

Supplementary Table S1

Characteristics of individual studies

Number	Author	Year	Country	Study Type	Quality score, range 0-5*	Number of patients	Agent	Indication	Dose	Route	Reported side effect	Mean interval period
7	Ammari et al	2015	Tunisia	Case report	2	1	Azathioprine	UC	-	-	CMV retinitis	A few months
8	Puga et al	2016	Spain	Case report	3	1	Mesalazine and Azathioprine	UC	100mg/24 hrs	-	Ocular toxoplasmosis	12 months
9	Doroshov et al	1981	USA	Cohort, prospective	-	4	Methotrexate	Neoplasm	200mg/kg	IV	Pruritus, burning, irritation, blurriness	2-7 days
10	Maesta et al	2018	USA	Cohort, retrospective	-	83	Methotrexate	GTD	1 mg/kg/24hr or 300mg/m2	IM or IV	Conjunctivitis, dry eye, blepharitis, eye pain	-
11	Lepore et al	1981	USA	Case report	2	1	Methotrexate	Lymphoma	12mg	intrathecal	Transient bilateral internuclear ophthalmoplegia	6 days after 14th and last dose
12	Johansson et al	1992	Sweden	Case report	2	1	Methotrexate	PsO	10mg/week	IM then oral	Visual field defects	3 yrs of treatment
13	Stebly et al	2006	Germany	Case report	3	1	Methotrexate	PsA	15 mg/week	IM	Visual field defects	long standing treatment
14	Balachandran et al	2002	Australia	Case report	3	1	Methotrexate	RA	15 mg/week	-	Optic neuropathy	-
15	Clare et al	2005	United Kingdom	Case report	2	1	Methotrexate	RA	7.5 mg/week	oral	Optic neuropathy	10 months of therapy
16	Rickalla et al	2005	United Kingdom	Case report	3	1	Methotrexate	GCA	25 mg/week	-	Primary intraocular lymphoma	9 months of therapy
17	Kobayashi et al	2016	Japan	Case report	3	1	Methotrexate	RA	6 mg/week	-	MALT lymphoma	8 years and 2 months of treatment
18	Kempson et al	2008	USA	Review	-	-	-	-	-	-	-	-
19	Kuroiwa et al	2011	Japan	Case report	3	1	Methotrexate	IOL	400 ug/0.1ml	intravitreal	Macula edema and cotton wool spots	-
20	Klemencic	2010	USA	Case report	3	1	Methotrexate	RA	12.5 mg/weekly	oral	Cotton wool spots	11 years of therapy
21	Gorovoy et al	2013	USA	Case report	3 and 4	2	Methotrexate	IOL	400 ug/0.1ml	intravitreal	Corneal epitheliopathy	case 1, post 6th injection. case 2, post 4th injection
23	Zacharias et al	2013	Brazil	Bench research	-	-	Human retinal cells	Mycophenolic acid	100 ug/ml	-	Decrease in cell viability and higher caspase activity	-
25	Barak et al	2004	USA	Case report	3	1	Leflunomide	RA	-	oral	Cystoid macula edema	2 weeks after initiation
27	Stak et al	2018	Singapore	Case report	3	1	Cyclosporine	SS	0.05% ophthalmic emulsion	topical	CMV anterior uveitis	3 months after initiation
28	Apaydin et al	1992	Turkey	Cohort, prospective	-	-	Cyclosporine	KTR	5 - 7.5 mg/kg/day plus steroid for ~30 months or 3 - 5 mg/kg/day plus steroid and azathioprine for ~20 months	-	No increased risk of macular hyperpigmentation or cataracts	-
29	Nakamaru et al	2003	Japan	Cohort, retrospective	-	67	Cyclosporine	KTR	Initial dose of 8 mg/kg and maintenance dose of 2 mg/kg/day	-	Potentiate steroid induced cataracts	Average follow up period ~ 5 years
30	Kotter et al	2006	Germany	Cohort study	-	117	Cyclosporin	BD	Within therapeutic range	-	-	-
31	Openshaw	2001	USA	Case report	3	1	Cyclosporin	MCL	-	-	diplopia with weakness in bilateral eye abduction, brain MRI showed patchy high signal abnormality on the T2 weighted and FLAIR sequences in subcortical white matter of the occipital lobes and brain stem	Approximately 2 months later
33	Kende et al	1979	USA	Cohort study	-	29	Cyclophosphamide	Childhood solid tumor patients	CTX 750 mg/m2 administered on alternate days for a total of 5 doses on days 1, 3, 5, 7, 9, total dose 3.75 gm/2	IV	blurred vision	day 2-9 of treatment with onset of symptoms, symptoms resolved in <1 hour to 14 days
34	Loprinzi et al	1990	USA	Cross sectional	-	-	Cyclophosphamide, methotrexate, and 5-fluorouracil combination	Breast cancer or malignant lymphoma	MTX 30-40 mg/m2, 5-FU 600 mg/M2 on days 1 and 8 of 28-day cycle, cyclophosphamide either oral 100mg/m2 on day 1 and 8 or IV 600 mg/m2 on day 1 and 8	IV	Tearing, pruritis, burning	11-17 days after starting cycle of chemotherapy
35	Stevens et al	2001	United Kingdom	Cohort study	-	128	Cyclophosphamide, methotrexate, and 5-fluorouracil combination	Breast cancer	unclear dosage	oral cyclophosphamide	sores of eyes, grittiness of eyes, dryness of eyes, increased lacrimation	lasted few days to 2 years
38	Santodomingo-Rubido et al	2003	United Kingdom	Case report	2	1	Sulfasalazine	RA	2g daily	oral	myopia	s/p 3 weeks of sulfasalazine, improved after stopping med for 2 weeks, stabilized after 6 weeks
39	Toussiroi et al	2016	France	Review	-	-	Anti-TNF alpha	Many	-	-	Paradoxical reactions	-
40	Cordero-Coma et al	2015	Spain and USA	Review	-	-	Anti-TNF alpha	Uveitis	-	-	-	-
41	Wending et al	2011	France	Cohort study	-	31	Anti-TNF alpha, rituximab	AS, PsA, RA, JIA	-	-	uveitis	-
42	Hashkes et al	2003	USA	Case report	3	1	Etanercept	Sarcoidosis	0.4mg/kg twice weekly	subQ	uveitis	2 months after therapy, also developed non-pruritic macular and follicular rash
43	Suzuki et al	2009	Japan	Case report	2	1	Etanercept	RA	25mg weekly	subQ	uveitis	Uncertain how long patient was on etanercept, but >3 months
44	Dragnev et al	2013	United Kingdom	Case report	3	1	Etanercept	RA	50mg weekly	subQ	uveitis	1 year of etanercept therapy
45	Seve et al	2012	France	Case report	3	1	Adalimumab	RA	40mg every other week	subQ	uveitis	3 years of adalimumab before parauveitis
46	Clementine et al	2010	USA	Case report	3	3	Infliximab, Etanercept	RA	-	-	Sarcoidosis	Case 1: infliximab treatment for 60 months, developed multigranulomatous sarcoidosis Case 2: 3 years of etanercept, developed sarcoidosis Case 3: etanercept for 2 years, developed sarcoidosis
47	Wladis et al	2016	USA	Case report	2	1	Adalimumab	PsA	40mg every other week	subQ	right-sided orbital pain and inflammation. Orbital biopsy of a focal lesion demonstrated sarcoid-like granulomatosis	-
48	Gaujoux-Viala et al	2012	France	Case series	4	3	Etanercept	RA	25 mg twice a week	-	Scleritis	Mean 21 months after treatment initiation
49	Shin et al	2006	USA	Case report and FDA postmarketing database review	2	16	Anti-TNF alpha (1) Infliximab and (2) Etanercept	RA, PsA, CD	-	-	GBS and MFS	21 months of therapy for case report patient, 1.5 months - several years for FDA database review patients
50	Theibich et al	2014	Denmark	Case series	2	2	(1) Infliximab and (2) Etanercept	PsA	-	-	Optic neuritis and visual disturbances	(1) 10 months (2) 2 months after initiation
51	Ratnarajan et al	2015	England	Case report	3	1	Infliximab	UC	-	-	Miller Fisher Syndrome	9 weeks after initiation (2 infusions)
52	Simsek et al	2007	Turkey	Review	-	-	Anti-TNF alpha	-	-	-	Optic neuritis	-
53	Winthrop et al	2012	USA	Cohort, retrospective	-	6	Anti-TNF alpha and Non-biologic DMARDs	RA, IBD, PsO, PsA, AS	-	-	Optic neuritis	123 days (range, 37-221 days) after anti-TNF initiation
54	Clifford et al	2004	United Kingdom	Case report	2	1	Etanercept	RA	-	-	Visual field defect	Symptoms noticed by patient the day after 1st injection; similar visual defect on other eye after 2nd injection; two further injections given (in a course of 5) before stopping treatment
55	Rosman et al	2006	USA	Double-blind, randomized, placebo-controlled phase II study	-	1	Infliximab	Pulmonary sarcoidosis	5mg/kg (group I) or placebo (group II) at weeks 0 and 2 and open-label infliximab 5mg/kg for all subjects at weeks 6 and 14	IV	Visual field defect	51 days after 4th infusion at week 14
56	Do et al	2008	Australia	Case report	3	1	Etanercept	RA	-	-	Demyelination	22 months of treatment
57	Papadia et al	2010	Switzerland	Case report	3	1	Infliximab	AS and HLA-B27 uveitis	5 mg/kg every 6 weeks	-	Demyelination	10 months after initiation
58	Drury et al	2015	United Kingdom	Case report	3	1	Adalimumab	CD	-	-	Internuclear ophthalmoplegia	18 months of treatment
59	Martorena-Alvarez et al	2012	Spain	Case report	3	1	Adalimumab	CD	160 mg on week 1, 80 mg on week 2, and 40 mg every other week thereafter	-	Diffuse retinopathy	1 month after initiation
60	Hsu et al	2014	Taiwan	Case report	2	1	Adalimumab	PsO	40 mg every 2 weeks	-	Central retinal vein occlusion and subsequent neovascular glaucoma	After 5th dose
61	Matet et al	2015	France	Case report	2	1	Adalimumab	CD	40mg every 2 weeks	subQ	Peripheral corneal infiltrates	36 hours after bimonthly dose
62	Schechet et al	2018	USA	Case report	3	1	Adalimumab	PsO	Initial 80 mg followed by 3 doses of 40 mg every other week	subQ	Acute retinal necrosis	4 days after fourth dose
63	Roos et al	2011	United Kingdom	Case report	3	1	Adalimumab	RA	40mg every 2 weeks	-	Right-sided dacryocystitis progressing to a widespread orbital cellulitis over 72 hrs	36 months of treatment
64	Kofoed et al	2018	Denmark	Case report	3	1	Adalimumab	CRMO	40 mg biweekly	subQ	Acute sinusitis complicated by orbital abscess	15 months of treatment
65	Caramaschi et al	2003	Italy	Case report	2	1	Etanercept	RA	25 mg 2x week	subQ	Orbital myositis	5 months after initiation
66	Couderc et al	2014	France	Case report	3	1	Etanercept	RA	50mg/week	subQ	Acute ocular myositis	6 years after initiation
67	Kalo et al	2012	Japan	Case report	3	1	Etanercept	Still's disease	50mg/week	IM	Angioedema of the periorbital region	After 4th injection (4 weeks after therapy)
68	Song et al	2018	South Korea	Case report	3	1	Etanercept	RA	25mg/week	subQ	primary intraocular lymphoma	8 months of treatment
69	Yakopson et al	2011	USA	Case report	2	1	Etanercept	RA	-	-	Postoperative eyelid infection with S. aureus	Patient undergoing treatment for RA, infection found at 1 week post op visit
70	Fanlotosa et al	2012	Spain	Case report	3	1	Etanercept	PsA	-	-	Sarcoid intermedial Uveitis	4 years of treatment
71	Glatre et al	2010	France	Case report	2	1	Etanercept	RA	-	-	HHV8 uveitis	-
72	Arriola-Villalobos et al	2008	Spain	Case report	2	1	Etanercept	HS	25-mg every 4 days for 3 months	IM	Bilateral Candida chorioretinitis	35 days after starting treatment
73	Lassoued et al	2007	France	Case report	3	2	(1) Etanercept (2) Infliximab	RA	(1) 25mg 2x week (2) 3mg/kg monthly injections	-	toxicoplasmic chorioretinitis.	(1) 4 weeks later (1) 3 months later
74	Hanafi et al	2018	Netherlands	Case report	2	1	Golimimumab	RA	-	-	Merkel cell carcinoma of the eyelid	6 months of therapy
75	Pull et al	2003	USA	Case report	2	1	Infliximab	CD	340 mg at time 0, 2, and 4 wk, and then at 2-month intervals	-	Retinal vein thrombosis	After 3rd dose of infliximab
76	Veerappan et al	2008	Ireland	Case report	2	1	Infliximab	UC	5 mg/kg on a 0-, 2- and 6-week	IV	Retinal vein thrombosis	2 weeks after his 6th infusion
77	Vergou et al	2010	Greece	Case report	2	1	Infliximab	PsO	3 years of therapy	IV	Central retinal vein occlusion	5 days after last infusion
78	Diniz et al	2011	Brazil	Case report	2	1	Infliximab	RA	3 mg/kg/dose at 2 month intervals	IV	Retinal venous branch occlusion	Following 6th infusion
79	Faszi-Spurio et al	2004	United Kingdom	Case report	3	1	Infliximab	RA	3 mg/kg monthly	IV	CMV retinitis	after 2 years of treatment
80	Madill et al	2014	United Kingdom	Case report	4	1	Infliximab + Adalimumab	CD	-	IV	Rosacea keratitis, corneal melts	4 months after initiation of therapy
81	Haerter et al	2004	Germany	Case report	3	1	Infliximab	RA	3 mg/kg/monthly	IV	CMV retinitis	Receiving treatment for 22 months
82	Roos et al	2006	United Kingdom	Case report	3	1	Infliximab	AS	5 mg/kg, six-times-weekly	-	Orbital Cellulitis	Following 4th dose
83	Agarwal et al	2007	United Kingdom	Case report	3	1	Infliximab	RA	3 mg/kg at week 0, 2 and 6	-	Endogenous endophthalmitis	Recently started on infliximab
84	Yoshida et al	2018	Japan	Case report	3	1	Infliximab	Surgically induced necrotizing scleritis	5 mg/kg at 0, 2 and 6 weeks, then once every 8 weeks	IV	Endophthalmitis associated with P. iliacinum	2 years after initiation of therapy
85	Sibley et al	2012	USA	Cohort Study	-	2	Anakinra	NOMID	1-5 mg/kg/day for at least 36 months	-	Nystagmus	Within the study period of 60 months
86	Heissigerová et al	2018	USA	Randomized, double-masked, placebo-controlled, phase 2 study	-	5	Sarilumab	Uveitis	200mg every 2 weeks for 16 weeks	-	Worsening uveitis and retinal infiltrates	Within the study period of 16 weeks
87	Roux et al	2011	France	Case report	3	1	Tocilizumab	RA	8 mg/kg/week	IV	Ophthalmic herpes zoster	After 9 months of treatment
88	Terada et al	2017	Japan	Case report	2	1	Tocilizumab	RA	8mg/kg at weeks 0 and 4	IV	HTLV-1 uveitis	Soon after second dose
89	Calvo-Rio et al	2017	Spain	Cohort, retrospective	-	1	Tocilizumab	JIA	8 mg/kg every 4 weeks	IV	Viral conjunctivitis	Within the study period of 12 months
90	Burzyn et al	2017	Canada	Case report	2	1	Tocilizumab	JIA	8mg/kg every 2 weeks	-	Bilateral papilloedema and vision loss	14 months after starting of tocilizumab
93	Martinez et al	2017	USA	Case report	3	1	Secukinumab	PsO	300 mg weekly	-	Endogenous endophthalmitis	4th week of treatment
95	Schuler et al	2016	Switzerland	Case report	3	1	Rituximab	RA and scleromalacia	2 x1000 mg 2 weeks apart (one cycle every 6 months)	IV	Acute retinal necrosis	4 months after 4th cycle
96	Dogra et al	2018	India	Case report	3	1	Rituximab	MPA	1g at week 0 and 2	-	Progressive outer retinal necrosis due to Varicella zoster virus-induced progressive outer retinal necrosis	1 month after 2nd infusion cycle
97	Marinella et al	2007	USA	Case report	3	1	Rituximab	BALT	725 mg (375 mg/m2)	IV	Transient bilateral conjunctivitis	20 minutes into the infusion
98	Bussone et al	2010	France	Case reports	4 and 3	2	Rituximab	GPA	(1)1000 mg on days 1 and 15 (2)375 mg/m ² /wk for 4 weeks	IV	Cystoid macular edema and scleritis	(1) 1 month (2) 2 months after initiation
99	Chan et al	2015	China	Cohort study	-	5	Rituximab	Low-grade B cell LPD or lymphoma	-	IV	CMV retinitis	6.4 months from last dose
100	Hashida et al	2012	Japan	Prospective, interventional case series	-	10	Rituximab	CD20-positive primary vitreoretinal lymphoma	1 mg/0.1ml/week for 4 weeks	Intravitreal	Transient IOP elevations and idocyclitis with mutton-fat keratic precipitates	3.8 ± 1.9 weeks after the first treatment course
102	Tsuboi et al	2014	Japan	Open-labeled, 1-year, prospective, and observational study	-	1	Abatacept	SS	500 mg for weight < 60 kg or 750 mg for weight ≥ 60 kg, administered at 0, 2, 4, and every 4 weeks, for 1 year	IV	Infectious cornea ulcer	within a 24 week period
105	Rentiya et al	2019	USA	Case reports	3	2	Interferon alpha	Hep C	180mcq weekly	-	Retinopathy	6 weeks to few months after therapy
106	Yang et al	2018	China	Case report	4	1	Interferon alpha-2b	Mucosal melanoma	20 MIU/m2 daily	-	Epicleritis	3 days after treatment
107	Ierkhass et al	2015	Morocco	Case report	3	1	Pegylated interferon	Hep C	-	-	Non-arteritic anterior ischemic optic neuropathy	4th month of treatment
108	Mangioni et al	2014	Italy	Case report	3	1	Pegylated interferon	Hep C	-	-	Neuromyelitis optica	4 months of treatment
109	Ortega-Ibarra et al	2013	Mexico	Case report	3	1	Pegylated interferon alpha-2b	Hep C	100 micrograms per week	-	Retinal thrombosis	4 weeks after treatment
110												