Trial eligibility criteria and patient baseline characteristics

S4 Table: Dataset

Data on all eligible trials. ID number corresponds to reference number.(1-50)(51-62).

ID number	1	2	3
Name of Biological Agent	ABA	ABA	ABA
Name of Co-allocation	PLA	PLA	MTX
DMARD History	TT IR	DMARD IR	DMARD IR
csDMARD Handling at Randomisation	CON	DIS	DIS
MTX Handling at Randomisation	CON	DIS	CON
TT Handling at Randomisation	DIS	DIS	NR
Max Disease Duration	NR	ES	NR
Min 66 SJC	10	10	10
Min 68 TJC	12	12	12
Min CRP	10 mg/mL<	NR	10 mg/mL<
Min ESR	NR	28	NR
RF status of all trial patients	Mix	Mix	Mix
Baseline female percentage	78.0	75.0	79.1
Baseline age	53.2	49.9	51.1
Baseline RF percentage	73.2	80.7*	80.7
Baseline anti-CCP percentage	NR	NR	NR
Baseline DAS28	6.5	7.0#	6.4
Baseline CRP	44.0	32.0	31.3
Baseline ESR	NR	32.8	NR
Baseline 66 SJC	22.4	23.7	21.6
Baseline 68 TJC	31.7	30.8	31.4
Baseline RA duration	11.9	3.3	8.6
Baseline MD global (VAS)	68.3	73.2	67.8
Baseline PT global (VAS)	69.4	72.2	62.7
Baseline pain (VAS)	70.5	70.2	64.2
Baseline HAQ	1.8	1.5*	1.7
n, randomised in active arm	262	32	433
n, randomised in control arm	131	32	219
Outcome week	24	12	26
Active arm: n, achieving ACR20	129	17	288
Active arm: total in ACR20 analysis	256	32	424
Active arm: n, achieving DAS28-remission	26	NR	63
Active arm: total in DAS28-remission analysis	256	NR	424
Control arm: n, achieving ACR20	26	10	85
Control arm: total in ACR20 analysis	133	32	214
Control arm: n, achieving DAS28-remission	1	NR	6
Control : total in DAS28-remission analysis	133	NR	214
Risk of Bias§	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L

Trial eligibility criteria and patient baseline characteristics

10	9	8	7	6	5	4
TOC	ABA	ABA	TOC	TOC	TOC	TOC
MTX	MTX	MTX	MTX	PLA	MTX	MTX
TT IR	DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD IR
DIS	DIS	DIS	DIS	CON	DIS	DIS
CON	CON	CON	CON	CON	CON	CON
DIS	DIS	NAIVE	DIS	NU	DIS	DIS
NR	NR	NR	NR	NR	NR	NR
6	10	10	6	6	6	10
8	12	12	8	8	8	10
10 mg/mL<	10 mg/mL<	10 mg/mL<	10 mg/mL<	10 mg/mL<	10 mg/mL<	10 mg/mL<
28	NR	NR	28	28	28	28
Mix	Mix	Mix	Mix	Mix	Mix	Mix
81.6	70.4	85.0	81.5	82.0	82.5	77.0
53.7	55.2	49.2	50.7	53.3	52.4	50.5
77.1	94.4	86.3	77.0	80.7*	82.5	87.9
NR	NR	NR	NR	NR	NR	NR
6.8	6.5¤	6.9	6.8	6.7	6.6	6.5
32.3	30.5	29.3	25.0	26.0	22.5	28.0
51.7	NR	48.4	50.5	48.5	46.4	41.0
18.9	21.6	20.8	20.1	19.4	17.0	16.7
31.1	30.0	31.1	32.3	29.8	28.6	23.8
12.0	9.3	8.1	7.6	6.9	9.2	10.9
66.9	62.7	63.6*	63.9	63.7	62.9	63.6
70.5	59.8	63.3*	64.2	66.0	62.9	65.4
64.4	63.3	60.2*	58.6	58.3	55.5	60.4
1.7	1.0	1.8	1.6	1.5	1.5	1.5*
175	115	156	205	805	399	50
160	119	110	204	415	392	49
24	26	28	24	24	24	16
85	69	104	120	488	224	36
170	115	156	205	803	398	49
40	NR	18	47	241	105	17
132	NR	156	171	803	315	49
16	42	46	54	101	106	20
158	119	110	204	413	393	49
1	NR	3	2	24	8	4
64	NR	110	121	413	212	49
L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/U/L	L/L/L/L/L

Trial eligibility criteria and patient baseline characteristics

17	16	15	14	13	12	11
ETA	RIT	RIT	RIT	RIT	INF	INF
MTX	MTX	MTX	MTX	MTX	MTX	MTX
DMARD naive	DMARD IR	DMARD IR	DMARD IR	TT IR	DMARD naive	DMARD IR
NU	DIS	NU	DIS	DIS	NAIVE	NU
NU	CON	CON	CON	CON	NAIVE	CON
NAIVE	DIS	NR	NAIVE	DIS	NAIVE	NAIVE
ES	NR	NR	NR	NR	EA	NR
10	8	8	8	8	6*	6
12	8	8	8	8	8*	6
20 mg/mL<	15 mg/mL<	15 mg/mL<	4.5-7 mg/mL<	15 mg/mL<	20 mg/mL<	20 mg/mL<
28	28	28	28	28	NR	28
Mix	Pos	Pos	Mix	Mix	Mix	Mix
76.5	80.0	77.5	83.4	81.0	81*	80.5
52.8	51.1	54.0	51.7	52.4	52.2	53.5
73.5	100.0	100.0	74.3	79.0	65.0	80.5
NR	NR	NR	NR	NR	NR	NR
5.5	6.8	6.9	6.5	6.9	6.6¤	6.4¤
27.8	31.5	30.5	24*	37.4	42.0	30.5
NR	40.5	52.5	NR	48.2	NR	NR
22.4	21.5	21.0	20.2	23.2	19.2*	19.0
33.7	33.5	32.0	29.5	33.5	28.3*	28.0
6.8	10.1	11.5	7.0	11.9	8.7*	8.7
63.6*	63.6*	63.6*	63.6*	63.6*	63.6*	63.0
63.3*	63.3*	63.3*	63.3*	63.3*	63.3*	64.0
60.2*	60.2*	60.2*	60.2*	60.2*	60.2*	68.5
1.5*	1.5*	1.5*	1.5*	1.9	1.3	1.8
229	128	40	172	311	10	86
229	128	40	172	209	10	88
24	24	24	24	24	14	30
187	66	29	86	152	6	42
231	122	40	170	298	10	83
62	NR	NR	16	45	NR	NR
205	NR	NR	170	298	NR	NR
166	34	15	40	36	2	17
228	122	40	172	201	10	84
26	NR	NR	4	4	NR	NR
193	NR	NR	172	201	NR	NR
L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	U/L/L/L/H/L	L/L/L/L/L/L

Trial eligibility criteria and patient baseline characteristics

24	23	22	21	20	19	18
GOL	ETA	ADA	ADA	ADA	ADA	ETA
MTX	PLA	PLA	MTX	MTX	PLA	MTX
DMARD naive	DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD IR
NU	DIS	DIS	DIS	DIS	CON	DIS
NAIVE	DIS	DIS	CON	CON	CON	CON
NAIVE	NR	NU	NAIVE	NAIVE	NR	NR
NR	NR	NR	NR	NR	NR	NR
4	10	10	6	6	6	6
4	12	12	9	9	9	6
15 mg/mL<	20 mg/mL<	20 mg/mL<	NR	10 mg/mL<	NR	NR
28	28	28	NR	NR	NR	NR
Mix	Mix	Mix	Mix	Mix	Mix	Mix
84.3	75.0	78.5	78.3	74.7	79.4	84.3
49.7	52.0	53.1	56.6	51.2	55.4	49.7
80.7*	79.0	80.7	80.7*	85.5	62.9	86.0
NR	NR	NR	NR	NR	NR	NR
6.2	7.2#	7.1	6.3¤	6.1¤	6.1¤	6.6#
25.0	44.0	54.8	25.8	18.0	15.0	23.3
NR	37.0	55.9	NR	NR	NR	28.7
15.4	25.0	20.2	17.1	19.2	21.1	19.0
28.2	34.0	34.6	28.3	27.7	27.5	28.0
3.2	11.5	11.1	11.7	11.0	10.4	13.0
61.0	69.0	67.7	58.8	61.7	59.8	61.7
6.0	69.5	72.2	57.4	53.5	53.4	60.0
6.3	66.0	70.1	55.0	56.1	55.4	52.0
1.5	1.7	1.9	1.6	1.5	1.4	1.5
159	81	113	67	207	318	59
160	83	110	62	200	318	30
24	13	26	24	24	24	24
98	48	52	45	131	168	42
159	78	113	67	207	318	59
40	NR	NR	NR	NR	NR	NR
159	NR	NR	NR	NR	NR	NR
79	18	21	9	59	111	8
160	80	110	62	200	318	30
18	NR	NR	NR	NR	NR	NR
160	NR	NR	NR	NR	NR	NR
L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L

31	30	29	28	27	26	25
TOC	ADA	ETA	CER	ADA	GOL	GOL
PLA	PLA	SSZ	PLA	PLA	PLA	MTX
DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD IR	TT IR	DMARD IR
DIS	DIS	NU	DIS	DIS	CON	NU
DIS	DIS	NU	DIS	DIS	CON	CON
NR	NU	NAIVE	NAIVE	NAIVE	NU	NAIVE
NR	NR	ES	NR	NR	NR	NR
6	10	6	9	10	4	4
6	12	10	9	12	4	4
10 mg/mL<	20 mg/mL<	20 mg/mL<	10 mg/mL<	20 mg/mL<	NR	15 mg/mL<
30	28	28	28	NR	NR	28
Mix	Mix	Mix	Mix	Mix	Mix	Mix
78.6	81.0	80.8	83.7	78.1	79.5	81.6
54.5	51.4	51.5	48.7	55.2	54.5	52.0
80.7	87.5	80.7*	100.0	87.6	72.5	83.3
NR	NR	NR	NR	NR	72.0	80.7
6.6#	7.1	6.9#	6.3	6.6¤	6.3	6.1
50.0	59.5	11.6	11.5	61.8	9.0	8.8
68.0	52.7	38.4	33.2	NR	NR	NR
13.8	19.5	19.2	20.6	19.2	14.0	12.4
18.0	31.0	31.3	29.0	24.1	26.5	23.0
8.3	9.7	6.2	9.5	9.2	9.7	5.7
63.6*	65.1	63.6*	72.0	75.2	63.0	58.6
63.3*	74.6	63.3*	66.0	68.0	66.5	55.8
60.2*	72.9	58.7	56.5	65.5	69.5	58.6
1.5*	1.7	1.6	1.5	1.5	1.7	1.3
55	70	104	111	91	153	89
54	70	52	109	87	155	133
12	12	24	24	24	14	14
43	40	74	50	40	54	49
55	70	100	111	91	153	89
NR	NR	NR	NR	NR	13	14
NR	NR	NR	NR	NR	153	89
6	7	14	10	12	28	44
53	70	50	109	87	155	133
NR	NR	NR	NR	NR	1	2
NR	NR	NR	NR	NR	155	133
L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L

Trial eligibility criteria and patient baseline characteristics

38	37	36	35	34	33	32
CER	CER	INF	ETA	GOL	RIT	TOC
MTX	MTX	MTX	MTX	MTX	MTX	PLA
DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD naive	DMARD IR
NU	DIS	NU	DIS	NU	NU	CON
CON	CON	CON	CON	CON	NAIVE	CON
NU	NU	NR	DIS	NAIVE	NR	DIS
ES	ES	NR	NR	NR	ES	NR
9	9	6	10	6	8	6
9	9	6	10	6	8	6
15 mg/mL<	15 mg/mL<	20 mg/mL<	NR	15 mg/mL<	10 mg/mL<	10 mg/mL<
30	30	28	NR	28	NR	28
Mix	Mix	Mix	Mix	Mix	Mix	Mix
83.9	82.9	78.1	86.5	80.0	81.0	81.0
52.0	51.7	55.2	49.2	54.5	48.0	55.4
77.7	80.7	80.7*	80.7*	80.7*	86.0	80.7*
NR	NR	NR	NR	NR	NR	NR
6.8	6.9	6.0¤	6.1¤	6.4	7.1	6.5
14.0	16.0	41.5	15.2	20.5	31.0	18.2
42.7	44.0	NR	NR	NR	NR	46.4
21.0	21.5	14.3	23.0	13.5	20.8	19.8
30.2	30.5	18.4	21.2	25.0	32.9	29.9
5.9	6.1	8.3	8.7*	6.9	0.4	8.6
64.8	63.6*	63.6*	77.5	60.5	63.6*	62.4
61.5	63.3*	63.3*	68.0	67.5	63.3*	62.1
61.2	60.2*	60.2*	56.4	70.0	60.2*	56.3
1.6	1.5*	1.5*	1.1	1.5	1.8	1.5*
246	393	50	29	35	251	412
127	199	50	29	35	252	207
24	24	14	12	16	24	24
141	228	30	26	21	183	183
246	388	49	29	35	250	409
23	NR	NR	NR	2	NR	157
246	NR	NR	NR	35	NR	409
11	27	11	10	13	147	52
127	198	47	29	35	250	205
1	NR	NR	NR	0	NR	3
127	NR	NR	NR	35	NR	205
L/L/L/L/H/L	L/L/L/L/L/L	L/L/L/L/L/L	U/L/U/U/L/L	L/L/L/L/U/L	L/L/L/L/L/L	L/L/L/L/L/L

Trial eligibility criteria and patient baseline characteristics

45	44	43	42	41	40	39
CER	TOF	TOF	GOL	ABA	ADA	INF
MTX	PLA	PLA	PLA	MTX	MTX	MTX
DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD naïve	DMARD IR	DMARD IR
DIS	DIS	DIS	DIS	NU	DIS	CON
CON	DIS	DIS	DIS	NAIVE	CON	CON
NAIVE	NU	DIS	NR	NR	NAIVE	NAIVE
NR	NR	NR	NR	EA	NR	NR
9	6	6	6	10	6	6
9	6	6	6	12	9	6
10 mg/mL<	4.5-7 mg/mL<	4.5-7 mg/mL<	20 mg/mL<	4.5-7 mg/mL<	NR	NR
28	28	28	28	NR	NR	NR
Mix	Mix	Mix	Mix	Pos	Mix	Mix
69.2	88.0	85.5	81.1	77.6	78.7	81.6
54.3	53.5	51.4	52.6	49.9	53.0	52.5
76.1	75.9	80.7*	80.7*	96.4	87.2	81.7
NR	NR	NR	NR	89.0	NR	NR
6.2	6.6	6.7	5.9	6.3	6.4	5.7¤
12.5	24.0	21.2	23.6	33.5	21.0	14.0
25.1	46.8	52.4	NR	NR	NR	NR
22.5	17.1	16.6	12.9	22.4	22.5	15.0
30.0	26.5	29.2	15.2	31.1	33.7	22.0
9.6	9.6	7.9	8.7	0.5	6.7	8.1
71.0	64.3	63.6*	58.6	63.6*	81.4	62.5
66.0	64.2	63.3*	54.3	63.3*	72.0	56.5
58.7	62.1	60.2*	55.4	60.2*	64.8	60.0
1.4	1.5	1.5	1.0	1.7	1.7	1.5
126	50	244	102	256	35	360
121	59	122	110	255	12	363
24	12	13	14	12	12	22
56	29	144	51	164	19	199
124	49	241	101	256	35	343
9	6	14	13	41	NR	106
97	49	229	97	256	NR	343
27	13	32	20	134	4	87
119	59	120	105	253	12	341
2	2	5	2	20	NR	48
65	59	104	94	253	NR	341
L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	L/L/L/L/L	U/L/L/L/L	L/L/L/L/H/L

Trial eligibility criteria and patient baseline characteristics

52	51	50	49	48	47	46
GOL	TOF	GOL	ABA	ADA	CER	CER
MTX	MTX	MTX	MTX	MTX	MTX	PLA
DMARD IR	DMARD IR	DMARD IR	DMARD IR	DMARD naive	DMARD IR	DMARD IR
NU	NU	NR	DIS	NU	NU	CON
CON	CON	CON	CON	NAIVE	CON	NU
NAIVE	NU	NU	DIS	NAIVE	NU	NU
NR	NR	NR	NR	EA	ES	ES
6	6	4	10	6	9	6
6	6	4	12	8	9	6
10 mg/mL<	4.5-7 mg/mL<	15 mg/mL<	10 mg/mL<	15 mg/mL<	15 mg/mL<	20 mg/mL<
NR	28	28	NR	28	30	28
Pos	Mix	Mix	Mix	Mix	Mix	Mix
81.6	82.0	83.9	79.5	74.0	84.9	74.4
52.7	53.3	50.8	53.4	50.5	51.2	55.7
80.7*	66.6	80.7*	80.7*	88.0	86.2	87.4
NR	70.7	NR	NR	84.0	NR	NR
6.0	6.6	5.6	6.0	6.0	6.3	6.2
19.0	15.3	20.5	33.9	28.5	15.0	16.5
NR	48.4	NR	NR	NR	46.9	50.0
12.0	16.7	11.6	17.1	12.5	17.0	14.6
23.3	28.1	13.2	21.7	16.0	19.3	16.9
4.7	7.7	8.7	7.3	4.3	5.7	5.6
63.6*	63.6*	56.2	63.6*	62.5	63.3	60.9
63.3*	63.3*	48.4	65.4	63.5	55.3	56.8
60.2*	60.2*	50.9	60.2*	65.0	58.2	56.8
1.6	1.5	1.0	1.4	1.6	1.1	1.1
395	204	89	62	515	82	116
197	108	90	66	517	77	114
14	26	14	24	26	12	12
231	101	62	47	361	63	78
395	196	86	61	515	82	116
NR	11	27	15	175	13	19
NR	177	86	61	515	82	116
49	30	24	14	295	22	17
197	106	88	66	517	77	114
NR	1	3	1	88	0	1
NR	92	88	66	517	77	114
L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L

Trial eligibility criteria and patient baseline characteristics

59	58	57	56	55	54	53
TOF	TOF	TOF	INF	ADA	TOF	CER
MTX	MTX	MTX	MTX	MTX	MTX	PLA
DMARD IR	TT IR	DMARD IR	DMARD naive	DMARD IR	DMARD IR	DMARD IR
DIS	DIS	NU	NU	DIS	DIS	CON
CON	CON	CON	NAIVE	CON	CON	CON
DIS	DIS	NU	NR	NR	DIS	NU
NR	NR	NR	EA	NR	NR	NR
6	6	6	6	6	6	6
6	6	6	8	9	6	8
4.5-7 mg/mL<	4.5-7 mg/mL<	4.5-7 mg/mL<	NR	NR	4.5-7 mg/mL<	10 mg/mL<
28	28	28	NR	NR	28	28
Mix	Mix	Mix	Mix	Mix	Mix	Mix
80.7	82.7	84.4	68.9	90.6	85.4	78.0
52.5	54.9	53.4	51.8	49.1	50.3	55.1
82.9	63.1	76.0	65.6	79.7	85.5	74.4
NR	72.1	85.0	58.0	NR	NR	66.3
6.1	6.5	6.3	5.3	5.0¤	6.0	6.4
18.4	18.0	14.9	36.9	2.4	19.5	9.2
NR	47.3	50.4	NR	NR	NR	37.6
14.9	16.7	14.1	11.4	12.5	14.7	17.0
21.5	28.3	23.7	13.8	19.7	17.1	23.1
9.1	12.2	9.0	0.4	6.8	8.4	5.6
53.3	64.9	58.2	63.6*	63.8	59.4	63.6*
57.4	63.3	56.8	63.3*	61.4	56.1	63.3*
53.1	63.2	57.3	60.2*	58.5	53.3	60.2*
1.3	1.6	1.4	1.4	1.4	1.3	1.5
71	133	321	15	65	28	851
69	132	160	14	63	28	212
12	13	26	22	24	12	12
40	55	159	13	40	26	435
71	132	309	15	65	27	851
10	8	19	NR	NR	NR	136
60	119	265	NR	NR	NR	851
25	32	39	4	23	4	55
69	131	154	14	63	28	212
4	2	2	NR	NR	NR	12
60	120	129	NR	NR	NR	212
L/L/L/L/L	L/L/L/L/L	L/L/L/L/H/L	L/L/H/L/H/L	L/L/L/L/L/L	L/L/L/L/L/L	L/L/L/L/L/L

Trial eligibility criteria and patient baseline characteristics

60	ADA	MTX	DMARD naive	DIS	NAIVE	NAIVE	EA	8	10	15 mg/mL<	28	Mix	81.4	54.0	84.4	84.1	6.6	30.0	60.8	16.9	13.2	0.3	66.0	65.2	60.2*	1.2	171	163	26	129	171	53	171	92	163	24	163	L/L/L/L/L/L
61	TOF	PLA	DMARD IR	CON	CON	NU	NR	4	4	4.5-7 mg/mL<	28	Mix	81.7	52.5	73.5	69.2	6.3	17.4	50.4	14.4	24.8	8.7	59.9	58.7	57.1	1.4	318	159	26	164	315	24	284	49	159	4	153	L/L/L/L/L/L
62	INF	MTX	DMARD IR	NU	CON	NR	NR	3	8	NR	28	Mix	85.0	48.4	80.7*	NR	6.4¤	24*	NR	19.2*	28.3*	7.5	63.6*	63.3*	60.2*	1.5*	87	86	18	66	87	NR	NR	42	86	NR	NR	L/L/L/L/U/L

ABA, abatacept; ACR20, American College of Rheumatology 20% improvement criteria; ADA, adalimumab; Anti-CCP, anti-cyclic citrullinated peptide; BL, baseline; CER, certolizumab; CON, continued; DAS28, disease activity score in 28 joints; DIS, Discontinued; csDMARD, conventional synthetic disease modifying antirheumatic drugs; ETA, etanercept; GOL, golimumab; HAQ, health assessment questionnaire; INF, infliximab; IR, inadequate responders; MD global, physicians global assessment (0-100); Min, minimum; MTX, metothrexate; NR, Not reported; NU, Not using; OR, odds ratio; PLA, placebo; PT global, patient global assessment; RIT, rituximab; RF, rheumatoid factor; SJC, swollen joint count; TJC, tender joint count; TOC, tocilizumab; TOF, tofacitinib; TT, Targeted therapy; VAS, visual analogue scale (0-100).

*Median values for the dataset imputed

Calculated from DAS28-ESR(4) formula: 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.70*Ln(ESR) + 0.014*GH

¤Calculated from DAS28-CRP(4) formula: 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.36*ln(CRP+1) + 0.014*GH + 0.96

§Risk of bias rated as L, low; U, unclear; H, high per domain: Allocation concealment/ Blinding of participants and personnel/ Blinding of outcome assessment/ Incomplete outcome data/ Selective reporting

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