

**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	

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

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

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

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

TCZ = Tocilizumab; RTX = Rituximab; ETN = [Etanercept](#); NA = not available;

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