

Table 1: Study characteristics of 51 randomized controlled trials

<u>First author</u>	<u>Year</u>	<u>Study design</u>	<u>Country/Region</u>	<u>No. of Centers</u>	<u>Overall N</u>	<u>From/to</u>	<u>Drugs analyzed</u>	<u>Trial name</u>
Burmester et al. (21)	2014	Phase IIa	NA	NA	1262	NA	TCZ	SUMMACTA
Cohen et al. (22)	2006	Phase IIIa	USA, EU, CAN, ISR	NA	520	NA	RTX	REFLEX
Combe et al. (23)	2006	NA	Europe, Australia	NA	254	NA	ETN	
Dougados et al. (24)	2014	Phase IIb	Europe	NA	556	NA	TCZ	ACT RAY
Emery et al. (25)	2006	Phase IIb	NA	NA	465	NA	RTX	
Emery et al. (26)	2010	Phase IIIa	11 countries	102	511	NA	RTX	SERENE
Emery et al. (27)	2008	Phase IV	EU, Latin America, Asia, Australia	NA	542	2004 - 2006	ETN	COMET
Emery et al. (28)	2008	Phase IIIa	USA, EU	NA	499	NA	TCZ	RADIATE
Gabay et al. (29)	2013	Phase IV	15 countries	76	452	NA	TCZ	ADACTA
Genovese et al. (30)	2004	NA	USA	41	244	NA	ETN	
Genovese et al. (31)	2008	Phase IIa	EU, South Am., Asia, Australia	18 countries	1220	2005 - 2006	TCZ	TOWARD
Gerlag et al. (32)	2010	Phase IIb	Eastern EU / 14 countries	61	482	NA	ETN	
Jobanputra et al. (33)	2012	Pragmatic	United Kingdom	NA	125	NA	ETN	RED SEA
Jones et al. (34)	2010	Phase III	USA, CAN, Israel	NA	673	NA	TCZ	AMBITION
Kameda et al. (35)	2010	Phase IV	Japan	NA	151	2005 - 2007	ETN	JESMER
Keystone et al. (36)	2004	NA	USA, CAN.	48	476	NA	ETN	
Keystone et al. (37)	2008	Phase III	USA, EU, CAN, ISR	114		NA	RTX	REFLEX
Kim et al. (38)	2012	Phase IV	Asia-Pacific	31	300	2007 - 2009	ETN	APPEAL
Kivitz et al. (39)	2014	Phase IIIa	not further spec.	NA	656	NA	TCZ	BREVACTA
Klareskog et al. (40)	2004	NA	EU	NA	682	2000 - 2001	ETN	TEMPO
Kosinski et al. (41)	2002	NA	not further spec.	NA	424	NA	ETN	
Kremer et al. (42)	2011	Phase IIIa	14 countries	121	1196	2004 - 2007	TCZ	LITHE
Machado et al. (43)	2014	Phase IV	Latin America	30	570	2009 - 2011	ETN	
Maini et al. (44)	2006	Phase II	EU	57	359	2001 - 2002	TCZ	CHARISMA
Mariette et al. (45)	2014	Phase III	France	44	234	2006 - 2011	RTX	SMART
McInnes et al. (46)	2015	Phase III	USA, CAN, UK	34	132	2007 - 2008	TCZ	MEASURE
Mease et al. (47)	2008	Phase IIb	not further spec.	95	367	NA	RTX	DANCER
Mease et al. (48)	2010	Phase III	USA	143	475	NA	RTX	SUNRISE
Moreland et al. (49)	1999	Phase III	USA	13	234	NA	ETN	

Moreland et al. (50)	2012	Phase IV	USA, Netherland	44	755	NA	ETN	TEAR
Nam et al. (51)	2014	Phase IIIa	England	NA	132	NA	ETN	EMPIRE
Nishimoto et al. (52)	2004	NA	Japan	NA	164	2001 - 2001	TCZ	
Nishimoto et al. (53)	2007	Phase III	Japan	28	306	NA	TCZ	SAMURAI
Nishimoto et al. (54)	2009	Phase III	Japan	25	127	2004 - 2005	TCZ	SATORI
Q'Deji et al. (55)	2013	NA	USA, CAN	20	353	2007 - 2010	ETN	RACAT
Ogata et al. (56)	2014	Phase IIIa	Japan	NA	348	NA	TCZ	MUSASHI
Pavelka et al. (57)	2014	Phase IV	EU; Lat. America; Asia	80	495	2008 - 2009	ETN	PRESERVE
Pope et al. (58)	2014	Phase IV	Canada	27	258	NA	ETN	CAMEO
Raffiner et al. (59)	2015	NA	Italy	1	524	2006 - 2012	ETN	
Rigby et al. (60)	2011	Phase IIIa	not further spec.	NA	748	NA	RTX	IMAGE
Rubbert-Roth et al. (61)	2010	Phase III	18 countries	81	378	NA	RTX	MIRROR
Smolen et al. (62)	2008	Phase III	17 countries	73	623	2005 - 2006	TCZ	OPTION
Smolen et al. (63)	2013	Phase IV	EU, Lat. America, A, Aust	80	834	2008 - 2009	ETN	PRESERVE
Strand et al. (64)	2006	NA	not further spec.	NA	161	NA	RTX	
Tada et al. (65)	2012	NA	Japan	7	70	2008 - 2010	ETN	PRECEPT
Takeuchi et al. (66)	2013	Phase III	Japan	40	550	NA	ETN	
van Riel et al. (67)	2006	NA	EU	60	315	2003 - 2004	ETN	ADORE
Weinblatt et al. (68)	1999	NA	not further spec.	NA	89	NA	ETN	
Weinblatt et al. (69)	2008	Phase IV	USA	63	200	NA	ETN	
Weinblatt et al. (70)	2013	Phase IIIb	USA	NA	886	2009 - 2010	TCZ	
Yazici et al. (71)	2012	Phase IIIb	not further spec.	NA	619	NA	TCZ	ROSE

TCZ = Tocilizumab; RTX = Rituximab; ETN = Etanercept; NA = not available;

Table 2: Study characteristics of 76 observational studies

First author	Year	Study design (Cohort, case series, registry)	Country/Region	Overall N	Calendar years	Drugs analyzed	Name Registry
Ajeganova et al. (72)	2011	Cohort	Sweden	215	2000 - 2007	RTX	
Atzeni et al. (73)	2012	Registry	Italy	2769	1999	ETN	
Backhaus et al. (74)	2015	Cohort	Germany	1603	2010 - 2011	TCZ	
Bingham et al. (75)	2009	Case series	CAN/USA	201	NA	ETN	
Blom et al. (76)	2011	Registry	Netherland	154	1997 - 2010	RTX	DREAM

Bobbio-Pallavicini et al. (77)	2007	Cohort	Italy	132	NA	ETN	
Bokarewa et al. (78)	2007	Case series	Sweden	48	2002 - 2005	RTX	
Bykerk et al. (79)	2015	Cohort	25 countries	1681	2008 - 2010	TCZ	
Cannon et al. (80)	2014	Registry	USA	1767	2003 - 2011	ETN	VARA
Carter et al. (81)	2012	Case series	USA	64	2008 - 2011	RTX	
Chatzidionysiou et al. (82)	2015	Registry	Sweden	7052	2005 - 2012	ETN	ARTIS
Chen et al. (83)	2013	Case series	Taiwan	56	NA	RTX	
Conigliaro et al. (84)	2014	Case series	Italy	82	NA	ETN	
Coulthard et al. (85)	2011	Registry	UK	1102	NA	ETN	BRAGSS
De Keyser et al. (86)	2014	Registry	Belgium	649	2006 - 2011	RTX	MIRA
Diaz-Torne et al. (87)	2014	Case series	Spain	33	NA	RTX	
Dougados et al. (88)	2012	Case series	France	120	NA	ETN	
Einarsson et al. (89)	2015	Registry	Sweden	2416	1999 - 2009	ETN	
Emery et al. (90)	2014	Cohort	11 countries	1312	NA	RTX	
Enevold et al. (91)	2014	Case series	Denmark	79	NA	TCZ	
Fabris et al. (92)	2013	Case series	Italy, UK	152	NA	RTX	
Feltelius et al. (93)	2005	Registry	Sweden	1073	1999 - 2005	ETN	
Fernandez-Nebro et al. (94)	2007	Cohort	Spain	161	1999 - 2006	ETN	
Finckh et al. (95)	2006	Registry	Switzerland	1198	1998 - 2004	ETN	SCQM
Finckh et al. (96)	2010	Registry	Switzerland	318	1998 - 2008	RTX	SCQM
Fortunet et al. (97)	2014	Cohort	France	220	2009 - 2011	ETN	
Gardette et al. (98)	2014	Cohort	France	114	NA	RTX	
Gibofsky et al. (99)	2011	Registry	USA	5032	2002 - 2003	ETN	
Gomez-Reino et al. (100)	2012	Cohort	Spain	1124	2006	RTX	MIRAR
Greenberg et al. (101)	2012	Registry	USA	2242	NA	ETN	CORONNA
Guls et al. (102)	2007	Case series	France	86	2000 - 2005	ETN	
Harrold et al. (103)	2015	Registry	USA	615	2006 - 2011	RTX	CORONNA
Hasan et al. (104)	2012	Case series	Kuwait	45	NA	RTX	
Hetland et al. (105)	2010	Registry	Denmark	8074	2000 - 2009	ETN	DANBIO
Hirabayashi et al. (106)	2013	Case series	Japan	285	2008 - 2009	TCZ	
Hirata et al. (107)	2014	Cohort	Japan	147	2003 - 2010	ETN	
Hyrich et al. (108)	2006	Registry	UK	2879	2001 - 2004	ETN	BSRBR
Izumi et al. (109)	2014	Cohort	Japan	115	2008 - 2011	TCZ	KEIO-TCZ
Jamnitski et al. (110)	2010	Case series	Netherlands	292	2004 - 2008	ETN	
Jancic et al. (111)	2013	Case series	Serbia	82	NA	ETN	
Kaneko et al. (112)	2012	Case series	Japan	31	2008 - 2008	TCZ	
Kawashiri et al. (113)	2010	Case series	Japan	45	NA	ETN	

Kawashiri et al. (114)	2011	Cohort	Japan	32	NA	TCZ	
Kekow et al. (115)	2012	Cohort	Germany	196	NA	RTX	
Kolima et al. (116)	2015	Registry	Japan	2176	2008 - 2009	TCZ	TBCR
Kume et al. (117)	2011	Case series	Japan	34	2006 - 2009	TCZ	
Kume et al. (118)	2014	Case series	Japan	86	NA	TCZ	
Laas et al. (119)	2008	Case series	Finland	91	1999 - 2003	ETN	
Leffers et al. (120)	2011	Registry	Denmark	328	2010 - 2011	TCZ	DANBIO
Listing et al. (121)	2006	Registry	Germany	1083	2001 - 2003	ETN	RABBIT
Listing et al. (122)	2013	Registry	Germany	8908	2001 - 2011	RTX	RABBIT
Marchesoni et al. (123)	2009	Registry	Italy	1114	1999	ETN	LOHREN
Mazilu et al. (124)	2014	Case series	Romania	74	2010	RTX	
McGonagle et al. (125)	2008	Case series	UK	39	2004 - 2007	RTX	
Montes et al. (126)	2014	Cohort	Spain, Greece	429	2000 - 2010	ETN	
Nakashima et al. (127)	2013	Registry	Japan	236	2008	TCZ	FRAB
Narvaez et al. (128)	2011	Case series	Spain	108	2007 - 2009	RTX	
Payet et al. (129)	2014	Registry	France	1709	NA	RTX	AIR
Perera et al. (130)	2006	Case series	Australia	50	NA	ETN	
Richez et al. (131)	2012	Cohort	France	45	NA	TCZ	
Scire et al. (132)	2013	Registry	Italy	2640	2007 - 2012	ETN	MonitorNet
Sebastiani et al. (133)	2014	Registry	Italy	338	1999	RTX	GISEA
Solau-Gervais et al. (134)	2012	Case series	France	108	2005 - 2008	RTX	
Soliman et al. (135)	2012	Registry	UK	646	2010	RTX	BSRBR
Song et al. (136)	2013	Cohort	Japan	93	2008	TCZ	
Su et al. (137)	2009	Case series	Taiwan	94	2004 - 2007	ETN	
Takeuchi et al. (138)	2011	Cohort	Japan	232	2008 - 2009	TCZ	REACTION
Thurlings et al. (139)	2008	Case series	Netherland	30	NA	RTX	
Valleala et al. (140)	2009	Case series	Finland	81	2005 - 2008	RTX	
Valleala et al. (141)	2015	Case series	Finland	151	2005 - 2011	RTX	
Van Dartel et al. (142)	2013	Registry	Netherland	2356	2003	ETN	DREAM
van Vollenhoven et al. (143)	2003	Registry	Sweden	97	NA	ETN	STURE
Vánčsa et al. (144)	2013	Case series	Hungary	77	NA	RTX	
Wakabayashi et al. (145)	2011	Case series	Japan	107	2008 - 2010	TCZ	
Wendler et al. (146)	2014	Case series	Germany	2484	NA	RTX	
Zink et al. (147)	2006	Registry	Germany	1458	2001 - 2003	ETN	RABBIT

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