Supplemental material

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Title: Efficacy and safety of biologic agents and tofacitinib in moderate-to-severe ulcerative colitis: a systematic overview of meta-analyses

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Table S1: Characteristics of included meta-analyses in the overview.

Author	Year	Exposure to biologics		Therapeutic agents					Efficacy outcomes			Safety outcomes	
		Naive	Prior exposure	ADA	GLM	IFX	VDZ	TFB	Clinical response	Clinical remission	Mucosal healing	AE	SAE
Motaghi et al.[37]	2019	x	-	-	-	x	-	-	-	x	-	x	x
Bonovas et al.[24]	2018	x	-	x	x	x	x	x	x	x	x	x	x
Lasa et al.[28]	2018	NR	NR	-	-	-	x	-	-	x	x	x	-
Paschos et al.[12]	2018	x	x	-	-	-	-	x	x	x	x	x	x
Singh et al.[31]	2018	x	x	x	x	x	x	x	-	x	x	-	x
Trigo-Vicente et al.[34]	2018	x	-	x	x	x	x	x	x	x	x	-	x
Cholapranee et al.[9]	2017	NR	NR	x	x	x	x	-	-	-	x	-	-
Archer et al.[17]	2016	x	-	x	x	x	-	-	x	x	-	-	-
Chen et al.[36]	2016	x	x	x	-	-	-	-	x	x	x	x	x
Moćko et al.[23]	2016	NR	NR	x	x	x	x	-	-	-	-	x	x
Vickers et al.[39]	2016	x	x	x	x	x	x	-	x	x	x	-	-
Zhang et al.[16]	2016	x	-	x	-	-	-	-	x	x	x	x	x
Galván-Banqueri et al.[10]	2015	x	-	x	x	x	-	-	x	x	x	-	-
Jin et al.[32]	2015	NR	NR	-	-	-	x	-	x	x	-	-	x
Lopez et al.[20]	2015	x	x	x	x	x	-	-	x	x	x	x	x
Mei et al.[22]	2015	NR	NR	x	x	x	x	-	x	x	x	-	x
Mosli et al.[27]	2015	NR	NR	-	-	-	x	-	x	x	-	x	x
Song and Zheng[30]	2015	NR	NR	x	x	x	-	-	x	-	x	-	x
Yang et al.[19]	2015	NR	NR	x	-	-	-	-	x	x	x	x	-
Bickston et al.[11]	2014	NR	NR	-	-	-	x	-	x	x	-	x	x
Danese et al.[35]	2014	x	-	x	x	x	x	-	x	x	x	x	x
Kawalec et al.[25]	2014	NR	NR	-	x	-	x	-	x	x	x	x	x
Lv et al.[38]	2014	NR	NR	x	-	x	-	-	-	x	x	-	x
Stidham et al.[29]	2014	NR	NR	x	x	x	-	-	x	x	-	-	-
Thorlund et al.[15]	2014	x	-	x	-	x	-	-	x	x	x	-	x

Wang et al.[13]	2014	NR	NR	-	-	-	x	-	x	x	-	-	x
Huang et al.[26]	2011	NR	NR	x	-	x	-	-	-	-	-	x	x
Ford et al.[18]	2011	x	-	-	-	x	-	-	-	x	-	x	x
Nikfar et al.[33]	2011	NR	NR	-	-	x	-	-	-	x	-	x	x
Gisbert et al.[21]	2007	NR	NR	-	-	x	-	-	x	x	-	x	-
Lawson et al.[14]	2006	x	-	-	-	x	-	-	x	x	-	x	x

NR, not reported

Table S2: Quality assessment of the included meta-analyses in the overview using AMSTAR 2.

Publication	**Items**																**Final rating**
	1	***2***	**3**	***4***	**5**	**6**	***7***	**8**	***9***	**10**	***11***	**12**	***13***	**14**	***15***	**16**	
Motaghi et al.[37], 2019	Y	N	N	N	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Bonovas et al.[24], 2018	Y	N	N	Y	N	Y	N	Y	Y	N	Y	Y	N	Y	Y	Y	Critically low
Lasa et al.[28], 2018	Y	N	N	pY	N	N	N	pY	N	N	Y	N	N	Y	Y	Y	Critically low
Paschos et al.[12], 2018	Y	Y	N	Y	Y	Y	N	pY	Y	N	Y	Y	Y	N	Y	Y	Low
Singh et al.[31], 2018	Y	Y	N	Y	Y	Y	N	pY	Y	N	Y	Y	Y	N	Y	Y	Low
Trigo-Vicente et al.,[34] 2018	Y	N	N	pY	Y	N	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Cholapranee et al.[9], 2017	Y	N	N	Y	Y	Y	N	pY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Archer et al.[17], 2016	Y	Y	N	pY	N	N	Y	Y	Y	N	N	Y	N	Y	Y	Y	Critically low
Chen et al.[36], 2016	Y	N	N	Y	Y	Y	N	pY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Moćko et al.[23], 2016	Y	Y	N	Y	Y	Y	N	pY	Y	N	Y	N	N	Y	Y	Y	Critically low
Vickers et al.[39], 2016	Y	Y	N	pY	Y	N	N	Y	Y	N	Y	N	N	Y	Y	Y	Critically low
Zhang et al.[16], 2016	Y	N	N	Y	Y	N	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Low
Galván-Banqueri et al.[10], 2015	Y	N	N	Y	Y	Y	N	Y	N	N	N	N	N	N	Y	N	Critically low
Jin et al.[32], 2015	Y	N	N	N	Y	N	N	Y	Y	N	Y	Y	Y	N	Y	Y	Critically low
Lopez et al.[20], 2015	Y	N	N	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Low
Mei et al.[22], 2015	Y	N	N	pY	N	N	N	Y	N	N	Y	N	N	N	Y	Y	Critically low
Mosli et al.[27], 2015	Y	N	N	pY	Y	N	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Song and Zheng[30], 2015	Y	N	N	N	N	Y	N	N	pY	N	Y	N	N	Y	Y	Y	Critically low
Yang et al.[19], 2015	Y	N	N	Y	Y	Y	N	N	N	N	Y	N	N	Y	Y	Y	Critically low

Bickston et al.[11], 2014	Y	N	N	pY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Low
Danese et al.[35], 2014	Y	Y	N	pY	N	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Low
Kawalec et al.[25], 2014	Y	N	N	Y	Y	Y	N	Y	N	N	Y	N	N	N	Y	Y	Critically low
Lv et al.[38], 2014	Y	N	N	N	Y	Y	Y	Y	pY	N	Y	Y	N	Y	Y	Y	Critically low
Stidham et al.[29], 2014	Y	N	N	N	Y	Y	N	Y	Y	N	Y	N	N	Y	Y	Y	Critically low
Thorlund et al.[15], 2014	Y	pY	N	pY	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	Y	Critically low
Wang et al.[13], 2014	Y	N	N	pY	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Low
Huang et al.[26], 2011	Y	N	N	pY	Y	N	N	Y	N	N	Y	N	N	Y	Y	N	Critically low
Ford et al.[18], 2011	Y	N	N	Y	Y	Y	N	pY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Nikfar et al.[33], 2011	Y	N	N	pY	Y	N	Y	Y	pY	N	Y	N	N	Y	Y	Y	Critically low
Gisbert et al.[21], 2007	Y	N	N	pY	N	N	Y	Y	pY	N	Y	Y	Y	Y	Y	Y	Low
Lawson et al.[14], 2006	Y	N	N	pY	Y	Y	Y	Y	Y	N	Y	N	N	N	Y	Y	Critically low

AMSTAR 2 items assessed (items in italics are considered critical): 1, PICO description; *2, protocol registered before the commencement of the review*; 3, study design included in the review; *4, adequacy of the literature search;* 5, two authors study selection; 6, two authors data extraction; *7, justification for excluding individual studies*; 8, included studies described in detail; *9, risk of bias assessment for the single studies being included in the review*; 10, source of funding of primary studies; *11, appropriateness of meta-analytical methods;* 12, impact of risk of bias of single studies on the results of the meta-analysis; *13, consideration of risk of bias when interpreting the results of the review;* 14, explanation and discussion of the heterogeneity observed; *15, assessment of presence and likely impact of publication bias*; 16, funding sources and conflict of interest declared.

Abbreviations: Y, yes; pY, partial yes; N, no.

Footnotes: **High:** 0–1 non-critical weakness. The systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest. **Moderate**: >1 non-critical weakness. The systematic review has more than one weakness, but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review. **Low:** 1 critical flaw with or without non-critical weaknesses. The review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest. **Critically low:** >1 critical flaw with or without non-critical weaknesses. The review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

Table S3: Indirect comparisons for efficacy and safety between biologic agents including adalimumab, golimumab, infliximab, and vedolizumab, as induction therapy, in ulcerative colitis. Significant estimates (p<0.05) are presented in bold.

Indirect comparison		**Estimates and 95% CIs**				
		Efficacy outcomes			**Safety outcomes**	
	Author, year	**Clinical response**	**Clinical remission**	**Mucosal healing**	**Adverse events**	**Serious adverse events**
IFX vs. ADA	Bonovas et al.[24], 2018	**OR, 2.01 (1.36–2.98)**	**OR, 2.10 (1.21–3.64)**	**OR, 1.87 (1.26–2.79)**	NR	NR
	Singh et al.[31], 2018	NR	**OR, 2.33 (1.17-4.54)**	**OR, 2.08 (1.35-3.23)**	NR	NR
	Trigo-Vicente et al.,[34] 2018	OR, 2.05 (0.84-5.17) [a, b]	OR, 2.06 (0.84-5.17) [a, b]	OR, 2.09 (0.91-4.99) [a,b]	NR	NR
	Trigo-Vicente et al.,[34] 2018	**OR, 2.10 (1.33-3.27) [b, c]**	**OR, 2.35 (1.35-4.14) [b, c]**	**OR, 2.01 (1.28-3.16) [b, c]**	NR	NR
	Cholapranee et al.[9], 2017	NR	NR	**OR, 2.22 (1.22-4.00)**	NR	NR
	Archer et al.[17], 2016	PS, -0.52 (-1.03-0.00) [b]		NR	NR	NR
	Vickers et al.[39], 2016	**OR, 2.19 (1.35-3.55)** [b]	**OR, 2.81 (1.49-5.49)** [b]	**OR, 2.23 (1.21-4.14)** [b]	NR	NR
	Galván-Banqueri et al.[10], 2015	**RiR, 1.46 (1.12-1.90)**	RiR, 1.68 (0.94-3.03)	**RiR, 1.49 (1.12-1.98)**	NR	NR
	Mei et al.[22], 2015 [d]	**OR, 2.44 (1.61-3.85)**	**OR, 3.03 (1.61-6.25)**	**OR, 2.44 (1.61-3.70)**	NR	NR
	Danese et al.[35], 2014	**OR, 2.36 (1.22-4.63)** [b]	OR, 2.79 (0.95-8.83) [b]	**OR, 2.02 (1.13-3.59)** [b]	NR	NR
	Stidham et al.[29], 2014	ReR, 2.15 (0.73-5.80) [b]	ReR, 2.08 (0.32-12.03) [b]	NR	NR	NR
	Thorlund et al.[15], 2014	**OR, 2.22 (1.12-4.35)**	**OR, 2.38 (1.03-5.88)**	**OR, 2.17 (1.19-4.00)**	NR	NR
IFX vs. GLM	Bonovas et al.[24], 2018	**OR, 1.67 (1.08–2.59)**	OR, 1.43 (0.76–2.71)	**OR, 1.75 (1.13–2.73)**	NR	NR
	Singh et al.[31], 2018	NR	OR, 1.49 (0.70-3.23)	**OR, 1.92 (1.20-3.03)**	NR	NR
	Trigo-Vicente et al.,[34] 2018	OR, 1.57 (0.64-4.02) [a, b]	OR, 1.24 (0.45-3.45) [a, b]	OR, 1.74 (0.75-4.14) [a, b]	NR	NR
	Trigo-Vicente et al.,[34] 2018	**OR, 1.60 (1.01-2.56) [b, c]**	OR, 1.42 (0.68-2.95) [b, c]	**OR, 1.67 (1.04-2.67) [b, c]**	NR	NR
	Cholapranee et al.[9], 2017	NR	NR	OR, 1.82 (0.87-3.70) [b]	NR	NR
	Archer et al.[17], 2016	PS, -0.42 (-1.00-0.17) [b]		NR	NR	NR
	Vickers et al.[39], 2016	OR, 1.61 (0.94-2.74) [b]	OR, 1.44 (0.65-3.14) [b]	OR, 1.79 (0.96-3.42) [b]	NR	NR
	Galván-Banqueri et al.[10], 2015	RiR, 1.15 (0.85-1.55)	RiR, 1.10 (0.56-2.17)	RiR, 1.25 (0.91-1.71)	NR	NR
	Mei et al.[22], 2015 [d]	OR, 1.52 (0.95-2.50)	OR, 1.39 (0.63-3.13)	**OR, 1.67 (1.05-2.70)**	NR	NR
	Danese et al.[35], 2014	OR, 1.96 (0.99-4.48) [b]	OR, 1.84 (0.58-6.92) [b]	OR, 1.80 (0.96-3.46) [b]	NR	NR
	Stidham et al.[29], 2014	ReR, 1.48 (0.38-4.69) [b]	ReR, 1.18 (0.13-10.63) [b]	NR	NR	NR
IFX vs. VDZ	Bonovas et al.[24], 2018	OR, 1.12 (0.57–2.22)	OR, 0.95 (0.33-2.74)	OR, 1.05 (0.53-2.09)	NR	NR
	Singh et al.[31], 2018	NR	OR, 0.96 (0.30-3.03)	OR, 1.14 (0.56-2.33)	NR	NR
	Trigo-Vicente et al.,[34] 2018	OR, 1.55 (0.59-4.21) [a, b]	OR, 1.08 (0.33-3.35) [a, b]	OR, 1.59 (0.66-4.05) [a, b]	NR	NR
	Trigo-Vicente et al.,[34] 2018	OR, 1.58 (0.9-2.79) [b, c]	OR, 1.23 (0.47-2.94) [b, c]	OR, 1.54 (0.87-2.69) [b, c]	NR	NR
	Cholapranee et al.[9], 2017	NR	NR	OR, 1.59 (0.71-3.45) [b]	NR	NR
	Vickers et al.[39], 2016	OR, 1.28 (0.61-2.56) [b]	OR, 1.14 (0.35- 3.33) [b]	OR, 1.16 (0.52-2.63) [b]	NR	NR
	Mei et al.[22], 2015 [d]	OR, 1.52 (0.80-2.94)	OR, 1.20 (0.37-3.85)	OR, 1.54 (0.81-2.94)	NR	NR

	Danese et al.[35], 2014	OR, 1.28 (0.48-3.45) [b]	OR, 1.18 (0.21-6.32) [b]	NR	NR	NR
ADA vs. GLM	Bonovas et al.[24], 2018	OR, 0.83 (0.55-1.26)	OR, 0.68 (0.36-1.31)	OR, 0.94 (0.61–1.43)	NR	NR
	Singh et al.[31], 2018	NR	OR, 0.65 (0.30-1.37)	OR, 0.91 (0.59-1.41)	NR	NR
	Trigo-Vicente et al.,[34] 2018	OR, 0.77 (0.49-1.21)	OR, 0.60 (0.29-1.25)	OR, 0.83 (0.53-1.32)	NR	NR
	Cholapranee et al.[9], 2017	NR	NR	OR, 0.81 (0.42-1.56) [b]	NR	NR
	Moćko et al.[23], 2016	NR	NR	NR	OR, 1.14 (0.60-2.30) [b]	OR, 1.14 (0.18-6.38) [b]
	Archer et al.[17], 2016	PS, -0.10 (–0.69-0.50) [b, e]		NR	NR	NR
	Vickers et al.[39], 2016	OR, 0.74 (0.47-1.18) [b]	OR, 0.51 (0.24-1.04) [b]	OR, 0.81 (0.51-1.27) [b]	NR	NR
	Galván-Banqueri et al.[10], 2015	RiR, 0.79 (0.59-1.04)	RiR, 0.66 (0.33-1.30)	RiR, 0.83 (0.61-1.14)	NR	NR
	Mei et al.[22], 2015 [d]	**OR, 0.62 (0.39-0.95)**	OR, 0.47 (0.20-0.98)	OR, 0.69 (0.44-1.06)	NR	NR
	Danese et al.[35], 2014	OR, 0.83 (0.47-1.67) [b]	OR, 0.66 (0.23-2.00) [b]	OR, 0.89 (0.52-1.56) [b]	NR	NR
	Stidham et al.[29], 2014	ReR, 1.46 (0.42-5.38) [b]	ReR, 1.75 (0.17-16.86) [b]	NR	NR	NR
ADA vs. VDZ	Bonovas et al.[24], 2018	OR, 0.56 (0.29–1.09)	OR, 0.45 (0.16–1.31)	OR, 0.56 (0.29–1.10)	NR	NR
	Singh et al.[31], 2018	NR	OR, 0.41 (0.13-1.33)	OR, 0.54 (0.27-1.09)	NR	NR
	Singh et al.[31], 2018	NR	OR, 0.41 (0.06-2.70) [f]	OR, 0.65 (0.24-1.75) [f]	NR	NR
	Trigo-Vicente et al.,[34] 2018	OR, 0.75 (0.43-1.32)	OR, 0.52 (0.20-1.24)	OR, 0.76 (0.43-1.32)	NR	NR
	Cholapranee et al.[9], 2017	NR	NR	OR, 0.70 (0.34-1.43) [b]	NR	NR
	Moćko et al.[23], 2016	NR	NR	NR	OR, 1.53 (0.75-3.29) [b]	OR, 1.53 (0.24-11.01) [b]
	Vickers et al.[39], 2016	OR, 0.59 (0.29-1.16) [b]	OR, 0.40 (0.12-1.16) [b]	OR, 0.52 (0.27-1.03) [b]	NR	NR
	Mei et al.[22], 2015 [d]	OR, 0.61 (0.33-1.12)	OR, 0.40 (0.12-1.22)	OR, 0.63 (0.33-1.18)	NR	NR
	Danese et al.[35], 2014	OR, 0.54 (0.21-1.35) [b]	OR, 0.42 (0.08-1.96) [b]	NR	NR	NR
GLM vs. VDZ	Bonovas et al.[24], 2018	OR, 0.67 (0.34–1.35)	OR, 0.66 (0.22–2.02)	OR, 0.60 (0.30–1.21)	NR	NR
	Singh et al.[31], 2018	NR	OR, 0.65 (0.19-2.17)	OR, 0.60 (0.30-1.20)	NR	NR
	Trigo-Vicente et al.,[34] 2018	OR, 1.0 (0.56-1.72)	OR, 0.86 (0.30-2.33)	OR, 0.92 (0.52-1.61)	NR	NR
	Cholapranee et al.[9], 2017	NR	NR	OR, 0.87 (0.38-1.96) [b]	NR	NR
	Moćko et al.[23], 2016	NR	NR	NR	OR, 1.33 (0.61-2.92) [b]	OR, 1.37 (0.17-12.69) [b]
	Vickers et al.[39], 2016	OR, 0.80 (0.39-1.61) [b]	OR, 0.79 (0.23-2.50) [b]	OR, 0.65 (0.32-1.32) [b]	NR	NR
	Mei et al.[22], 2015 [d]	OR, 0.99 (0.51-1.92)	OR, 0.87 (0.24-3.03)	OR, 0.92 (0.48-1.75)	NR	NR
	Danese et al.[35], 2014	OR, 0.65 (0.23-1.61) [b]	OR, 0.64 (0.11-3.13) [b]	NR	NR	NR

Abbreviations: ADA, adalimumab; CI, confidence interval; GLM, golimumab; IFX, infliximab; NA, non-applicable, NR, not reported; OR, odds ratio; P, p-value; PS, probit score; ReR, Relative risk; RiR, Risk ratio; VDZ, vedolizumab; vs., versus.

[a] IFX dosage 3.5 mg/kg

[b] CrI, credible interval

[c] IFX dosage 5 mg/kg

[d] The presented odds ratios in the study of Mei et al. 2015 [22] are for the opposite associations (i.e., for example infliximab vs. placebo – not placebo vs. infliximab)

[e] GLM versus ADA

[f] Patients with prior exposure to anti-TNF agents

Table S4: Indirect comparisons for efficacy and safety between biologic agents including adalimumab, golimumab, infliximab, and vedolizumab (VDZ), as maintenance therapy, in ulcerative colitis. Significant estimates (p<0.05) are presented in bold.

Outcome/ Biologic therapy		**Estimates and 95% CIs**				
		Efficacy			**Safety**	
	Author, year	**Clinical response**	**Clinical remission**	**Mucosal healing**	**Adverse events**	**Serious adverse events**
IFX vs. ADA	Singh et al.[31], 2018	NR	OR, 1.18 (0.62-2.22)	OR, 1.32 (0.75-2.28)	NR	OR, 0.67 (0.37-1.20) [a]
	Trigo-Vicente et al.[34], 2018	NR	OR, 1.16 (0.51-2.61) [a] (dosage: 5 mg)	OR, 1.98 (0.91-3.95) [a] (dosage: 5 mg)	NR	OR, 0.39 (0.04-1.97) [a] (dosage: 3.5 mg) OR, 0.69 (0.34-1.38) [a] (dosage: 5 mg)
	Cholapranee et al.[9], 2017	NR	NR	OR, 1.92 (0.69-5.26) [a]	NR	NR
	Archer et al.[17], 2016	PS, -0.20 (-1.09-0.69) [a, b]	PS, -0.29 (-1.41, 0.85) [a, b]	NR	NR	NR
	Archer et al.[17], 2016	PS, -0.67 (-2.04, 0.66) [a, c]	PS, 0.78 (-0.53, 2.14) [a, c]	NR	NR	NR
	Moćko et al.[23], 2016	NR	NR	NR	OR, 0.93 (0.26-3.57)	OR, 0.71 (0.29-1.79) [a]
	Vickers et al.[39], 2016	OR, 1.24 (0.51-3.15) [d]	OR, 0.63 (0.24-1.63) [a]	OR, 1.31 (0.57-3.12) [a]	NR	NR
	Galván-Banqueri et al.[10], 2015	RiR, 1.51 (0.87-2.60)	RiR, 1.19 (0.59-2.04)	RiR, 1.54 (0.86-2.79)	NR	NR
	Mei et al.[22], 2015 [e]	OR, 1.69 (0.82-3.45)	OR, 0.95 (0.18-4.55)	OR, 1.14 (0.22-5.26)	NR	OR, 0.75 (0.32-1.72)
	Stidham et al.[29], 2014	ReR, 1.70 (0.17-16.59) [a]	ReR, 1.18 (0.19-8.02) [a]	NR	NR	NR
	Thorlund et al.[15], 2014	OR, 1.88 (0.89-4.00) [a]	OR, 1.39 (0.57-3.23) [a]	OR, 2.00 (0.90-4.35) [a]	NR	OR, 0.81 (0.29-2.33) [a]
IFX vs. GLM	Singh et al.[31], 2018	NR	NR	NR	NR	OR, 0.46 (0.20-1.04)
	Trigo-Vicente et al.[34], 2018	NR	OR, 1.51 (0.68-3.34) [a] (dosage: 100 mg)	OR, 1.87 (0.88-4.04) [a] (dosage: 100 mg)	NR	OR, 0.24 (0.03-1.35) [a] (dosage: IFX 3.5 mg, GLM 100 mg) OR, 0.44 (0.18-1.04) [a] (dosage: IFX 5 mg, GLM 100 mg)
	Trigo-Vicente et al.[34], 2018	NR	OR, 1.56 (0.70-3.46) [a] (dosage: 50 mg)	OR, 1.92 (0.91-4.15) [a] (dosage: 50 mg)	NR	OR, 0.42 (0.04-2.48) [a] (dosage: IFX 3.5 mg, GLM 50 mg) OR, 0.75 (0.28-1.96) (dosage: IFX 5 mg, GLM 50 mg)
	Cholapranee et al.[9], 2017	NR	NR	OR, 1.89 (0.60-5.88) [a]	NR	NR
	Archer et al.[17], 2016	PS, 0.18 (-0.68-1.01) [a, b] (dosage: 100 mg)	PS, 0.51 (-0.48-1.45) [a, b] (dosage: 100 mg)	NR	NR	NR
	Archer et al.[17], 2016	PS, 0.07 (-0.75-0.91) [a, b] (dosage: 50 mg)	PS, 0.52 (-0.46-1.49) [a, b] (dosage: 50 mg)	NR	NR	NR

	Archer et al.[17], 2016	PS, -0.56 (-1.85-0.73) [a] (dosage: 100 mg)	PS, -0.08 (-1.37-1.24) [a, c] (dosage: 100 mg)	NR	NR	NR
	Archer et al.[17], 2016	PS, -0.18 (-0.51-1.10) [a] (dosage: 50 mg)	PS, -0.29 (-1.57-1.02) [a, c] (dosage: 50 mg)	NR	NR	NR
	Moćko et al.[23], 2016	NR	NR	NR	OR, 0.86 (0.21-3.70) [a]	OR, 0.53 (0.17-1.54) [a]
	Vickers et al.[39], 2016	OR, 0.73 (0.31-1.77) [a, d]	OR, 0.69 (0.29-1.77) [a]	NR	NR	NR
	Galván-Banqueri et al.[10], 2015	NR	RiR, 1.37 (0.75-2.50) (dosage: 100 mg)	NR	NR	NR
	Galván-Banqueri et al.[10], 2015	NR	RiR, 1.40 (0.77-2.56) (dosage: 50 mg)	NR	NR	NR
	Mei et al.[22], 2015 [d]	OR, 1.61 (0.80-3.23)	OR, 1.45 (0.29-7.14)	OR, 1.96 (0.40-10.0)	NR	OR, 0.56 (0.23-1.32)
	Stidham et al.[29], 2014	ReR, 1.47 (0.15-14.43) [a]	ReR, 1.22 (0.18-8.43) [a]	NR	NR	NR
IFX vs. VDZ	Singh et al.[31], 2018	NR	NR	NR	NR	OR, 1.56 (0.63-3.85)
	Trigo-Vicente et al.[34], 2018	NR	OR, 0.71 (0.30-1.66) [a]	OR, 0.88 (0.39-1.99) [a]	NR	OR, 0.31 (0.03-1.97) [a] (dosage: 3.5 mg) OR, 0.56 (0.19-1.60) [a] (dosage 5 mg)
	Cholapranee et al.[9], 2017	NR	NR	OR, 0.85 (0.26-2.86) [a]	NR	NR
	Mei et al.[22], 2015 [d]	OR, 0.87 (0.42-1.79)	OR, 1.18 (0.24-6.25)	OR, 0.82 (0.17-4.00)	NR	OR, 0.74 (0.27-2.04)
	Moćko et al.[23], 2016	NR	NR	NR	OR, 1.22 (0.30-5.36) [a]	OR, 0.87 (0.33-2.29) [a]
	Vickers et al.[39], 2016	**OR, 0.31 (0.11-0.88) [a, d]**	**OR, 0.34 (0.12-0.97) [a]**	OR, 0.41 (0.15-1.15) [a]	NR	NR
ADA vs. GLM	Singh et al.[31], 2018	NR	NR	NR	NR	OR, 0.68 (0.30-1.56)
	Trigo-Vicente et al.[34], 2018	NR	OR, 1.31 (0.63-2.70) [a] (dosage: 100 mg)	OR, 0.99 (0.52-1.90) [a] (dosage: 100 mg)	NR	OR, 0.63 (0.28-1.38) [a] (dosage: 100 mg)
	Trigo-Vicente et al.[34], 2018	NR	OR, 1.34 (0.65-2.82) [a] (dosage: 50 mg)	OR, 1.02 (0.53-1.95) [a] (dosage: 50 mg)	NR	OR, 1.09 (0.45-2.67) [a] (dosage: 50 mg)
	Cholapranee et al.[9], 2017	NR	NR	OR, 0.98 (0.37-2.63) [a]	NR	NR
	Archer et al.[17], 2016	PS, -0.38 (-1.36-0.59) [a, c] (dosage: 100 mg)	PS, -0.79 (-1.96-0.42) [a, b, f] (dosage: 100 mg)	NR	NR	NR
	Archer et al.[17], 2016	PS, -0.29 (-1.24-0.67) [a, c] (dosage: 50 mg)	PS, -0.82 (-1.96-0.39) [a, b, f] (dosage: 50 mg)	NR	NR	NR
	Archer et al.[17], 2016	PS, -0.12 (-1.36-1.11) [a, c] (dosage: 100 mg)	PS, 0.87 (-0.38-2.11) [a, c, f] (dosage: 100 mg)	NR	NR	NR
	Archer et al.[17], 2016	PS, -0.49 (-1.77-0.77) [a, c] (dosage: 50 mg)	PS, 1.08 (-0.18-2.31) [a, c, f] (dosage: 50 mg)	NR	NR	NR
	Moćko et al.[23], 2016	NR	NR	NR	OR, 0.94 (0.29-2.95) [a]	OR, 0.73 (0.27-1.93) [a]
	Vickers et al.[39], 2016	OR, 0.59 (0.27-1.18) [a, d]	OR, 1.11 (0.51-2.33) [a]	NR	NR	NR
	Galván-Banqueri et al.[10], 2015	NR	RiR, 1.18 (0.62-2.25) (dosage: 50 mg)	NR	NR	NR
	Galván-Banqueri et al.[10], 2015	NR	1.16 (0.61-2.20) (dosage: 100 mg)	NR	NR	NR
	Mei et al.[22], 2015 [d]	OR, 0.95 (0.49-1.92)	OR, 1.52 (0.32-8.33)	OR, 1.69 (0.38-8.33)	NR	OR, 0.73 (0.30-1.79)

	Stidham et al.[29], 2014	ReR, 1.14 (0.11-10.92) [a]	ReR, 1.04 (0.16-6.96) [a]	NR	NR	NR
ADA vs. VDZ	Singh et al.[31], 2018	NR	NR	NR	NR	OR, 2.33 (0.94-5.88)
	Trigo-Vicente et al.[34], 2018	NR	OR, 0.61 (0.28-1.35) [a]	**OR, 0.46 (0.23-0.95)** [a]	NR	OR, 0.81 (0.29-2.18) [a]
	Cholapranee et al.[9], 2017	NR	NR	OR, 0.45 (0.17-1.27) [a]	NR	NR
	Moćko et al.[23], 2016	NR	NR	NR	OR, 1.30 (0.43-4.14) [a]	OR, 1.20 (0.56-2.70) [a]
	Vickers et al.[39], 2016	OR, 0.25 (0.10-0.60) [a, d]	OR, 0.55 (0.20-1.35) [a]	**OR, 0.31 (0.14-0.75)** [a]	NR	NR
	Vickers et al.[39], 2016	OR, 0.49 (0.11-2.27) [a, g]	OR, 0.29 (0.03-2.50) [a, g]	**OR, 0.15 (0.02-0.74)** [a, g]	NR	NR
	Mei et al.[22], 2015 [d]	OR, 0.52 (1.03-0.25)	OR, 1.23 (0.26-6.67)	OR, 0.71 (0.15-3.85)	NR	OR, 0.99 (0.36-3.70)
GLM vs. VDZ	Singh et al.[31], 2018	NR	OR, 1.12 (0.05-25.00)	OR, 0.69 (0.09-5.56)	NR	**OR, 3.45 (1.16-10.0)** [a]
	Trigo-Vicente et al.[34], 2018	NR	OR, 0.47 (0.21-1.03) [a] (dosage: 100 mg)	**OR, 0.47 (0.22-0.99)** [a] (dosage: 100 mg)	NR	OR, 1.27 (0.41-3.97) [a] (dosage: 100 mg)
	Trigo-Vicente et al.[34], 2018	NR	OR, 0.46 (0.20-1.00) [a] (dosage: 50 mg)	**OR, 0.45 (0.22-0.95)** [a] (dosage: 50 mg)	NR	OR, 0.74 (0.22-2.45) [a] (dosage: 50 mg)
	Cholapranee et al.[9], 2017	NR	NR	OR, 0.46 (0.14-1.45) [a]	NR	NR
	Moćko et al.[23], 2016	NR	NR	NR	OR, 1.39 (0.39-5.24) [a]	OR, 1.66 (0.61-4.67) [a]
	Vickers et al.[39], 2016	OR, 0.43 (0.18-0.96) [a,d]	OR, 0.49 (0.20-1.19) [a]	NR	NR	NR
	Mei et al.[22], 2015 [d]	OR, 0.54 (0.27-1.06)	OR, 0.81 (0.17-4.17)	OR, 0.42 (0.09-2.04)	NR	OR, 1.35 (0.47-3.85)

Abbreviations: ADA, adalimumab; CI, confidence interval; GLM, golimumab; IFX, infliximab; NA, non-applicable, NR, not reported; OR, odds ratio; P, p-value; ReR, Relative risk; RiR, Risk ratio; VDZ, vedolizumab; vs., versus.

[a] CrI, credible interval

[b] Maintenance 8–32 weeks for patients starting in response

[c] Maintenance 32-52 weeks for patients starting in response

[d] Durable clinical response

[e] The presented odds ratios in the study of Mei et al. 2015[22] are for the opposite associations (i.e., for example infliximab vs. placebo – not placebo vs. infliximab)

[f] GLM vs. ADA

[g] Patients with prior exposure to anti-TNF agents

Table S5: Indirect comparisons for efficacy and safety between tofacitinib and biologic agents including adalimumab, golimumab, infliximab, and vedolizumab, as induction, maintenance, and induction and/or maintenance therapy, in ulcerative colitis. Significant estimates ($p<0.05$) are presented in bold.

Indirect comparison		**Estimates and 95% CIs**				
		Efficacy outcomes			**Safety outcomes**	
Induction therapy	**Author, year**	**Clinical response**	**Clinical remission**	**Mucosal healing**	**Adverse events**	**Serious adverse events**
TFB vs. IFX	Bonovas et al.[24], 2018	OR, 0.68 (0.41-1.16)	OR, 0.61 (0.31-1.20)	OR, 0.68 (0.38-1.20)	NR	NR
	Singh et al.[31], 2018	NR	OR, 0.52 (0.23-1.20)	OR, 0.60 (0.34-1.11)		
	Trigo-Vicente et al.,[34] 2018	NR	OR, 0.56 (0.20-1.61) [a] (dosage 3.5 mg) OR, 0.49 (0.23-1.08) [a] (dosage 5 mg)	OR, 0.62 (0.24-1.60) [a] (dosage 3.5 mg) OR, 0.64 (0.36-1.2) [a] (dosage 5 mg)	NR	NR
TFB vs. ADA	Bonovas et al.[24], 2018	OR, 1.37, (0.84-2.22)	OR, 1.28 (0.65-2.56)	OR, 1.27 (0.71-2.22)	NR	NR
	Singh et al.[31], 2018	NR	OR, 1.22 (0.52-2.86)	OR, 1.28 (0.72-2.29)	NR	NR
	Singh et al.[31], 2018	NR	**OR, 8.75 (1.27-60.36) [b]**	**OR, 4.29 (1.63-11.33) [b]**	NR	NR
	Trigo-Vicente et al.,[34] 2018	NR	OR, 1.15 (0.55-2.52) [a]	OR, 1.30 (0.72-2.41) [a]	NR	NR
TFB vs. GLM	Bonovas et al.[24], 2018	OR, 1.14 (0.68-1.89)	OR, 0.88 (0.41-1.89)	OR, 1.18 (0.65-2.17)	NR	NR
	Singh et al.[31], 2018	NR	OR, 0.78 (0.31-1.96)	OR, 1.17 (0.64-2.12)		
	Trigo-Vicente et al.,[34] 2018	NR	OR, 0.69 (0.29-1.70) [a]	OR, 1.08 (0.60-1.99) [a]	NR	NR
TFB vs. VDZ	Bonovas et al.[24], 2018	OR, 0.76 (0.37-1.60)	OR, 0.58 (0.19-1.82)	OR, 0.71 (0.32-1.57)	NR	NR
	Singh et al.[31], 2018	NR	OR, 0.50 (0.14-1.79)	OR, 0.70 (0.31-1.55)	NR	NR
	Singh et al.15, 2018	NR	OR, 3.60 (0.37-35.13) [b]	OR, 2.79 (0.96-8.15) [b]	NR	NR
	Trigo-Vicente et al.,[34] 2018	NR	OR, 0.60 (0.21-1.63) [a]	OR, 0.99 (0.51-1.97) [a]	NR	NR
Maintenance therapy						
TFB vs. IFX	Singh et al.[31], 2018	NR	NR	NR	NR	OR, 1.03 (0.40-2.65) (TFB dosage: 5 mg) OR, 1.15 (0.45-2.90) (TFB dosage: 10 mg)
	Trigo-Vicente et al.,[34] 2018	NR	OR, 2.03 (0.90-4.59) [a]	OR, 1.48 (0.68-3.22) [a]	NR	OR, 2.01 (0.33, 19.24) [a] (dosage: 3.5 mg) OR, 1.12 (0.41, 3.12) (dosage: 5 mg)
TFB vs. ADA	Singh et al.[31], 2018	NR	NR	NR	NR	OR, 0.69 (0.27-1.77) (dosage: 5 mg) OR, 0.77 (0.30-1.94)

						(dosage: 10 mg)
	Trigo-Vicente et al.,[34] 2018	NR	**OR, 2.34 (1.12-4.95)** [a]	**OR, 2.80 (1.46-5.50)** [a]	NR	OR, 0.77 (0.30, 1.94) [a]
TFB vs. GLM	Trigo-Vicente et al.,[34] 2018	NR	**OR, 3.06 (1.47-6.41)** [a] (dosage 100 mg) **OR, 3.15 (1.52-6.71)** [a] (dosage 50 mg)	**OR, 2.77 (1.39-5.64)** [a] dosage 100 mg **OR, 2.85 (1.43-5.81)** [a] (dosage 50 mg)	NR	OR, 0.49 (0.17, 1.43) [a] (dosage: 100 mg) OR, 0.84 (0.27, 2.66) [a] (dosage: 50 mg)
	Singh et al.[31], 2018	NR	OR, 0.86 (0.04-17.92) (dosage: 5 mg)	OR, 1.12 (0.14-8.86) (dosage: 5 mg)	NR	OR, 0.47 (0.16-1.42) (dosage: 5 mg)
	Singh et al.[31], 2018	NR	OR, 1.12 (0.05-23.20) (dosage: 10 mg)	OR, 1.57 (0.20-12.47) (dosage: 10 mg)	NR	OR, 0.53 (0.18-1.56) (dosage: 10 mg)
TFB vs. VDZ	Trigo-Vicente et al.,[34] 2018	NR	OR, 1.44 (0.64-3.23) [a]	OR, 1.30 (0.61-2.82) [a]	NR	OR, 0.62 (0.18, 2.10) [a]
	Singh et al.[31], 2018	NR	OR, 0.97 (0.03-28.68) (dosage: 5 mg)	OR, 0.77 (0.08-7.72) (dosage: 5 mg)	NR	OR, 1.60 (0.50-5.15) (dosage: 5 mg)
	Singh et al.[31], 2018	NR	OR, 1.26 (0.04-37.14) (dosage: 10 mg)	OR, 1.08 (0.11-10.88) (dosage: 10 mg)	NR	OR, 1.79 (0.56-5.67) (dosage: 10 mg)
Induction and/or maintenance		NR				
TFB vs. IFX	Bonovas et al.[24], 2018	NR	NR	NR	OR, 0.65 (0.41-1.02)	OR, 0.96 (0.53-1.72)
TFB vs. ADA	Bonovas et al.[24], 2018	NR	NR	NR	OR, 0.85 (0.60-1.20)	OR, 0.85 (0.47-1.56)
TFB vs. GLM	Bonovas et al.[24], 2018	NR	NR	NR	OR, 0.83 (0.59-1.18)	OR, 0.79 (0.40-1.56)
TFB vs. VDZ	Bonovas et al.[24], 2018	NR	NR	NR	OR, 0.99 (0.64-1.54)	OR, 1.71 (0.82-3.57)

Abbreviations: ADA, adalimumab; CI, confidence interval; GLM, golimumab; IFX, infliximab; NR, not reported; OR, odds ratio; P, p-value; TFB, tofacitinib; VDZ, vedolizumab; vs., versus.

[a] Credible interval

[b] Patients with prior exposure to anti-TNF agents

Table S6: Characteristics of meta-analyses that studied the safety of biologic therapies i.e., adalimumab, golimumab, infliximab, and vedolizumab, in ulcerative colitis (UC). Significant estimates (p<0.05) are presented in bold.

Outcome/ Biologic therapy	Author, year	Dosage	Trials (n.)	Subjects (n.)	UC cases (n.)	Estimates and 95% CIs	Heterogeneity (I^2 or P-value)	Small-study effects
Induction therapy								
Adverse events								
ADA	Chen et al.[36], 2016	160/80 mg	3	1149	573	RiR, 1.10 (0.95-1.27)	I^2=0%, P=0.69	NA
	Chen et al.[36], 2016	80/40 mg	2	536	217	RiR, 1.16 (0.94-1.42)	I^2=0%, P=0.40	NA
	Moćko et al.[23], 2016	NR	2	849	530	OR, 1.20 (0.78-1.90) [a]	NR	NA
	Yang et al.[19], 2015	160/80 mg	2	963	480	RiR, 1.00 (0.93-1.09)	I^2=0%, P=0.60	NA
GLM	Moćko et al.[23], 2016	NR	1	732	402	OR, 1.04 (0.63-1.73) [a]	NA	NA
	Kawalec et al.[25], 2014	NR	2	1354	947	RiR, 1.01 (0.86-1.18)	I^2=0%, P=0.63	NA
IFX	Motaghi et al.[37], 2019	5 mg/kg	5	858	428	OR, 1.40 (0.98-1.99)	I^2=0%, P=0.68	NA
	Ford et al.[18], 2011	NR	3	739	492	ReR, 1.07 (0.99-1.15)	NR	NA
	Nikfar et al.[33], 2011	5 or 10 mg	3	659	445	ReR, 1.07 (0.99-1.14)	NR, P=0.76	NA
	Gisbert et al.[21], 2007	5 or 10 mg/kg	2	784	516	**OR, 1.52 (1.03-2.24)**	I^2=48.4%, P=0.12	NA
VDZ	Moćko et al.[23], 2016	NR	1	374	225	OR, 0.78 (0.43-1.39) [a]	NA	NA
	Kawalec et al.[25], 2014	NR	1	374	225	ReR, 0.86 (0.68-1.09)	NA	NA
Serious adverse events								
ADA	Chen et al.[36], 2016	160/80 mg	3	1149	573	RiR, 0.79 (0.54-1.14)	I^2=0%, P=0.40	NA
	Chen et al.[36], 2016	80/40 mg	2	536	217	RiR, 0.44 (0.19-1.00)	I^2=0%, P=0.61	NA
	Moćko et al.[23], 2016	NR	2	849	530	OR, 0.48 (0.16-1.37) [a]	NR	NA
GLM	Moćko et al.[23], 2016	NR	1	732	402	OR, 0.43 (0.11-1.79) [a]	NA	NA
	Kawalec et al.[25], 2014	NR	2	1354	947	RiR, 0.56 (0.33-0.95)	I^2=0%, P=0.36	NA
IFX	Motaghi et al.[37], 2019	5 mg/kg	5	858	428	OR, 0.71 (0.50-1.03)	I^2=0%, P=0.76	NA
	Ford et al.[18], 2011	NR	4	782	515	ReR, 0.64 (0.41-1.00)	NR	NA
	Nikfar et al.[33], 2011	5 or 10 mg	3	149	84	ReR, 0.83 (0.44-1.54)	NR, P=0.06	NA
VDZ	Moćko et al.[23], 2016	NR	1	374	225	OR, 0.31 (0.06-1.47) [a]	NA	NA
	Jin et al.[32], 2015	0.5-10 mg/kg or 300 mg	3	1122	901	OR, 0.75 (0.20-2.87)	I^2=77.9%, P=0.01	NA
	Kawalec et al.[25], 2014	NR	2	555	343	RiR, 0.75 (0.16-3.51)	I^2=80%, P=0.02	NA
Maintenance therapy								

Adverse events								
ADA	Chen et al.[36], 2016	40 mg	2	790	434	**RiR, 1.28 (1.06-1.54)**	I^2=5%, P=0.30	NA
	Moćko et al.[23], 2016	NR	2	990	434	OR, 1.33 (0.68-2.62) [a]	NR	NA
GLM	Moćko et al.[23], 2016	NR	1	464	308	OR, 1.42 (0.55-3.58) [a]	NA	NA
	Kawalec et al.[25], 2014	NR	1	464	308	RiR, 1.11 (0.97-1.26)	NR	NA
IFX	Moćko et al.[23], 2016	NR	1	242	121	OR, 1.23 (0.42-3.90) [a]	NA	NA
VDZ	Moćko et al.[23], 2016	NR	1	925	650	OR, 1.03 (0.41-2.47) [a]	NA	NA
	Kawalec et al.[25], 2014	NR	2	419	284	RiR, 0.96 (0.87-1.05)	I^2=0%, P=0.50	NA
Serious adverse events								
ADA, IFX	Lv et al.[38], 2014	160/80/40 mg; 5 or 10 mg/kg	4	1973	1225	ReR, 0.83 (0.69-1.00)	I^2=47%, P=0.13	NA
ADA	Singh et al.[31], 2018		3	NR	NR	OR, 1.10 (0.73-1.67)	NR	NA
	Chen et al.[36], 2016	40 mg	2	790	434	RiR, 1.09 (0.76-1.56)	I^2=0%, P=0.48	NA
	Moćko et al.[23], 2016	NR	2	990	434	OR, 1.10 (0.66-1.87) [a]	NR	NA
	Lv et al.[38], 2014	160/80/40 mg	1	517	257	ReR, 1.12 (0.74-1.69)	NA	NA
	Mei et al.[22], 2015[b]	NR	NR	NR	NR	OR, 1.22 (0.51-2.54)	NR	NA
	Thorlund et al.[15], 2014	160/80 or 160 mg	1	517	257	OR, 0.98 (0.49-1.95) [a]	NA	NA
GLM	Singh et al.[31], 2018		1	NR	NR	OR, 1.61 (0.80-3.26)	NA	NA
	Moćko et al.[23], 2016	NR	1	464	308	OR, 1.53 (0.70-3.51) [a]	NA	
	Mei et al.[22], 2015 [b]	NR	NR	NR	NR	OR, 1.53 (0.79-2.98)	NR	NA
	Kawalec et al.[25], 2014	NR	1	464	308	RiR, 1.48 (0.79-2.76)	NA	NA
IFX	Singh et al.[31], 2018		2	NR	NR	OR, 0.74 (0.49-1.12)	NR	NA
	Moćko et al.[23], 2016	NR	1	242	121	OR, 0.80 (0.38-1.66) [a]	NA	NA
	Mei et al.[22], 2015 [b]	NR	NR	NR	NR	OR, 0.84 (0.47-1.54)	NR	NA
	Thorlund et al.[15], 2014		1	364	243	OR, 0.79 (0.37-1.70) [a]	NA	NA
VDZ	Singh et al.[31], 2018		1	NR	NR	OR, 0.47 (0.21-1.06)	NA	NA
	Moćko et al.[23], 2016	NR	1	925	650	OR, 0.92 (0.49-1.70) [a]	NA	
	Mei et al.[22], 2015 [b]	NR	NR	NR	NR	OR, 1.14 (0.50-2.60)	NR	NA
	Kawalec et al.[25], 2014	NR	2	419	284	RiR, 0.51 (0.26-0.99)	I^2=18%, P=0.27	NA
Induction and/or maintenance therapy								
Adverse events								
ADA, GLM, IFX	Lopez et al.[20], 2015	NR	6	3348	2135	RiR, 1.04 (0.99-1.09)	I^2=0%, P=0.58	NA
ADA, IFX	Huang et al.[26], 2011	NR	6	1304	776	OR, 1.07 (0.55-2.09)	I^2=79%, P<0.001	NA

ADA	Bonovas et al.[24], 2018	160/80/40 mg	3	1149	570	OR, 1.19 (0.80-1.78)	I^2=50%, P=0.14	NA
	Zhang et al.[16], 2016	160/80 or 80/40 mg	2	1093	610	ReR, 1.02 (0.94-1.10)	I^2=0%, P=0.37	NA
	Lopez et al.[20], 2015	NR	2	1093	610	RiR, 1.00 (0.93-1.07)	I^2=0%, P=0.37	NA
GLM	Bonovas et al.[24], 2018	200/100 mg	3	1034	517	OR, 1.40 (0.73-2.67)	I^2=70%, P=0.03	NA
	Lopez et al.[20], 2015	NR	2	1527	1041	RiR, 1.08 (0.97-1.19)	I^2=0%, P=0.43	NA
IFX	Bonovas et al.[24], 2018	5 mg/kg	4	776	387	**OR, 1.48 (1.00-2.19)**	I^2=0%, P=0.64	NA
	Lopez et al.[20], 2015	NR	2	728	484	RiR, 1.06 (0.99-1.14)	I^2=0%, P=0.44	NA
VDZ	Bonovas et al.[24], 2018	300 mg	2	849	697	OR, 0.98 (0.67-1.43)	I^2=0%, P=0.85	NA
	Mosli et al.[27], 2015	NR	1	941	657	RiR 1.00 (0.93-1.07)	NA	NA
	Bickston et al.[11], 2014	0.5, 2, 6 or 10 mg/kg	2	941	657	RiR, 0.99 (0.93-1.07)	NR	NA
Serious adverse events								
ADA, GLM, IFX	Lopez et al.[20], 2015	NR	6	NR	NR	RiR, 0.81 (0.58-1.15)	NR	NA
ADA, GLM, IFX	Song and Zheng[30], 2015	NR	8	2590	1550	OR, 0.69 (0.53-0.88)	I^2=26%, P=0.22	NA
ADA, IFX	Huang et al.[26], 2011	NR	7	1347	799	OR, 0.65 (0.48-0.89)	I^2=6%, P=0.38	NA
ADA	Bonovas et al.[24], 2018	160/80/40 mg	3	1149	570	OR, 0.82 (0.55-1.23)	I^2=0%, P=0.43	NA
	Zhang et al.[16], 2016	160/80 or 80/40 mg	2	1093	610	ReR, 1.09 (0.78-1.53)	I^2=0%, P=0.84	NA
	Thorlund et al.[15], 2014	160/80 or 160 mg	2	576	353	OR, 0.79 (0.43-1.42) [a]	NR	NA
GLM	Bonovas et al.[24], 2018	200/100 mg	3	1034	517	OR, 0.70 (0.19-2.61)	I^2=78%, P=0.01	NA
IFX	Bonovas et al.[24], 2018	5 mg/kg	4	776	387	OR, 0.73 (0.50-1.06)	I^2=0%, P=0.65	NA
	Thorlund et al.[15], 2015	160/80 or 160 mg	2	364	241	OR, 0.65 (0.36-1.13) [a]	NR	NA
VDZ	Bonovas et al.[24], 2018	300 mg	2	849	697	**OR, 0.39 (0.18-0.81)**	I^2=36%, P=0.21	NA
	Mosli et al.[27], 2015	NR	3	1122	775	RiR, 1.02 (0.73-1.42)	NR	
	Wang et al.[13], 2014	0.5, 2, 6, 10 mg/kg or 300 mg	3	578	362	ReR, 1.01 (0.72-1.41)	I^2=0%, P=0.51	NA
	Bickston et al.[11], 2014	0.5, 2, 6 or 10 mg/kg	3	1122	775	RiR, 1.02 (0.73-1.42)	NR	NA

ADA and GLM were administered subcutaneously (SC) and IFX and VDZ intravenously (IV).

Abbreviations: ADA, adalimumab; CI, confidence interval; GLM, golimumab; IFX, infliximab; NA, non-applicable, NR, not reported; OR, odds ratio; ReR, relative risk; RiR, Risk ratio; P, p-value; VDZ, vedolizumab.

[a] CrI, credible interval

[b] The presented odds ratios in the study of Mei et al. 2015[22] are for the opposite associations (i.e., for example infliximab vs. placebo – not placebo vs. infliximab)

Table S7: Indirect comparisons between biologic therapies including adalimumab, golimumab, infliximab, and vedolizumab, as induction and/or maintenance therapy, in ulcerative colitis (UC) in terms of safety. Significant estimates ($p<0.05$) are presented in bold.

Biologic therapy		**Estimates and 95% CIs**	
	Author, year	**Adverse events**	**Serious adverse events**
IFX vs. ADA	Bonovas et al.[24], 2018	OR, 1.31 (0.81-2.01)	OR, 0.89 (0.52-1.54)
	Thorlund et al.[15], 2014	NR	OR, 0.83 (0.36-1.89) [a]
IFX vs. GLM	Bonovas et al.[24], 2018	OR, 1.28 (0.81-2.05)	OR, 0.83 (0.45-1.54)
IFX vs. VDZ	Bonovas et al.[24], 2018	OR, 1.52 (0.88-2.62)	OR, 1.78 (0.89-3.55)
ADA vs. GLM	Bonovas et al.[24], 2018	OR, 0.98 (0.68-1.42)	OR, 0.93 (0.50-1.75)
ADA vs. VDZ	Bonovas et al.[24], 2018	OR, 1.16 (0.73-1.85)	OR, 2.00 (0.99-4.02)
GLM vs. VDZ	Bonovas et al.[24], 2018	OR, 1.18 (0.75-1.87)	**OR, 2.15 (1.00-4.59)**

Abbreviations: ADA, adalimumab; CI, confidence interval; GLM, golimumab; IFX, infliximab; NR, not reported; OR, odds ratio; VDZ, vedolizumab; vs., versus.

[a] CrI, credible interval