

DMARD	Study	Study design	Total N	Intervention	Intervention sample size	Fever	Nausea/vomiting	Loss of appetite or weight	Diarrhea	Pain	Pruritus
BIOLOGIC AGENTS											
Abatacept	Golmia et al., 2008 ¹	Case report	1	Abatacept	1	-	-	-	-	-	-
	Ruperto et al., 2008 ²	RCT	190	Abatacept	190	12	19	-	17	35	-
				Total	191	12	19	-	17	35	-
Adalimumab	Burmester et al., 2009 ³	Series	171	Adalimumab	171	-	-	-	-	-	-
	Cimaz et al., 2010 ⁴	Case report	1	Adalimumab	1	-	-	-	-	-	-
	Lovell et al., 2008 ⁵	RCT	171	Adalimumab	85	-	2	-	-	-	-
	Lovell et al., 2008 ⁵	RCT	171	Adalimumab + MTX	86	-	4	-	-	-	-
				Total	343	-	6	-	-	-	-
Anakinra	Canna et al., 2009 ⁶	Case reports	3	Anakinra	3	-	-	-	-	-	-
	Ilowite et al., 2009 ⁷	RCT	86	Anakinra	86	14	13	-	7	92	26
	Kone-Paut et al., 2007 ⁸	Case report	1	Anakinra	1	1	-	-	-	-	1
	Lequerre et al., 2008 ⁹	Series	20	Anakinra	20	-	-	-	-	2	-
	Ohlsson et al., 2008 ¹⁰	Series	7	Anakinra	7	-	-	-	-	-	3
	Zeft et al., 2009 ¹¹	Series	32	Anakinra	32	-	-	-	-	-	-
				Total	149	15	13	-	7	94	30

DMARD	Study	Study design	Total N	Intervention	Intervention sample size	Fever	Nausea/vomiting	Loss of appetite or weight	Diarrhea	Pain	Pruritus
Etanercept	Bloom, 2000 ¹²	Case report	1	Etanercept	1	-	-	-	-	-	-
	Bout-Tabaku et al., 2007 ¹³	Case report	1	Etanercept	1	-	-	-	-	-	-
	Dalocchio et al., 2010 ¹⁴	Case reports	8	Etanercept	8	-	-	-	-	-	-
	Elwood et al., 2003 ¹⁵	Case report	1	Etanercept	1	-	-	-	-	-	-
	Fathalla et al., 2008 ¹⁶	Case report	1	Etanercept	1	-	-	-	-	-	-
	Giannini et al., 2009 ¹⁷	Series	103	Etanercept	103	-	-	-	-	1	-
	Horneff et al., 2009 ¹⁸	Series	20	Etanercept	20	2	2	-	-	3	1
	Horneff et al., 2009 ¹⁹	Series	604	Etanercept	100	-	4	-	-	2	-
	Hung et al., 2005 ²⁰	Case reports	3	Etanercept	3	2	-	-	-	-	-
	Kimura et al., 2005 ²¹	Series	82	Etanercept	82	-	-	-	-	12	3
	Kunzmann et al., 2005 ²²	Case report	1	Etanercept	1	-	-	-	-	-	-
	Lepore et al., 2003 ²³	Case report	1	Etanercept	1	-	-	-	-	-	-
	Livermore et al., 2002 ²⁴	Case report	1	Etanercept	1	-	-	-	-	-	-
	Lovell et al., 2000 ²⁵	Series	69	Etanercept	69	-	10	-	-	25	1

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	Lovell et al., 2003 ²⁶	Series	58	Etanercept	58	6	8	-	-	63	
	Mangge et al., 2003 ²⁷	Case report	1	Etanercept	1	-	-	-	-	-	-
	Mene et al., 2010 ²⁸	Case report	1	Etanercept	1	-	-	-	-	-	-
	Mori et al., 2005 ²⁹	Series	22	Etanercept	22	-	2	-	-	5	-
	Morishita et al., 2010 ³⁰	Case reports	2	Etanercept	2	-	-	-	-	-	-
	Peek et al., 2006 ³¹	Case report	1	Etanercept	1	-	-	-	-	-	-
	Prince et al., 2009 ³²	Series	146	Etanercept	146	7	9	1	-	7	-
	Quartier et al., 2003 ³³	Series	61	Etanercept	61	-	-	1	1	9	-
	Ramanan et al., 2003 ³⁴	Case report	1	Etanercept	1	-	-	-	-	-	-
	Robinson et al., 2003 ³⁵	Series	21	Etanercept	21	-	-	-	-	-	-
	Skytta et al., 2000 ³⁶	Case reports	2	Etanercept	2	-	-	-	-	-	2
	Smith et al., 2005 ³⁷	RCT	12	Etanercept	7	-	-	-	-	-	-
	Takei et al., 2001 ³⁸	Series	8	Etanercept	8	-	-	-	-	-	-
	Tauber et al., 2005 ³⁹	Case reports	2	Etanercept	2	-	-	-	-	-	-
	Tauber et al., 2006 ⁴⁰	Case reports	2	Etanercept	2	-	-	-	-	-	-

DMARD	Study	Study design	Total N	Intervention	Intervention sample size	Fever	Nausea/vomiting	Loss of appetite or weight	Diarrhea	Pain	Pruritus
	Tynjala et al., 2007 ⁴¹	Series	45	Etanercept	24	-	-	-	-	-	-
	Tzaribachev et al., 2008 ⁴²	Series	25	Etanercept	25	1	-	-	-	-	-
	Wiegering et al., 2010 ⁴³	Case report	1	Etanercept	1	-	-	-	-	-	-
	Aikawa et al., 2009 ⁴⁴	Case report	1	Etanercept + MTX	1	-	-	-	-	-	-
	Billiau et al., 2010 ⁴⁵	Series	16	Etanercept + MTX	16	-	-	-	-	-	-
	Fitch et al., 2006 ⁴⁶	Case report	1	Etanercept + MTX	1	-	-	-	-	-	-
	Giannini et al., 2009 ¹⁷	Series	294	Etanercept + MTX	294	-	-	-	-	6	-
	Holl-Wieden et al., 2008 ⁴⁷	Case report	1	Etanercept + MTX	1	-	-	-	-	-	-
	Horneff et al., 2004 ⁴⁸	Series	322	Etanercept + MTX	322	5	2	-	-	12	6
	Horneff et al., 2009 ¹⁹	Series	604	Etanercept + MTX	504	2	3	-	4	19	-
	Kuemmerle-Deschner et al., 2007 ⁴⁹	Series	12	Etanercept + MTX	12	-	-	-	-	-	-
	Yildirim-Toruner et al., 2008 ⁵⁰	Correspondence	1	Etanercept + MTX	1	-	-	-	-	-	-
				Total	1929	25	40	2	5	164	13

DMARD	Study	Study design	Total N	Intervention	Intervention sample size	Fever	Nausea/vomiting	Loss of appetite or weight	Diarrhea	Pain	Pruritus
				Incidence – Etanercept		1%	2%	0%	0%	9%	1%
IVIG	Aggarwal et al., 2004 ⁵¹	Series	214	IVIG	1	-	-	-	-	-	-
	de Castro et al., 2003 ⁵²	Case reports	5	IVIG	1	-	-	-	-	-	-
	Prieur et al., 1990 ⁵³	Series	16	IVIG	16	-	-	-	-	-	-
	Silverman et al., 1994 ⁵⁴	RCT	31	IVIG	14	2	-	-	-	1	-
	Uziel et al., 1996 ⁵⁵	Series	27	IVIG	27	-	-	-	-	-	-
				Total	60	2	-	-	-	1	-
Infliximab	Armbrust et al., 2004 ⁵⁶	Case report	1	Infliximab	1	-	-	-	-	-	-
	Becker et al., 2004 ⁵⁷	Case reports	3	Infliximab	3	-	-	-	-	-	-
	Billiau et al., 2002 ⁵⁹	Case reports	3	Infliximab	3	-	-	-	-	-	-
	Corona et al., 2004 ⁵⁸	Series	9	Infliximab	9	-	-	-	-	-	-
	Katsicas et al., 2005 ⁶⁰	Series	6	Infliximab	6	-	-	-	-	-	4
	Lahdenne et al., 2003 ⁶¹	Series	24	Infliximab	14	-	-	-	-	-	-
	Mangge et al., 2003 ⁶²	Case report	1	Infliximab	1	-	-	-	1	1	-

DMARD	Study	Study design	Total N	Intervention	Intervention sample size	Fever	Nausea/vomiting	Loss of appetite or weight	Diarrhea	Pain	Pruritus
	Morishita et al., 2010 ³⁰	Case reports	2	Infliximab	2	-	-	-	-	-	-
	Pipitone et al., 2005 ⁶³	Case report	1	Infliximab	1	-	-	-	-	-	-
	Simonini et al., 2008 ⁶⁴	Series	15	Infliximab	15	-	-	-	-	-	-
	Tutar et al., 2004 ⁶⁵	Case reports	2	Infliximab	2	2	-	-	-	-	-
	Tyler et al., 2007 ⁶⁶	Case report	1	Infliximab	1	-	-	-	-	-	-
	Tynjala et al., 2007 ⁴¹	Series	45	Infliximab	21	-	-	-	-	-	-
	Ruperto et al., 2007 ⁶⁷	RCT	122	Infliximab + MTX	60	-	-	-	-	-	-
	Ruperto et al., 2010 ⁶⁸	Post-RCT open-label trial	78	Infliximab + MTX	78	18	17	-	-	19	-
	Yildirim-Toruner et al., 2008 ⁵⁰	Case reports	2	Infliximab	2	-	-	-	-	-	-
				Total	219	20	17	-	1	20	4
Leflunomide	Foeldvari and Wierk, 2010 ⁶⁹	Series	58	Leflunomide	58	-	-	-	7	-	-
	Silverman et al., 2005 ⁷⁰	RCT	94	Leflunomide	47	4	13	-	7	32	-
	Silverman et al., 2005 ⁷¹	Series	27	Leflunomide	27	-	8	-	7	24	-
				Total	132	4	21		21	56	

DMARD	Study	Study design	Total N	Intervention	Intervention sample size	Fever	Nausea/vomiting	Loss of appetite or weight	Diarrhea	Pain	Pruritus
Tocilizumab	Woo et al., 2005 ⁷²	RCT	18	Tocilizumab	18	-	-	-	-	-	1
	Yokota et al., 2008 ⁷³	RCT	56	Tocilizumab	56	-	-	-	-	-	-
				Total	74	-	-	-	-	-	1
				Total – Biologics	3097	78	116	2	44	370	48
				Incidence – Biologics		3%	4%	0%	2%	12%	2%
NON-BIOLOGIC AGENTS											
Azathioprine	Aggarwal et al., 2004 ⁵¹	Series	214	Azathioprine	5	-	-	-	-	-	-
	de Castro et al., 2003 ⁵²	Case reports	5	Azathioprine	2	-	-	-	-	-	-
	Kvien et al., 1986 ⁷⁴	RCT	32	Azathioprine	17	1	1	-	-	1	-
	Lin et al., 2000 ⁷⁵	Series	24	Azathioprine	24	-	-	-	-	-	-
	Savolainen et al., 1997 ⁷⁶	Series	129	Azathioprine	129	-	1	-	-	9	1
	de Castro et al., 2003 ⁵²	Case reports	5	Azathioprine + MTX	5	-	1	-	-	-	-
				Total	182	1	3			10	1

DMARD	Study	Study design	Total N	Intervention	Intervention sample size	Fever	Nausea/vomiting	Loss of appetite or weight	Diarrhea	Pain	Pruritus
Cyclosporine A	de Castro et al., 2003 ⁵²	Case reports	5	Cyclosporine A	2	-	-	-	-	-	-
	Gattinara et al., 1994 ⁷⁷	Case reports	50 35 w/ JRA	Cyclosporine A	50	-	-	-	-	-	-
	Gerloni et al., 2001 ⁷⁸	Series	41	Cyclosporine A	41	-	-	-	-	1	-
	de Castro et al., 2003 ⁵²	Case reports	5	Cyclosporine A + MTX	1	-	-	-	-	-	-
	Krugmann et al., 2000 ⁷⁹	Case report	1	Cyclosporine A + MTX	1	-	-	-	-	-	-
	Mateicka et al., 1994 ⁸⁰	Series	3	Cyclosporine A	3	-	-	-	-	-	-
	Murphy et al., 1993 ⁸¹	Case report	1	Cyclosporine A	1	-	-	-	-	-	-
	Ostensen et al., 1988 ⁸²	Series	14	Cyclosporine A	14	-	-	-	-	-	-
	Pistoia et al., 1993 ⁸³	Series	9	Cyclosporine A	9	-	-	-	-	-	-
	Ruperto et al., 2006 ⁸⁴	Series	329	Cyclosporine A	329	-	-	-	-	-	-
	Ravelli et al., 2002 ⁸⁵	Series	17	Cyclosporine A + MTX	17	-	-	-	-	-	-
					Total	468	-	-	-	-	1

DMARD	Study	Study design	Total N	Intervention	Intervention sample size	Fever	Nausea/vomiting	Loss of appetite or weight	Diarrhea	Pain	Pruritus	
Penicillamine	Aggarwal et al., 2004 ⁵¹	Series	214	Penicillamine	23	-	-	-	-	-	-	
	Kvien et al., 1985 ⁸⁶	RCT	77	Penicillamine	38	-	-	-	-	1	-	
	Prieur et al., 1985 ⁸⁷	RCT	74	Penicillamine	74	-	-	-	-	-	-	
	Sahn et al., 1989 ⁸⁸	Case report	1	Penicillamine	1	-	-	-	-	-	-	
	Brewer et al., 1986 ⁸⁹	RCT	162	Penicillamine	54	-	-	-	-	-	-	
	Kvien et al., 1985 ⁹⁰	RCT	72	Penicillamine	24	-	-	-	-	-	-	
	Swartz et al., 1984 ⁹¹	Case report	1	Penicillamine	1	-	-	-	-	-	-	
					Total	215	-	-	-	-	1	-
	Methotrexate	Aggarwal et al., 2004 ⁵¹	Series	214	Methotrexate	118	-	-	-	-	-	-
Arakawa et al., 2003 ⁹²		Case report	1	Methotrexate	1	-	-	-	-	-	-	
Becker et al., 2010 ⁹³		Series	220	Methotrexate	220	-	-	-	-	-	-	
Chedeville et al., 2005 ⁹⁴		Series	27	Methotrexate	27	-	4	-	-	-	-	
Cleary et al., 2002 ⁹⁵		Case report	1	Methotrexate	1	-	-	-	-	-	-	
Corona et al., 1993 ⁹⁶		Series	34	Methotrexate	34	-	-	-	-	-	-	
Cron et al., 1998 ⁹⁷		Case report	1	Methotrexate	1	-	-	-	-	-	-	

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	de Castro et al., 2003 ⁵²	Case reports	5	Methotrexate	4	-	-	-	-	-	-
	Douglas Graham et al., 1992 ⁹⁸	Series	62	Methotrexate	62	-	14	-	-	-	-
	Falcini et al., 1997 ⁹⁹	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Giannini et al., 1992 ¹⁰⁰	RCT	127	Methotrexate	86	-	-	-	-	-	-
	Giannini et al., 2009 ¹⁷	Series	197	Methotrexate	197	-	-	-	-	-	-
	Gottlieb et al., 1997 ¹⁰¹	Series	25	Methotrexate	25	-	-	-	-	-	-
	Graham et al., 1992 ¹⁰²	Series	62	Methotrexate	62	-	14	-	-	-	-
	Halle et al., 1991 ¹⁰³	Series	30	Methotrexate	30	-	6	-	-	-	-
	Huang et al., 1996 ¹⁰⁴	Series	26	Methotrexate	26	-	-	-	-	-	-
	Hunstad et al., 2007 ¹⁰⁵	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Keim et al., 1990 ¹⁰⁶	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Lee et al., 2006 ¹⁰⁷	Series	84	Methotrexate	46	-	15	-	-	-	-
	Lee et al., 2009 ¹⁰⁸	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Lin et al., 2000 ¹⁰⁹	Series	52	Methotrexate	52	-	11	-	11	-	-

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	Londino et al., 1998 ¹¹⁰	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Martini et al., 1991 ¹¹¹	Series	27	Methotrexate	27	-	-	-	-	-	-
	Muzaffer et al., 1996 ¹¹²	Case reports	2	Methotrexate	2	-	-	-	-	-	-
	Ortiz-Alvarez et al., 2004 ¹¹³	Series	89	Methotrexate	89	-	-	-	-	-	-
	Padeh et al., 1997 ¹¹⁴	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Ravelli et al., 1996 ¹¹⁵	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Ravelli et al., 1998 ¹¹⁶	Series	256	Methotrexate	256	-	-	-	-	-	-
	Ravelli et al., 2001 ¹¹⁷	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Riddle et al., 2006 ¹¹⁸	Series	57	Methotrexate	20	-	9	3	2	3	
	Rose et al., 1990 ¹¹⁹	Series	29	Methotrexate	29	-	-	-	-	-	-
	Ruperto et al., 2004 ¹²⁰	RCT	595	Methotrexate	595	-	26	6	-	-	-
	Russo et al., 2000 ¹²¹	Series	20	Methotrexate	20	-	1	2	-	1	-
	Savolainen et al., 2001 ¹²²	Case reports	2	Methotrexate	2	-	-	-	-	-	-

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	Schmeling et al., 2005 ¹²³	Series	58	Methotrexate	58	-	-	-	-	-	-
	Silverman et al., 2005 ⁷⁰	RCT	94	Methotrexate	47	1	16	-	8	22	-
	Speckmaier et al., 1989 ¹²⁴	Series	12	Methotrexate	12	-	-	-	-	-	-
	Takeyama et al., 2006 ¹²⁵	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Truckenbrodt et al., 1986 ¹²⁶	Series	19	Methotrexate	12	-	-	-	-	-	-
	van der Meer et al., 2007 ¹²⁷	Series	29	Methotrexate	29	-	20	-	-	-	-
	Wallace et al., 1992 ¹²⁸	Series	13	Methotrexate	13	-	2	-	-	-	-
	Yildirim et al., 2000 ¹²⁹	Case report	1	Methotrexate	1	-	-	-	-	-	-
	Kocharla et al., 2009 ¹³⁰	Series	588	Methotrexate + folic acid	198	-	-	-	-	-	-
				Total	2411	1	138	11	21	26	-
				Incidence – Methotrexate		0%	6%	1%	2%	2%	-
Sulfasalazine	Balci et al., 2009 ¹³¹	Case report	1	Sulfasalazine	1	-	-	-	-	-	-
	Burgos-Vargas et al., 2002 ¹³²	RCT	33	Sulfasalazine	17	-	-	-	-	4	-
	Chen et al., 2002 ¹³³	Series	24	Sulfasalazine	24	-	2	-	-	2	-

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	de Castro et al., 2003 ⁵²	Case reports	5	Sulfasalazine	1	-	-	-	-	-	-
	Hertzbergerten Cate et al., 1991 ¹³⁴	Series	3	Sulfasalazine	3	3	2	-	-	-	-
	Imundo et al., 1996 ¹³⁵	Series	139	Sulfasalazine	139	5	-	-	-	3	-
	Joos et al., 1991 ¹³⁶	Series	41	Sulfasalazine	41	-	-	-	-	-	-
	van Rossum et al., 1998 ¹³⁷	RCT	69	Sulfasalazine	35	-	10	10	5	26	1
	van Rossum et al., 2007 ¹³⁸	Series	61	Sulfasalazine	32	1	-	-	-	-	-
	Aggarwal et al., 2004 ⁵¹	Series	214	Sulfasalazine	28	-	-	-	-	-	-
	Ansell et al., 1991 ¹³⁹	Series	51	Sulfasalazine	51	1	1	-	2	1	-
	Gedalia et al., 1993 ¹⁴⁰	Series	10	Sulfasalazine	10	-	-	-	-	-	-
	Gunnarson et al., 1997 ¹⁴¹	Series	8	Sulfasalazine	8	-	-	-	-	-	-
	Huang et al., 1998 ¹⁴²	Series	15	Sulfasalazine	15	-	1	-	2	1	-
	Huang et al., 1998 ¹⁴³	Case report	1	Sulfasalazine	1	-	-	-	-	-	-

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	Kummerle-Deschner et al., 1995 ¹⁴⁴	Case report	1	Sulfasalazine	1	-	-	-	-	-	1
	Ozdogan et al., 1986 ¹⁴⁵	Series	18	Sulfasalazine	18	-	1	-	2	1	-
	Pinana et al., 2010 ¹⁴⁶	Case report	1	Sulfasalazine	1	-	-	-	-	-	-
	Settas et al., 1991 ¹⁴⁷	Series	18	Sulfasalazine	18	-	8	4	-	6	-
	Varbanova et al., 1999 ¹⁴⁸	Series	32	Sulfasalazine	32	-	1	-	-	1	-
				Total	476	10	26	14	11	45	1
				Incidence – Sulfasalazine		2%	5%	3%	2%	9%	0%
OTHER											
	Flato et al., 1998 ¹⁴⁹	Series	117	DMARDs	28	-	2	-	2	3	2
	Lomater et al., 1994 ¹⁵⁰	Series	7	Plaquenil + MTX + gold salts	7	-	1	-	-	-	-
	Barash et al., 199 ¹⁵¹	Case reports	2	Penicillamine + gold	2	-	-	-	-	-	-