This table is a supplement to the publication "Seeing Clearly: Balancing Perceptions and Facts of Anti-TNFs in SpA and Uveitis."

Supplementary Table 1. Level II study results on the rates of uveitis according to study and type of treatment.

	Study	Design	Patient Population/ Study Duration	Treatment	No. Patients	No. Uveitis Flares	Rate per 100 Patient-years (95% CI)	p value vs. PBO or DMARD Control*	Study Strengths	Study Limitations
Pooled analyses	Braun et al. 2005[23]	Meta-analysis of RCTs, OL extensions	AS & Hx of uveitis/ 6-24 weeks DB; ≤3 years OL (4 RCTs, 3 OL)	PBO	190	11	15.6 (7.8-27.9)	N/A	RCT + OL data; history of anterior uveitis provided; 4 studies gave follow-up data on uveitis incidence	OL data (loss of blinding)
				IFX DB+OL	90‡	5	3.4 (1.1-8.0)	0.005		
				ETN DB+OL	297‖	34	7.9 (5.5-11.1)	0.05		
				Anti-TNF, Total	387	39	6.8 (NR)	0.01		
	Sieper et al. 2010[24]	Systematic review of RCTs, AC, OL extensions	AS/ 12-24 weeks DB, ≥5 years OL	PBO	249	16	19.3 (11.0-29.8)	N/A	RCT + longer-term OL data	Uveitis history not specified on case report form; PBO and SSZ exposure much shorter than for ETN
				ETN DB	508	12	8.6 (4.5-14.2)	0.031		
				SSZ	187	8	14.7 (6.4-26.5)	N/A		
				ETN AC	379	12†	10.7 (5.5-17.6)	0.486		
				ETN DB+OL	1074	136	12.0 (10.0-14.1)	N/A		
	Wu et al. 2014[25]	Meta-analysis of parallel or cross-over RCTs	AS/ 12-30 weeks (6 trials)	Soluble receptor PBO	206	10	NR	N/A	All RCTs (blinding maintained); large N	Shorter duration of exposure
				Soluble receptor (ETN)	457	3	NR	0.04		
				Monoclonal Abs PBO	156	6	NR	N/A		
				Monoclonal Abs (CZP, IFX)	280	4	NR	0.18		
				PBO, Total	362	16	NR	N/A		
				Anti-TNF, Total	737	7	NR	0.01		
Prospective studies	Cobo-Ibáñez et al. 2008[26]	Prospective OS	SpA patients with previous AAU who received anti-TNF treatment at a single centre/2 years	Prior to ADA	150	0	0	NR	Prospective; controlled for exposure time	Single centre; patients were their own controls; small N
				ADA		0	0	NR		
				Prior to ETN		10	34.29	NR		
				ETN		NR	60	NR		
				Prior to IFX		9	61.73	NR		
				IFX		NR	2.64	NR		
	Rudwaleit et al. 2009[27]	Prespecified subanalysis – prospective OL study¶	AS/≤20 weeks	Pre-treatment (historical data)¶	1250	187.5	15 (NR)	N/A	Large N	OL; patients were their own controls
				ADA		27	7.4 (NR)	<0.001		
	van Denderen et al. 2014[28]	Prospective OL study¶	AS/ ≥12 weeks	Pre-treatment (historical data)¶	77	52	68 (NR)	N/A	Prospective	OL data (loss of blinding); patients were their own controls
				ADA		19	14 (NR)	<0.0001		

Continues ➤

Retrospective studies

Study	Design	Patient Population/ Study Duration	Treatment	No. Patients	No. Uveitis Flares	Rate per 100 Patient-years (95% CI)	p value vs. PBO or DMARD Control*	Study Strengths	Study Limitations
Guignard et al. 2006[31]	Retrospective OS¶	SpA & ≥1uveitis flare/ Dec 97-Dec 04	Pre-treatment: Anti-TNF antibody¶	33	NR	50.6 (NR)	N/A	Data available for disease duration; long follow-up period; used all patients at the centre (limiting selection bias)	Retrospective; small N; single centre (risk of selection bias); differences in populations (e.g., less DMARD and corticosteroid use in ETN group); patients were their own controls
			Anti-TNF antibody (ADA, IFX)		NR	6.8 (NR)	0.001		
			Pre-treatment: Soluble TNF receptor¶	13	NR	54.6 (NR)	N/A		
			Soluble TNF receptor		NR	58.5 (NR)	0.92		
			Pre-treatment: All anti-TNF¶	46	NR	51.8 (NR)	N/A		
			All anti-TNF		NR	21.4 (NR)	0.03		
Lim et al. 2007[36]	Retrospective registry-based OS	Uveitis cases reported to 2 spontaneous reporting databases prior to Jan 06 (most likely RA)¶	ADA	2	2	NR	N/A	Corrected for different number of patients taking each medication	Underlying systemic diagnoses unknown for >50% of cases; medication duration exposure missing for >50% of available reports; limited control for confounding; spontaneous reporting; reporting of dechallenge-rechallenge phenomenon incomplete for both databases
			ETN	20	20	NR	N/A		
			IFX	4	4	NR	N/A		
Fouache et al. 2009[30]	Retrospective OS	SpA/ Dec 00-Jan 08	Conventional DMARDs	112	3	NR	N/A	Conventional DMARD control group; diagnoses based on expert opinion	Single centre
			ADA	296	0	0 (NR)	0.303**		
			ETN		3	1 (NR)			
			IFX		0	0 (NR)			
Wendling et al. 2014[35]	Retrospective claims database study	Anti-TNF naive AS & no Hx of uveitis/05-11	ADA	717	17††	NR	N/A	Large N; assessed for confounders, including NSAID use, age, sex	Retrospective; lack of disease data/AS duration; did not assess potential impact of SSZ
			ETN	1087	49††	NR	N/A		
			IFX	311	10††	NR	N/A		
Lian et al. 2015[32]	Retrospective OS	SpA patients with uveitis admitted to a south China hospital/Jan 12-Mar 14	MTX	39	34‡‡	NR	N/A	Included HLA-B27 status	Retrospective; small N; single centre
			ADA	16	1‡‡	NR	N/A		
			ADA + MTX	32	3‡‡	NR	N/A		
			ETN	21	8‡‡	NR	N/A		
			ETN + MTX	53	6‡‡	NR	N/A		
			IFX + MTX	12	2‡‡	NR	N/A		
			IFX	9	1‡‡	NR	N/A		
Rudwaleit et al. 2016[29]	Post-hoc of RCT, OL extension	AxSpA/ 24 weeks DB, 96 weeks OL	Placebo	107	4	10.3 (2.8-26.3)	N/A	RCT + longer-term OL data	Retrospective post-hoc; greater proportion of patients with uveitis in placebo; OL data (loss of blinding)
			CZP DB	218	3	3.0 (0.6-8.8)	NR		
			CZP DB+OL	315	24	4.9 (3.2-7.4)	NR		

*p-values compare anti-TNF vs. placebo in placebo-controlled trials, or vs. sulfasalazine in the active comparator trial; †Includes two patients with an event during screening and one with an event during post-study follow-up; ‡Includes all 34 patients from infliximab arm of double-blind phase of Braun et al., 2002;[58] ¶Includes 141 patients from etanercept arms of the double-blind phase; ¶Investigators tried to exclude patients whose underlying disease was associated with uveitis using a priori criteria, this study was included because it is likely there were still SpA patients included in the analysis and it is frequently cited in the SpA/anti-TNF/uveitis literature; **Overall paradoxical adverse events in patients receiving anti-TNFs vs. controls (5 psoriasis, 3 AAU and 4 IBD; ††Patients with ≥1 uveitis event, number of uveitis flares not reported; ‡‡Number of patients with uveitis relapse, number of uveitis flares not reported.

AAU: acute anterior uveitis; Ab: antibody; AC: active comparator; ADA: adalimumab; AS: ankylosing spondylitis; CI: confidence interval; CZP: certolizumab pegol; DB: double-blind; DMARD: disease-modifying anti-rheumatic drug; ETN: etanercept; Hx: history; IBD: inflammatory bowel disease; IFX: infliximab; MTX: methotrexate; NR: not reported; NSAID: non-steroidal anti-inflammatory drug; OL: open-label; OS: observational study; PBO: placebo; RA: rheumatoid arthritis; RCT: randomized controlled trial; SpA: spondyloarthritis; SSZ: sulfasalazine; TNF: tumour necrosis factor.