., 2007	-6.5	11.1	140	-0.6	8.4	148	51.0%	-5.90 [-8.18, -3.62]	
Total (95% CI)			189			194	100.0%	-3.16 [-8.64, 2.33]	
Total (95% CI) 189 194 100.0% -3.16 [-8.64, 2.33] Heterogeneity: Tau ² = 14.00; Chi ² = 9.33, df = 1 (P = 0.002); l ² = 89% -3.16 [-8.64, 2.33] -3.16 [-8.64, 2.33] Test for overall effect: Z = 1.13 (P = 0.26) -3.16 [-8.64, 2.33] -3.16 [-8.64, 2.33]									-20 -10 0 10 20 Favours Adalimumab Favours Placebo

Comparison 2. Baricitinib versus placebo

Analysis 2.1. Baricitinib 4mg versus placebo in Rheumatoid Arthritis at 24 weeks.



Comparison 3. Sarilumab versus placebo

Analysis 3.1. Sarilumab versus placebo in Rheumatoid Arthritis at 24 weeks.

	Experimental			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight IV, Random, 95% CI		IV, Random, 95% Cl
5.1.1 150mg									
Strand et al., 2016	-8.6	0.5	311	-5.8	0.5	252	26.0%	-2.80 [-2.88, -2.72]	•
Strand et al., 2017	-9.9	0.8	126	-6.8	0.9	98	23.9%	-3.10 [-3.33, -2.87]	+
Subtotal (95% CI)			437			350	50.0%	-2.93 [-3.22, -2.64]	◆
Heterogeneity: Tau ² =	0.04; Ch	i² = 5.	94, df=	: 1 (P =	0.01)	; I² = 8 3	1%		
Fest for overall effect:	Z = 19.70) (P <	0.0000	1)					
5.1.2 200mg									
Strand et al., 2016	-9.2	0.5	320	-5.8	0.5	252	26.0%	-3.40 [-3.48, -3.32]	•
Strand et al., 2017	-10.1	0.8	136	-6.8	0.9	98	24.0%	-3.30 [-3.52, -3.08]	÷
Subtotal (95% CI)			456			350	50.0%	-3.39 [-3.47, -3.31]	•
Heterogeneity: Tau² =	0.00; Ch	i² = 0.	68, df=	: 1 (P =	0.41)	; I ² = 09	6		
Fest for overall effect:	Z = 85.78	}(P <	0.0000	1)					
									•
Fotal (95% CI)			893			700	100.0%	-3.15 [-3.51, -2.78]	•
Heterogeneity: Tau² =	0.13; Ch	i ^z = 10	03.71, d	if = 3 (P	< 0.0	00001);	I² = 97%	-	
Fest for overall effect:	Z = 16.95	5 (P ≺	0.0000	1)					Favours Sarilumab Favours Placebo
Fest for subgroup diff	erences:	Chi² =	= 8.82,	df = 1 (F	P = 0.	003), I ^z	= 88.7%		

Comparison 4. Tocilizumab versus placebo

Analysis 4.1.	Tocilizumab versus placebo in Rheumatoid Arthritis at 24 weeks.
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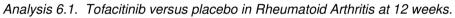
	Expe	rimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
6.1.1 8mg									
Smolen et al., 2008	-8.6	5.47	205	-4	7.28	204	26.2%	-4.60 [-5.85, -3.35]	
Strand et al. , 2012	-8.83	5.79	129	-4.22	4.5	60	21.1%	-4.61 [-6.12, -3.10]	_
Teitsma et al., 2017 Subtotal (95% Cl)	-7.4	9.5	106 440	-4.7	9.4	108 372	10.2% 57.5%		◆
Heterogeneity: Tau ² =	0.00; Ch	i ² = 1.9	90, df =	2 (P = I	0.39); I	z = 0%			
Test for overall effect:	Z = 9.50	(P < 0.	00001)					
6.1.2 4mg									
Smolen et al., 2008	-7.3	7.1	213	-4	7.28	204	23.5%	-3.30 [-4.68, -1.92]	
Strand et al. , 2012 Subtotal (95% CI)	-6.66	6.27	105 318	-4.22	4.5	60 264		-2.44 [-4.09, -0.79] - 2.95 [-4.01, -1.89]	•
Heterogeneity: Tau ² = Test for overall effect: 2					0.43); I	²= 0%			
Total (95% CI)			758			636	100.0%	-3.69 [-4.59, -2.79]	◆
Heterogeneity: Tau ² = Test for overall effect: J Test for subgroup diffe	Z = 8.06	(P < 0.	00001)				_	-4 -2 0 2 4 Favours Tocilizumab Favours Placebo

Comparison 5. Golimumab versus placebo

Analysis 5.1. Golimumab 100mg versus placebo in Rheumatoid Arthritis at 24 weeks.

	Exp	eriment	tal	Control				Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixe	d, 95% Cl		
Bingham et al., 2014	-7.96	10.79	395	-2.54	10.22	197	65.4%	-5.42 [-7.20, -3.64]	-8-			
Genovese et al., 2012	-7.16	8.58	89	-2.16	9.53	124	34.6%	-5.00 [-7.45, -2.55]				
Total (95% CI)			484			321	100.0%	-5.27 [-6.71, -3.84]	•			
Heterogeneity: Chi ² = 0.				= 0%					-10 -5		10	
Test for overall effect: Z	= 7.18 (F	° < 0.00	001)						Favours Golimumab	Favours Plac	ebo	

Comparison 6. Tofacitinib versus placebo



	Expe	erimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
8.1.1 5mg									
Strand et al., 2014	-6.27	10.9	117	-1.11	11.1	114	7.6%	-5.16 [-8.00, -2.32]	
Strand et al., 2016a	-5.8	8.57	294	-2.1	7.27	147	26.1%	-3.70 [-5.23, -2.17]	_
Strand et al., 2016b Subtotal (95% CI)	-5.85	8.02	185 596	-1.57	7.74	96 357		-4.28 [-6.21, -2.35] - 4.11 [-5.22, -3.01]	•
Heterogeneity: Chi ² =	0.83, df=	= 2 (P =	0.66);	l² = 0%					
Test for overall effect:	Z = 7.29	(P < 0.	00001)						
8.1.2 10mg									
Strand et al., 2014	-4.57	11.51	125	-1.11	11.1	114	7.4%	-3.46 [-6.33, -0.59]	
Strand et al., 2016a	-6.9	8.52	291	-2.1	7.27	147	26.1%	-4.80 [-6.33, -3.27]	
Strand et al., 2016b	-6.88	7.98	183	-1.57	7.74	96	16.4%	-5.31 [-7.24, -3.38]	_ _
Subtotal (95% CI)			599			357	49.9%	-4.77 [-5.87, -3.66]	◆
Heterogeneity: Chi ² = Test for overall effect:									
Total (95% CI)			1195			714	100.0%	-4.44 [-5.22, -3.66]	◆
Heterogeneity: Chi ² =	2.61, df=	= 5 (P =	0.76);	l² = 0%				-	
Test for overall effect:	Z=11.1	3 (P < 0	.00001	0					-4 -2 U 2 4 Eavours Tofacitinib Eavours Placebo
Test for subgroup diff	erences:	Chi ² =	0.68, d	f=1 (P	= 0.41), I ² = 0	%		

Comparison 7. Secukinumab versus placebo

Analysis 7.1.	Secukinumab	versus placebo in	Spondyloarthritis a	at 16 weeks.
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	Expe	rimen	tal	Co	ontro	1		Mean Difference		Mean D	ifference	9	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	om, 95%	CI	
9.1.1 150mg													
Deodhar et al., 2016	-6.8	0.8	125	-2.5	0.9	122	26.3%	-4.30 [-4.51, -4.09]	-				
Marzo-Ortega et al., 2017	-8.1	1.1	72	-3.3	1.1	74	23.8%						
Subtotal (95% CI)			197			196			•				
Heterogeneity: Tau ² = 0.10	: Chi ² = 5	.57. df	= 1 (P	= 0.02);	$ ^{2} = 8$	32%							
Test for overall effect: Z = 1													
9.1.2 75mg													
Deodhar et al., 2016	-6.6	0.9	124	-2.5	n 9	122	26.1%	-4.10 [-4.32, -3.88]					
Marzo-Ortega et al., 2017		1.1		-3.3									
Subtotal (95% CI)	0.1		197	0.0		196		-3.76 [-4.45, -3.08]	•				
Heterogeneity: Tau ² = 0.22 Test for overall effect: Z = 1				P = 0.00	1); I²	= 91%							
Total (95% CI)			394			392	100.0%	-4.15 [-4.60, -3.71]	•				
Heterogeneity: Tau ² = 0.19); Chi ² = 31.78, df = 3 (P < 0.00001); I ² = 91%						%					+	+
Test for overall effect: Z = 1				0.00	0017		~		-4	-2	0	2	4
Test for subgroup difference			· ·				~		Favours Se	cukinumab	Favour	s Placeb	0

Comparison 8. Etanercept versus placebo

Analysis 8.1. Etanercept 50mg versus placebo in Spondyloarthritis at 12 weeks.

