Supplemental Digital Content

Supplementary Table 1. Online search strategy.

Note that the inclusion of morbidities, in addition to ulcerative colitis and Crohn's disease, for which biologics are a treatment option, allowed this search to be run simultaneously for conditions of interest to the study sponsor in addition to inflammatory bowel disease (IBD). Only publications related to IBD were considered for this review.

(a) MEDLINE® In-Process & Other Non-Indexed Citations

S/N	Search terms	Parameter
1	exp Arthritis: Rheumatoid/ or exp Arthritis: Psoriatic/ or exp Spondylarthritis/ or exp Spondylitis: Ankylosing/ or exp Spondylarthropathies/ or exp Colitis: Ulcerative/ or exp Crohn Disease/ or exp Psoriasis/ or exp Arthritis: Juvenile/	Disease
2	rheumatoid arthritis.tw.	
3	(psoria$ adj2 (arthrit$ or arthropath$)).tw.	
4	(spondyloarthritis or spondyloarthritides or spondyloarthropathies).tw.	
5	(Axial SpA or axial spondyloarthritis or axSpA or ax-SpA).tw.	
6	(ankylosing spondylitis or 'AS').tw.	
7	(bekhterev or bechterew or marie strumpell or rheumatoid spondylitis or ankylos* or spondyl* or axial).tw.	
8	(Non$radiographic or radiograph* or nr-axSpA).tw.	
9	Ulcerative colitis.tw.	
10	crohn$.tw.	
11	psoria$.tw.	
12	((Juvenile adj2 arthritis) or JIA or JRA).tw.	
13	or/1-12	
14	(Infliximab or Remicade or Avakine).mp.	Intervention
15	(golimumab or CNTO 148 or CNTO148 or Simponi).mp.	
16	(certolizumab or CDP870 or CDP 870 or PHA738144 or PHA 738144 or Cimzia).mp.	
17	(certolizumab adj2 pegol).mp.	

S/N	Search terms	Parameter
18	(Etanercept or Enbrel or ETA or ETN).mp.	
19	(Tocilizumab or actemra or atlizumab).mp.	
20	(Rituximab or rituxan or Mabthera).mp.	
21	(Ustekinumab or stelara or CNTO 1275 or CNTO-1275).mp.	
22	(Abatacept or BMS 188667 or ctla4 ig).mp.	
23	(Secukinumab or cosentyx or AIN457 or vedolizumab or entyvio).mp	
24	(biosimilars or biologics or CT-P13 or inflectra or remsima).mp.	
25	or/14-24	
26	randomized controlled trial.pt.	Study Design
27	controlled clinical trial.pt.	
28	randomi?ed.ab.	
29	placebo.tw.	
30	drug therapy.fs.	
31	clinical trials as topic.sh.	
32	randomly.ab.	
33	trial.ab.	
34	groups.ab.	
35	(crossover or cross-over or cross over).tw.	
36	((singl$ or double$ or triple$ or treble$) and (blind$ or mask$)).tw:sh.	
37	Epidemiologic Studies/ or exp Case-Control Studies/ or exp Cohort Studies/ or exp Cross-Sectional Studies/ or exp Control Groups/ or Longitudinal Studies/ or Prospective Studies/ or Retrospective Studies/ or Comparative Study/ or research design/ or Observational Study/	
38	(case control or case-control).ti:ab.	
39	((follow up or follow-up) adj (study or studies)).ti:ab.	
40	(Longitudinal or retrospective or prospective or comparative or cohort or cross sectional or cross-sectional).ti:ab.	
41	((observ$ or registry) adj3 (study or studies)).ti:ab.	
42	(Epidemiolog$ adj (study or studies or analysis)).ti:ab.	
43	or/26-42	
44	exp "Costs and cost analysis"/ or cost-benefit analysis/	
45	Economics: Pharmaceutical/ or Economics: Medical/ or Economics/ or exp Economics: Hospital/ or Economics: Dental/ or Economics: Nursing/	
46	(economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti:ab.	
47	(expenditure$ not energy).ti:ab.	
48	(value adj1 money).ti:ab.	
49	budget$.ti:ab.	

S/N	Search terms	Parameter
50	or/44-49	Pharmaco-economics
51	((energy or oxygen) adj cost).ti:ab.	
52	(metabolic adj cost).ti:ab.	
53	((energy or oxygen) adj expenditure).ti:ab.	
54	or/51-53	
55	50 not 54	
56	Quality-Adjusted Life Years/	
57	exp "Outcome and Process Assessment (Health Care)"/ or exp "Outcome Assessment (Health Care)"/ or exp Treatment Outcome/ or exp "Quality of Life"/	
58	((sf or short form or shortform) and "6").tw.	
59	(EuroQol or standard gamble or time trade off or time tradeoff or TTO or EQ5D or EQ-5D or health utilit$ index).tw.	
60	((Health and utilit* and index) or HUI* or SF-6D or sf6* or sf 6* or short form 6* or shortform 6* or sf six or sfsix or short form six or shortform six or QALY or quality adjusted life year* or quality-adjusted life year or quality adjusted life-year* or quality-adjusted life-year* or SF-36 or sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty-six or short form thirty six or short form health survey or willingness to pay).tw.	
61	((utilit* and score*) or (utilit* and weight*) or Rosser or (health and utilit*) or (utilit* and value) or disutility*).tw.	
62	(outcome and measure$).tw.	
63	(health and outcome$).tw.	
64	or/56-63	
65	43 or 55 or 64	
66	13 and 25 and 65	
67	(editorial or comment$ or letter or note or case series or case study or case studies or case report).pt. or (editorial/ or letter/ or case study/ or case report/ or note/)	
68	animal/ not (animal/ and human/)	
69	or/67-68	
70	66 not 69	
71	limit 70 to english language	
72	**limit 71 to yr=2009 to present**	

(b) Embase®

S/N	Search terms	Parameter

S/N	Search terms	Parameter
1	exp rheumatoid arthritis/ or exp psoriatic arthritis/ or exp spondylarthritis/ or exp ankylosing spondylitis/ or exp spondyloarthropathy/ or exp ulcerative colitis/ or exp Crohn disease/ or exp Psoriasis/ or exp juvenile rheumatoid arthritis/	Disease
2	rheumatoid arthritis.tw.	
3	(psoria$ adj2 (arthrit$ or arthropath$)).tw.	
4	(spondyloarthritis or spondyloarthritides or spondyloarthropathies).tw.	
5	(Axial SpA or axial spondyloarthritis or axSpA or ax-SpA).tw.	
6	(ankylosing spondylitis or 'AS').tw.	
7	(bekhterev or bechterew or marie strumpell or rheumatoid spondylitis or ankylos* or spondyl* or axial).tw.	
8	(Non$radiographic or radiograph* or nr-axSpA).tw.	
9	Ulcerative colitis.tw.	
10	crohn$.tw.	
11	psoria$.tw.	
12	((Juvenile adj2 arthritis) or JIA or JRA).tw.	
13	or/1-12	
14	exp infliximab/ or exp adalimumab/ or exp golimumab/ or exp certolizumab pegol/ or exp etanercept/ or exp tocilizumab/ or exp rituximab/ or exp secukinumab/ or exp ustekinumab/ or exp abatacept/	Intervention
15	(Infliximab or Remicade or Avakine).mp.	
16	(Adalimumab or Humira or Hum?ra).mp.	
17	(golimumab or CNTO 148 or CNTO148 or Simponi).mp.	
18	(certolizumab or CDP870 or CDP 870 or PHA738144 or PHA 738144 or Cimzia).mp.	
19	(certolizumab adj2 pegol).mp.	
20	(Etanercept or Enbrel or ETA or ETN).mp.	
21	(Tocilizumab or actemra or atlizumab).mp.	
22	(Rituximab or rituxan or Mabthera).mp.	
23	(Ustekinumab or stelara or CNTO 1275 or CNTO-1275).mp.	

S/N	Search terms	Parameter
24	(Abatacept or orencia or BMS 188667 or ctla4 ig).mp.	
25	(Secukinumab or cosentyx or AIN457 or vedolizumab or entyvio).mp	
26	(biosimilars or biologics or CT-P13 or inflectra or remsima).mp.	
27	or/14-26	
28	clinical trial/	Study Design
29	random$.tw.	
30	randomized controlled trial/	
31	trial$.tw.	
32	controlled study/	
33	double blind procedure/	
34	placebo$.tw.	
35	placebo/	
36	(singl$ adj (blind$ or mask$)).tw.	
37	factorial$.ti:ab.	
38	(crossover$ or cross-over$).ti:ab.	
39	(double$ adj (blind$ or mask$)).tw.	
40	assign$.ti:ab.	
41	allocat$.ti:ab.	
42	volunteer$.ti:ab.	
43	Crossover Procedure/	
44	Single Blind Procedure/	
45	((triple$ or treble$) adj (blind$ or mask$)).tw.	
46	epidemiology/ or exp case control study/ or exp cohort analysis/ or exp cross-sectional study/ or exp control group/ or clinical study/ or longitudinal study/ or prospective study/ or retrospective study/ or comparative study/ or observational study/	
47	(Epidemiolog$ adj (study or studies or analysis)).ti:ab.	

S/N	Search terms	Parameter
48	(case control or case-control).ti:ab.	
49	((follow up or follow-up) adj (study or studies)).ti:ab.	
50	(Longitudinal or retrospective or prospective or comparative or cohort or cross sectional or cross-sectional).ti:ab.	
51	((observ$ or registry) adj3 (study or studies)).ti:ab.	
52	or/28-51	
53	health-economics/ or exp economic-evaluation/ or exp health-care-cost/ or exp pharmacoeconomics/	
54	(econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti:ab.	
55	(expenditure$ not energy).ti:ab.	
56	(value adj2 money).ti:ab.	
57	budget$.ti:ab.	
58	or/53-57	
59	(metabolic adj cost).ti:ab.	
60	((energy or oxygen) adj cost).ti:ab.	
61	((energy or oxygen) adj expenditure).ti:ab.	
62	or/59-61	
63	58 not 62	
64	exp quality adjusted life year/	
65	exp treatment outcome/	
66	exp "quality of life"/	
67	exp outcome assessment/	
68	((sf or short form or shortform) and "6").tw.	
69	(EuroQol or standard gamble or time trade off or time tradeoff or TTO or EQ5D or EQ-5D or health utilit$ index).tw.	Pharmaco-economics
70	((Health and utilit* and index) or HUI* or SF-6D or sf6* or sf 6* or short form 6* or shortform 6* or sf six or sfsix or short form six or shortform six or QALY or quality adjusted life year* or quality-adjusted life year or quality adjusted life-year* or quality-adjusted life-year* or SF-36 or sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty-six	

S/N	Search terms	Parameter
	or short form thirty six or short form health survey or willingness to pay).tw.	
71	((utilit* and score*) or (utilit* and weight*) or Rosser or (health and utilit*) or (utilit* and value) or disutility*).tw.	
72	or/64-71	
73	52 or 63 or 72	
74	13 and 27 and 73	
75	(editorial or comment* or letter or note or case series or case study or case studies or case report).pt. or (editorial/ or letter/ or case study/ or case report/ or note/)	
76	animal/ not (animal/ and human/)	
77	or/75-76	
78	74 not 77	
79	**limit 78 to (english language and yr=2009 to present**	

(c) Cochrane Library

S/N	Search terms	Parameter
#1	MeSH descriptor: [Arthritis: Rheumatoid] explode all trees	Disease
#2	MeSH descriptor: [Arthritis: Psoriatic] explode all trees	
#3	MeSH descriptor: [Spondylarthritis] explode all trees	
#4	MeSH descriptor: [Spondylitis: Ankylosing] explode all trees	
#5	MeSH descriptor: [Spondylarthropathies] explode all trees	
#6	MeSH descriptor: [Colitis: Ulcerative] explode all trees	
#7	MeSH descriptor: [Crohn Disease] explode all trees	
#8	MeSH descriptor: [Psoriasis] explode all trees	
#9	MeSH descriptor: [Arthritis: Juvenile] explode all trees	
#10	(psoria* near/2 (arthrit* or arthropath*)):ti:ab:kw	
#11	rheumatoid arthritis:ti:ab:kw	
#12	(spondyloarthritis or spondyloarthritides or spondyloarthropathies):ti:ab:kw	
#13	(Axial SpA or axial spondyloarthritis or axSpA or ax-SpA):ti:ab:kw	
#14	(bekhterev or bechterew or marie strumpell or rheumatoid spondylitis or ankylos* or spondyl* or axial):ti:ab:kw	

#15	(Non*radiographic or radiograph* or nr-axSpA).ti:ab:kw.	
#16	Ulcerative colitis:ti:ab:kw	
#17	crohn*:ti:ab:kw	
#18	psoria*:ti:ab:kw	
#19	((Juvenile near/2 arthritis) or JIA or JRA):ti:ab:kw	
#20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19	
#21	(Infliximab or Remicade or Avakine):ti:ab:kw	Intervention
#22	(golimumab or CNTO 148 or CNTO148 or Simponi):ti:ab:kw	
#23	(certolizumab or CDP870 or CDP 870 or PHA738144 or PHA 738144 or Cimzia):ti:ab:kw	
#24	(certolizumab near/2 pegol):ti:ab:kw	
#25	(Etanercept or Enbrel or ETA or ETN):ti:ab:kw	
#26	(Tocilizumab or actemra or atlizumab):ti:ab:kw	
#27	(Rituximab or rituxan or Mabthera):ti:ab:kw	
#28	(Ustekinumab or stelara or CNTO 1275 or CNTO-1275):ti:ab:kw	
#29	(Abatacept or orencia or BMS 188667):ti:ab:kw	
#30	(Secukinumab or corsentyx or AIN457 or vedolizumab or entyvio):ti:ab:kw	
#31	(biosimilars or biologics):ti:ab:kw	
#32	#21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31	
#33	#20 and #32	
#34	**#33 Publication Year from 2009 to 2014: in Cochrane Reviews (Reviews and Protocols): Other Reviews: Trials: Technology Assessments and Economic Evaluations**	

(d) Cross-referencing of MEDLINE® In-Process & Other Non-Indexed Citations

S/N	**Search terms**	**Parameter**
1	exp Arthritis: Rheumatoid/ or exp Arthritis: Psoriatic/ or exp Spondylarthritis/ or exp Spondylitis: Ankylosing/ or exp Spondylarthropathies/ or exp Colitis: Ulcerative/ or exp Crohn Disease/ or exp Psoriasis/ or exp Arthritis: Juvenile/	Disease
2	rheumatoid arthritis.tw.	
3	(psoria$ adj2 (arthrit$ or arthropath$)).tw.	
4	(spondyloarthritis or spondyloarthritides or spondyloarthropathies).tw.	
5	(Axial SpA or axial spondyloarthritis or axSpA or ax-SpA).tw.	

S/N	Search terms	Parameter
6	(ankylosing spondylitis or 'AS').tw.	
7	(bekhterev or bechterew or marie strumpell or rheumatoid spondylitis or ankylos* or spondyl* or axial).tw.	
8	(Non$radiographic or radiograph* or nr-axSpA).tw.	
9	Ulcerative colitis.tw.	
10	crohn$.tw.	
11	psoria$.tw.	
12	((Juvenile adj2 arthritis) or JIA or JRA).tw.	
13	or/1-12	
14	(Infliximab or Remicade or Avakine).mp.	
15	(Adalimumab or Humira or Hum?ra).mp.	
16	(golimumab or CNTO 148 or CNTO148 or Simponi).mp.	
17	(certolizumab or CDP870 or CDP 870 or PHA738144 or PHA 738144 or Cimzia).mp.	
18	(certolizumab adj2 pegol).mp.	
19	(Etanercept or Enbrel or ETA or ETN).mp.	
20	(Tocilizumab or actemra or atlizumab).mp.	Intervention
21	(Rituximab or rituxan or Mabthera).mp.	
22	(Ustekinumab or stelara or CNTO 1275 or CNTO-1275).mp.	
23	(Abatacept or BMS 188667 or ctla4 ig).mp.	
24	(Secukinumab or cosentyx or AIN457 or vedolizumab or entyvio).mp	
25	(biosimilars or biologics or CT-P13 or inflectra or remsima).mp.	
26	or/14-25	
27	randomized controlled trial.pt.	
28	controlled clinical trial.pt.	
29	randomi?ed.ab.	
30	placebo.tw.	
31	drug therapy.fs.	
32	clinical trials as topic.sh.	
33	randomly.ab.	
34	trial.ab.	
35	groups.ab.	
36	(crossover or cross-over or cross over).tw.	
37	((singl$ or double$ or triple$ or treble$) and (blind$ or mask$)).tw:sh.	Study Design
38	Epidemiologic Studies/ or exp Case-Control Studies/ or exp Cohort Studies/ or exp Cross-Sectional Studies/ or exp Control Groups/ or Longitudinal Studies/ or Prospective Studies/ or Retrospective Studies/ or Comparative Study/	

S/N	Search terms	Parameter
	or research design/ or Observational Study/	
39	(case control or case-control).ti:ab.	
40	((follow up or follow-up) adj (study or studies)).ti:ab.	
41	(Longitudinal or retrospective or prospective or comparative or cohort or cross sectional or cross-sectional).ti:ab.	
42	((observ$ or registry) adj3 (study or studies)).ti:ab.	
43	(Epidemiolog$ adj (study or studies or analysis)).ti:ab.	
44	or/27-43	
45	immunogenicity.tw.	Immunogenicity Terms
46	anti-drug antibod$.tw.	
47	anti-infliximab antibod$.tw.	
48	"antibod$ to infliximab".tw.	
49	anti-ifx antibod$.tw.	
50	anti-inf antibod$.tw.	
51	anti-certolizumab pegol antibod$.tw.	
52	anti-certolizumab antibod$.tw.	
53	"antibod$ to certolizumab".tw.	
54	anti-czp antibod$.tw.	
55	anti-abatacept antibod$.tw.	
56	"antibod$ to abatacept".tw.	
57	anti-CTLA4 antibod$.tw.	
58	"antibod$ to CTLA4".tw.	
59	anti-aba antibod$.tw.	
60	anti-adalimumab antibod$.tw.	
61	"antibod$ to adalimumab".tw.	
62	anti-ada antibod$.tw.	
63	anti-etanercept antibod$.tw.	
64	"antibod$ to etanercept".tw.	
65	anti-eta antibod$.tw.	
66	anti-etn antibod$.tw.	
67	anti-golimumab antibod$.tw.	
68	"antibod$ to golimumab".tw.	
69	anti-glm antibod$.tw.	
70	anti-rituximab antibod$.tw.	
71	antibod$ to rituximab".tw.	

S/N	Search terms	Parameter
72	anti-rtx antibod$.tw.	
73	“anti-secukinumab antibod$” or “anti-vedolizumab antibod$”.tw.	
74	"antibod$ to secukinumab" or "antibod$ to vedolizumab".tw.	
75	“anti-sec antibod$” or “anti-vdm antibod$”.tw.	
76	anti-tocilizumab antibod$.tw.	
77	"antibod$ to tocilizumab".tw.	
78	anti-tcz antibod$.tw.	
79	anti-ustekinumab antibod$.tw.	
80	"antibod$ to ustekinumab".tw.	
81	anti-ust antibod$.tw.	
82	or/45-81	
83	13 and 26 and 44 and 82	
84	(editorial or comment* or letter or note or case series or case study or case studies or case report).pt. or (editorial/ or letter/ or case study/ or case report/ or note/)	
85	animal/ not (animal/ and human/)	
86	or/84-85	
87	83 not 86	
88	limit 87 to english language	
89	**limit 88 to ed=2009 to present**	

e) Cross-referencing Embase®

S/N	Search terms	Parameter
1	exp rheumatoid arthritis/ or exp psoriatic arthritis/ or exp spondylarthritis/ or exp ankylosing spondylitis/ or exp spondyloarthropathy/ or exp ulcerative colitis/ or exp Crohn disease/ or exp Psoriasis/ or exp juvenile rheumatoid arthritis/	
2	rheumatoid arthritis.tw.	Disease
3	(psoria$ adj2 (arthrit$ or arthropath$)).tw.	
4	(spondyloarthritis or spondyloarthritides or spondyloarthropathies).tw.	
5	(Axial SpA or axial spondyloarthritis or axSpA or ax-SpA).tw.	

S/N	Search terms	Parameter
6	(ankylosing spondylitis or 'AS').tw.	
7	(bekhterev or bechterew or marie strumpell or rheumatoid spondylitis or ankylos* or spondyl* or axial).tw.	
8	(Non$radiographic or radiograph* or nr-axSpA).tw.	
9	Ulcerative colitis.tw.	
10	crohn$.tw.	
11	psoria$.tw.	
12	((Juvenile adj2 arthritis) or JIA or JRA).tw.	
13	or/1-12	
14	exp infliximab/ or exp adalimumab/ or exp golimumab/ or exp certolizumab pegol/ or exp etanercept/ or exp tocilizumab/ or exp rituximab/ or exp ustekinumab/ or exp abatacept/	Intervention
15	(Infliximab or Remicade or Avakine).mp.	
16	(Adalimumab or Humira or Hum?ra).mp.	
17	(golimumab or CNTO 148 or CNTO148 or Simponi).mp.	
18	(certolizumab or CDP870 or CDP 870 or PHA738144 or PHA 738144 or Cimzia).mp.	
19	(certolizumab adj2 pegol).mp.	
20	(Etanercept or Enbrel or ETA or ETN).mp.	
21	(Tocilizumab or actemra or atlizumab).mp.	
22	(Rituximab or rituxan or Mabthera).mp.	
23	(Ustekinumab or stelara or CNTO 1275 or CNTO-1275).mp.	
24	(Abatacept or orencia or BMS 188667 or ctla4 ig).mp.	
25	(Secukinumab or cosentyx or AIN457).mp	
26	(biosimilars or biologics or CT-P13 or inflectra or remsima).mp.	
27	or/14-26	
28	clinical trial/	Study Design
29	random$.tw.	
30	randomized controlled trial/	

S/N	Search terms	Parameter
31	trial$.tw.	
32	controlled study/	
33	double blind procedure/	
34	placebo$.tw.	
35	placebo/	
36	(singl$ adj (blind$ or mask$)).tw.	
37	factorial$.ti:ab.	
38	(crossover$ or cross-over$).ti:ab.	
39	(double$ adj (blind$ or mask$)).tw.	
40	assign$.ti:ab.	
41	allocat$.ti:ab.	
42	volunteer$.ti:ab.	
43	Crossover Procedure/	
44	Single Blind Procedure/	
45	((triple$ or treble$) adj (blind$ or mask$)).tw.	
46	epidemiology/ or exp case control study/ or exp cohort analysis/ or exp cross-sectional study/ or exp control group/ or clinical study/ or longitudinal study/ or prospective study/ or retrospective study/ or comparative study/ or observational study/	
47	(Epidemiolog$ adj (study or studies or analysis)).ti:ab.	
48	(case control or case-control).ti:ab.	
49	((follow up or follow-up) adj (study or studies)).ti:ab.	
50	(Longitudinal or retrospective or prospective or comparative or cohort or cross sectional or cross-sectional).ti:ab.	
51	((observ$ or registry) adj3 (study or studies)).ti:ab.	
52	or/28-51	
53	immunogenicity.tw.	Immunogenicity Terms
54	anti-drug antibod$.tw.	

S/N	Search terms	Parameter
55	anti-infliximab antibod$.tw.	
56	"antibod$ to infliximab".tw.	
57	anti-ifx antibod$.tw.	
58	anti-inf antibod$.tw.	
59	anti-certolizumab pegol antibod$.tw.	
60	anti-certolizumab antibod$.tw.	
61	"antibod$ to certolizumab".tw.	
62	anti-czp antibod$.tw.	
63	anti-abatacept antibod$.tw.	
64	"antibod$ to abatacept".tw.	
65	anti-CTLA4 antibod$.tw.	
66	"antibod$ to CTLA4".tw.	
67	anti-aba antibod$.tw.	
68	anti-adalimumab antibod$.tw.	
69	"antibod$ to adalimumab".tw.	
70	anti-ada antibod$.tw.	
71	anti-etanercept antibod$.tw.	
72	"antibodies to etanercept".tw.	
73	anti-eta antibod$.tw.	
74	anti-etn antibod$.tw.	
75	anti-golimumab antibod$.tw.	
76	"antibod$ to golimumab".tw.	
77	anti-glm antibod$.tw.	
78	anti-rituximab antibod$.tw.	
79	"antibod$ to rituximab".tw.	

S/N	Search terms	Parameter
80	anti-rtx antibod$.tw.	
81	“anti-secukinumab antibod$” or “anti-vedolizumab antibod$”.tw.	
82	"antibod$ to secukinumab" or "antibod$ to vedolizumab".tw.	
83	“anti-sec antibod$” or “anti-vdm antibod$”.tw.	
84	anti-tocilizumab antibod$.tw.	
85	"antibod$ to tocilizumab".tw.	
86	anti-tcz antibod$.tw.	
87	anti-ustekinumab antibod$.tw.	
88	"antibod$ to ustekinumab".tw.	
89	anti-ust antibod$.tw.	
90	or/53-90	
91	13 and 27 and 52 and 90	
92	(editorial or comment* or letter or note or case series or case study or case studies or case report).pt. or (editorial/ or letter/ or case study/ or case report/ or note/)	
93	animal/ not (animal/ and human/)	
94	or/92-93	
95	91 not 94	
96	limit 95 to english language	
97	**limit 96 to em=2009 to present**	

Supplementary Table 2. Conference proceedings search strategy.

Conference:	**Advances in Inflammatory Bowel Disease Crohn's and Colitis**		
Year:	2013–2015		
Search method:	Screening the title identified two potential relevant abstracts		
Search results:	Two abstracts identified		
Conference:	**Congress of the European Crohn's and Colitis Organisation (ECCO)**		
Year:	2013–2015		
Search method:	Both oral and poster presentations were hand-searched from the conference website		
Search results:	Forty-four abstracts identified		
Conference:	**The International Society for Pharmacoeconomics and Outcomes Research (ISPOR)**		
Year:	2009–2015		
Search method:	The ISPOR scientific presentations database was searched with keywords listed in the table below. Thereafter: the titles and abstracts of the retrieved articles were screened for relevance		
	Keyword	**Hits**	**Relevant abstract**
	Rheumatoid arthritis in title	651	0
	Immunogenicity in abstract	15	0
	Anti-drug antibodies in abstract	0	0
	Psoriatic arthritis in title	88	0
	Juvenile idiopathic arthritis in title	14	0
	Ankylosing spondylitis in title	78	0
	Psoriasis in title	279	0
	Crohn's disease in title	4	0
	Ulcerative colitis in title	52	0
	Non-radiographic axial spondyloarthritis in title	6	0
	Antibodies in abstract	92	0
Search results:	No abstract was identified		

Supplementary Table 3. Study data to extract.

Information to extract (comprehensive)	
Study information	The following study information was extracted: • Author • Study name • Study intervention • Disease indication • Study design • Study duration • Number of patients (per treatment arm) • Study setting • Study outcomes • Country(ies)/centers • Study limitation(s)
Treatment data	The following information was extracted regarding biologic interventions: • Dose • Frequency • Concomitant medication • Route of administration

Information to extract (comprehensive)	
Baseline	The following baseline variables were extracted: • Age • Gender • Race • Disease duration • Proportion of patient with immunosuppressive therapy • Biologic experienced patients • CRP • ESR • IBDQ • PGA • Concomitant or prior IS • Prior biologics
Safety outcomes	The following safety outcomes were extracted: • Incidence of AEs due to dose intensification because of immunogenicity • Infusion/injection site reaction • Thromboembolic events and/or other types of AEs
Efficacy outcomes	The following efficacy outcomes were extracted: • Proportion of patients with antibody presence/detection (based on type of method for detection e.g. ELISA vs. radioimmunoassay) • Proportion of refractory patients or patients who relapsed (number of patients who initially responded but lost response later) • Efficacy outcomes (CDAI: Mayo: etc.) • Duration of clinical response • Proportion of patients requiring dose intensification due to presence of ADAbs • Proportion of patient with relative gain in efficacy following dose intensification • Treatment discontinuations due to lack of efficacy
Drug survival outcomes	The following drug survival outcomes were extracted: • Treatment discontinuations due to any cause

Information to extract (comprehensive)	
Pharmacokinetic outcomes	The following pharmacokinetic outcomes were extracted: • Biologic serum concentration
Pharmacoeconomics and treatment-related outcomes	The following pharmacoeconomic outcomes were extracted: • Costs associated with ADAbs management • ADAbs associated costs per patient • HRQoL (e.g. QALY)

ADAbs: anti-drug antibodies; AEs: adverse events; CDAI: Crohn's Disease Activity Index; CRP: C-reactive protein; ELISA: enzyme-linked immunosorbent assay; ESR: erythrocyte sedimentation rate; HRQoL: health-related quality of life; IBDQ: Inflammatory Bowel Disease Questionnaire; IS: immunosuppressant; PGA: physician's global assesment; QALY: quality-adjusted life years.

Supplementary Table 4. Characteristics of included studies.

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Eckert *et al.*: 2013 (CA)	CD	ADA: sc 40/20 mg or 20/10 mg eow or qw	189	RCT	NR	52 weeks	Pharmacokinetics & immunogenicity	9[a]
Hanauer *et al.*: 2006	CD	ADA: sc 40 mg w 0 and 20 mg w 2 ADA: sc 80 mg w 0 and 40 mg w 2 ADA: sc 160 mg w 0 and 80 mg w 2	299	RCT	Multicenter	4 weeks	Safety: efficacy: & immunogenicity	5[b]
Hyams *et al.*: 2014 (CA)	CD	ADA: sc 160/80 mg or 80/40 mg w 0: 2: and 40/20 mg or 20/10 mg eow	188	RCT	NR	52 weeks	Safety: efficacy: & immunogenicity	8[a]
Sandborn *et al.*: 2007a	CD	ADA: sc 20: 40: 80: or 160 mg w 0 and 2: 40 mg qw or eow	276	RCT	Multicenter International	56 weeks	Safety: CDAI remission: & immunogenicity	4[b]
Bodini *et al.*: 2014 (CA)	CD	ADA: NR	23	Prospective cohort study	Single center	104 weeks	Efficacy: pharmacokinetics: & immunogenicity	7[a]
Imaeda *et al.*: 2014	CD	ADA: sc 40 mg eow	40	Prospective cohort study	Single center	NR	Efficacy & immunogenicity	16[c]
Karmiris *et al.*: 2009 Baert *et al.*: 2014	CD	ADA: sc 160/80 or 80/40 mg w 0 and 2 or 40 mg w 2 and 40 mg qw or eow	209	Prospective cohort study	Single center	NR	Safety: efficacy: dose escalation: discontinuation: & immunogenicity	18[c] 17[c]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Johnston *et al.*: 2015 (CA)	CD	ADA: NR	90	Prospective cohort study	Multicenter	NR	Immunogenicity	5[a]
Ward *et al.*: 2015b (CA)	CD	ADA: NR	80	Prospective cohort study	Multicenter	NR	Immunogenicity	6[a]
vande Casteele *et al.*: 2015 (CA)	CD	ADA: sc: 160 mg: w 0: 80 mg w 2: 40 mg every 4 wks	23	Prospective cohort study	Single center	12 weeks	Safety: efficacy: & immunogenicity	5[a]
Zittan *et al.*: 2015 (CA)	CD	ADA: NR	91	Prospective cohort study	NR	NR	Safety: efficacy: pharmacokinetics: & immunogenicity	6[a]
West *et al.*: 2008	CD	ADA: sc 160 mg w 0: 80 mg w 2: and 40 mg eow	30	Retrospective cohort study	Multicenter	NR	Efficacy	16[c]
Awni *et al.*: 2013 (CA)	UC	ADA: sc 160 or 80 mg w 0: 2: and then 40 mg qw or eow	360	RCT	NR	52 weeks	Pharmacokinetics & immunogenicity	8[a]
Sandborn *et al.*: 2012b	UC	ADA: sc 160 mg w 0: 80 mg w 2: then 40 mg eow	518	RCT	Multicenter International	52 weeks	Safety: efficacy: pharmacokinetics: & immunogenicity	3[b]
Suzuki *et al.*: 2014	UC	ADA: sc 160/80 mg or 80/40 mg w 0: 2 and 40 mg at wk then eow	343	RCT	Multicenter	52 weeks	Safety & efficacy	4[b]
Ben-Bassat *et al.*: 2013a (CA)	CD or UC cohort	ADA: sc 40 mg qw: 40 mg eow or 80 mg eow	57	Prospective cohort study	NR	NR	Safety: efficacy: & immunogenicity	7[a]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Roblin *et al.*: 2014a	CD or UC cohort	ADA: NR	40	Prospective cohort study	Single center	NR	Efficacy: pharmacokinetics: & immunogenicity	17[c]
Roblin *et al.*: 2014b	CD or UC cohort	ADA: sc 40 mg eow: then INF 5 mg/kg w 0: 2: 6: and every 8 wks (non-responders)	180	Prospective cohort study	Single center	NR	Efficacy: pharmacokinetics: & immunogenicity	18[c]
Steenholdt *et al.*: 2015 (CA)	CD or UC cohort	ADA: NR	72	Prospective cohort study	Single center	NR	Efficacy and immunogenicity	6[a]
Velayos *et al.*: 2013 (CA)	CD or UC cohort	ADA: NR	54	Prospective cohort study	Single center	NR	Efficacy: pharmacokinetics: & immunogenicity	1[a]
Yarur *et al.*: 2013 (CA)	CD or UC cohort	ADA: NR	66	Prospective cohort study	NR	NR	Pharmacokinetics & immunogenicity	7[a]
Sandborn *et al.*: 2011a	CD	CZP: sc 400 mg w 0: 2: and 4	439	RCT	Multicenter International	6 weeks	CDAI responders & immunogenicity	3[b]
Schreiber *et al.*: 2005	CD	CZP: sc 100: 200 or 400 mg w 0: 4: and 8	372	RCT	Multicenter International	12 weeks	Safety: efficacy: & CDAI responders	4[b]
Schreiber *et al.*: 2007 Sandborn *et al.*: 2007b	CD	CZP: sc 400 mg w 0: 2: 4: and every 4 wk	PRECISE 1: 976 PRECISE 2: 930	RCT	Multicenter International	80 weeks	Safety: efficacy: CDAI responders: & immunogenicity	4[b]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Lichtenstein *et al.*: 2010 Sandborn *et al.*: 2011b								
Stefan *et al.*: 2014 (CA)	CD	CZP: sc 400 mg w 0: 2: 4: and every 4 wk	594	RCT & LTE	Multicenter International	364 weeks	Safety & efficacy	4[b]
Sandborn *et al.*: 2014b	UC	GLM: sc 100/50 mg or 200/100 mg or 400/200 mg w 0 and 2	1064	RCT	Multicenter International	6 weeks	Safety: efficacy: & immunogenicity	3[b]
Sandborn *et al.*: 2014a	UC	RCT: GLM: sc 50 or 100 mg every 4 wks nRCT: GLM: sc 100 mg every 4 wks	ALL: 1:228 RCT: 464 nRCT: 764	RCT & nRCT	Multicenter International	54 weeks	Safety: efficacy: & immunogenicity	3[b]
Feagan *et al.*: 2014	CD	INF: i.v. 5 mg/kg w 1: 3: 7: 14: 22: 30: 38: and 46 INF plus MTX (10–25 mg/wk): 5 mg/kg w 1: 3: 7: 14: 22: 30: 38: and 46	132	RCT	Multicenter	50 weeks	Safety: efficacy: & immunogenicity	5[b]
Hanauer *et al.*: 2004	CD	INF: i.v. 5 mg/kg w 2 and 6 and every 8 wks INF: i.v. 5 mg/kg w 2 and 6 and 10 mg/kg every 8 wks	580	RCT	Multicenter International	72 weeks	Safety: efficacy: discontinuation: & immunogenicity	4[b]
Hyams *et al.*: 2007	CD	INF: i.v. 5 mg/kg w 0: 2: 6: and every 8 or 12 wks from wk 14	112	RCT	Multicenter International	54 weeks	Safety & immunogenicity	3[b]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Sands *et al.*: 2004	CD	INF: i.v. 5 mg/kg w 0: 2: 6: and every 8 wks	306	RCT	Multicenter International	54 weeks	Safety: efficacy: & immunogenicity	3[b]
Steenholdt *et al.*: 2014a Steenholdt *et al.*: 2013 Steenholdt *et al.*: 2014b	CD	INF: i.v. 5 mg/kg every 4 wks: then ADA: sc 80 mg w 0 and then 40 mg eow	69	RCT	Multicenter	12 weeks	Safety: efficacy: cost analysis: & immunogenicity	2[b]
van Assche *et al.*: 2008	CD	INF plus IS (continued IS (AZA: 2-2.5 mg/kg: 6-MP: 1–1.25 mg/kg: MTX: 15 mg/wk)): i.v. 5 mg/kg every 8 wks INF plus IS (discontinued IS): i.v. 5 mg/kg every 8 wks	80	RCT	Multicenter	104 weeks	Safety: efficacy: pharmacokinetics: & immunogenicity	2[b]
Colombel *et al.*: 2010	CD	INF: i.v. 5- mg/kg w 0: 2: 6: and every 8 wks INF plus AZA (2.5 mg/kg): i.v. 5- mg/kg w 0: 2: 6: and every 8 wks	817	RCT & LTE	Multicenter	50 weeks	Efficacy: CDAI remission: & immunogenicity	4[b]
Baert *et al.*: 2003 Magdelaine-Beuzelin *et al.*: 2009	CD	INF: i.v. 5 mg/kg w 0: 2: and 6	125	Prospective cohort study	NR	NR	Safety: pharmacokinetics: & immunogenicity	15[c]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Ben-Bassat *et al.*: 2013b (CA)	CD	INF: i.v. 5 mg/kg NR	234	Prospective cohort study	NR	NR	Efficacy: pharmacokinetics: & immunogenicity	6[a]
Echarri *et al.*: 2015 (CA)	CD	INF: NR	36	Prospective cohort study	NR	NR	Efficacy and immunogenicity	6[a]
Farrell *et al.*: 2003	CD	INF: i.v. 5 mg/kg w 0: 2: and 6 and NR	53	Prospective cohort study	NR	16 weeks	Safety: efficacy: & immunogenicity	15[c]
Imaeda *et al.*: 2012	CD	INF: i.v. 5 mg/kg every 6-8 wks	58	Prospective cohort study	Single center	NR	Immunogenicity	16[c]
Lazebnik *et al.*: 2011 (CA)	CD	INF: i.v. 5 mg/kg w 0: 2: 6: and every 8 wks	15	Prospective cohort study	Single center	52 weeks	Efficacy & immunogenicity	9[a]
Levesque *et al.*: 2014	CD	INF: i.v. ≤5 mg/kg w 0 and 8	327	Prospective cohort study	Multicenter	8 weeks	Efficacy: pharmacokinetics: & immunogenicity	16[c]
Maser *et al.*: 2006	CD	INF: i.v. 5 mg/kg w 0: 2: 6: and every 6: 7: or 8 wks	105	Prospective cohort study	Single center	NR	Safety: efficacy: endoscopic improvement: & immunogenicity	14[c]
Vermeire *et al.*: 2007	CD	INF: i.v. NR w 0 or w 0: 2: and 6 INF plus IS (AZA: 2–2.5 mg/kg: 6-MP: 1–1.25 mg/kg: MTX: 15 mg/wk): i.v. NR w 0 or w 0: 2: and 6	174	Prospective cohort study	Multicenter	NR	Safety: efficacy: pharmacokinetics: & immunogenicity	15[c]
Stein *et al.*: 2014 (CA)	CD	INF: NR	82	Prospective cohort study	NR	52 weeks	Safety & efficacy	7[a]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Hukkinen *et al.*: 2014	CD	INF: i.v.: 5 mg/kg: w 0: 2: 6: and the every 8 wks	13	Retrospective cohort study	NR	NR	Safety & efficacy	17[c]
Ainsworth *et al.*: 2008	CD	INF: NR	70	Retrospective cohort study	Single center	8 weeks	Efficacy: pharmacokinetics: & immunogenicity	17[c]
Bortlik *et al.*: 2013	CD	INF: i.v. NR w 0: 2: 6: and every 8 wks	184	Retrospective cohort study	Single center	NR	Efficacy: pharmacokinetics: & immunogenicity	14[c]
Bar-yoseph *et al.*: 2015 (CA)	CD	INF: NR	136	Retrospective cohort study	Multicenter	104 weeks	Efficacy	5[a]
Drobne *et al.*: 2015	CD	INF: NR	533	Retrospective cohort study	Single center	NR	Efficacy & immunogenicity	14[c]
Church *et al.*: 2014	CD	INF: i.v. 5 mg/kg w 0: 2: 6: NR	195	Retrospective chart review	Single center	NR	Efficacy: drug survival: & immunogenicity	17[c]
Rutgeerts *et al.*: 2005 ACT I	UC	INF: i.v. 5 or 10 mg/kg w 0: 2: 6: and every 8 wks	364	RCT	Multicenter International	54 weeks	Safety: Mayo responders: & immunogenicity	4[b]
Rutgeerts *et al.*: 2005 ACT II	UC	INF: i.v. 5 or 10 mg/kg w 0: 2: 6: and every 8 wks	364	RCT	Multicenter International	30 weeks	Safety: Mayo responders: & immunogenicity	4[b]
Brandse *et al.*: 2014 (CA)	UC	INF: i.v. 5 mg/kg w 0: 2: and 6	15	Prospective cohort study	Multicenter	6 weeks	Efficacy & pharmacokinetics	5[a]
Brandse *et al.*: 2015a (CA)	UC	INF: NR	20	Prospective cohort study	NR	NR	Immunogenicity	8[a]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Murthy *et al.*: 2012 (CA)	UC	INF: i.v. 5 mg/kg NR	134	Prospective cohort study	NR	NR	Efficacy: pharmacokinetics: & immunogenicity	4[a]
Seow *et al.*: 2010	UC	INF: i.v. 5 or 10 mg/kg w 0: 2: 6: and then every 6: 7: or 8 wks	115	Prospective cohort study	NR	NR	Efficacy: endoscopic improvement: & mayo responders	18[c]
Ungar *et al.*: 2015 (CA)	UC	INF: NR	28	Prospective cohort study	NR	NR	Immunogenicity	6[a]
Hayes *et al.*: 2014	UC	INF: i.v. 5 mg/kg every 8 wks INF plus IS (NR): i.v. 5 mg/kg every 8 wks	85	Retrospective chart review	Single center	NR	Safety: efficacy: concomitant therapy: & immunogenicity	16[c]
Vande Casteele *et al.*: 2012a (CA)	CD or UC cohort	INF: NR	270	RCT	NR	NR	Dose escalation	6[a]
Cardile *et al.*: 2013 (CA)	CD or UC cohort	INF: NR	15	Prospective cohort study	NR	NR	Immunogenicity & pharmacokinetics	6[a]
Daperno *et al.*: 2013 (CA)	CD or UC cohort	INF: NR	71	Prospective cohort study	NR	NR	Pharmacokinetics & immunogenicity	4[a]
Eser *et al.*: 2013 (CA)	CD or UC cohort	INF: NR	90	Prospective cohort study	NR	NR	Immunogenicity	6[a]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Guidi *et al.*: 2015 (CA)	CD or UC cohort	INF: NR	102	Prospective cohort study	NR	NR	Efficacy	6[a]
Hamalainen *et al.*: 2013	CD or UC cohort	INF: i.v. 5 mg/kg w 0: 2: 6: and every 8 wks	37	Prospective cohort study	Single center	NR	Pharmacokinetics & immunogenicity	16[c]
Kong *et al.*: 2011 (CA)	CD or UC cohort	INF: NR	30	Prospective cohort study	Single center	NR	Efficacy & immunogenicity	6[a]
Leclerc *et al.*: 2014 (CA)	CD or UC cohort	INF: NR	93	Prospective cohort study	NR	NR	Efficacy: pharmacokinetics: & immunogenicity	2[a]
Lowenberg *et al.*: 2014 (CA)	CD or UC cohort	INF: NR	81	Prospective cohort study	NR	NR	Efficacy: HRQoL: & immunogenicity	3[a]
Malickova *et al.*: 2013	CD or UC cohort	INF: i.v. 5 mg/kg w 0: 2: 6: and every 8 wks	30	Prospective cohort study	NR	14 weeks	Biomarkers	10[c]
Martin Arranz *et al.*: 2014 (CA)	CD or UC cohort	INF: NR	126	Prospective cohort study	Single center	NR	Safety: efficacy: & immunogenicity	8[a]
Pallagi-Kunstár *et al.*: 2014	CD or UC cohort	INF: NR	67	Prospective cohort study	Single center	NR	Safety: efficacy: pharmacokinetics: & immunogenicity	14[c]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Paul *et al.*: 2013	CD or UC cohort	INF: i.v. 5 mg/kg every 8 wks then 10 mg/kg every 8 wks	52	Prospective cohort study	Single center	NR	Efficacy: concomitant medication: & immunogenicity	17[c]
Rivera *et al.*: 2014 (CA)	CD or UC cohort	INF: NR	69	Prospective cohort study	NR	NR	Pharmacokinetics & immunogenicity	7[a]
Rosenthal *et al.*: 2012 (CA)	CD or UC cohort	INF: NR	38	Prospective cohort study	NR	NR	Pharmacokinetics & immunogenicity	5[a]
Schatz *et al.*: 2011 (CA)	CD or UC cohort	INF: NR	50	Prospective cohort study	Single center	NR	Efficacy & immunogenicity	7[a]
Ungar *et al.*: 2014	CD or UC cohort	INF: i.v. 5 mg/kg every 8 wks	182	Prospective cohort study	Single center	208 weeks	Efficacy: pharmacokinetics: & immunogenicity	16[c]
Ward *et al.*: 2015a (CA)	CD or UC cohort	INF: NR	79	Prospective cohort study	NR	NR	Immunogenicity	5[a]
Wolf *et al.*: 2013 (CA)	CD or UC cohort	INF: NR	174	Prospective cohort study	Multicenter	NR	Efficacy & immunogenicity	6[a]
Ben-Horin *et al.*: 2015	CD or UC cohort	INF: NR	86	Prospective cohort study	Single center	NR	Pharmacokinetics	15[c]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Geethan *et al.*: 2014 (CA)	CD or UC cohort	INF: NR	38	Prospective cohort study	NR	NR	Efficacy & immunogenicity	7[a]
Hoekman *et al.*: 2015	CD or UC cohort	INF: i.v.: 5 mg/kg: w 0: 2: 6: and the every 8 wks	39	Prospective cohort study	Multicenter	NR	Safety & efficacy	17[c]
Singh *et al.*: 2014	CD or UC cohort	INF: i.v.: 5 mg/kg w 0: 2: and 6	58	Prospective cohort study	Multicenter	54 weeks	Efficacy & pharmacokinetics	18[c]
Warman *et al.*: 2015	CD or UC cohort	INF: i.v.: 5 mg/kg every 8 wks	113	Prospective cohort study	Single center	NR	Efficacy	16[c]
Zitomersky *et al.*: 2015	CD or UC cohort	INF: NR	134	Prospective cohort study	Single center	NR	Efficacy: pharmacokinetics: & immunogenicity	16[c]
Ben-Horin *et al.*: 2010	CD or UC cohort	INF: i.v. 5 mg/kg every 8 wks	62	Prospective observational study	Single center	NR	Efficacy & immunogenicity	14[c]
Billiet *et al.*: 2015 (CA)	CD or UC cohort	INF: NR	201	Retrospective cohort study	NR	NR	Efficacy	6[a]
Brandse *et al.*: 2015b (CA)	CD or UC cohort	INF: NR	324	Retrospective cohort study	Single center	NR	Immunogenicity	7[a]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Cleynen *et al.*: 2015 (CA)	CD or UC cohort	INF: NR	604	Retrospective cohort study	NR	NR	Safety and immunogenicity	6[a]
Dauer *et al.*: 2013 (CA)	CD or UC cohort	INF: NR	17	Retrospective cohort study	Single center	NR	Safety & immunogenicity	5[a]
Marits *et al.*: 2014	CD or UC cohort	INF: NR	79	Retrospective cohort study	NR	NR	Pharmacokinetics & immunogenicity	14[c]
Pariente *et al.*: 2012	CD or UC cohort	INF: i.v. 5 or 10 mg/kg NR	76	Retrospective cohort study	Multicenter	NR	Safety: efficacy: & immunogenicity	22[c]
Steenholdt *et al.*: 2011 Steenholdt *et al.*: 2012b	CD or UC cohort	INF: NR	106	Retrospective cohort study	Single center	NR	Pharmacokinetics & immunogenicity	19[c]
Vande Casteele *et al.*: 2012b (CA)	CD or UC cohort	INF: NR	57	Retrospective cohort study	NR	NR	Immunogenicity	
Vande Casteele *et al.*: 2013	CD or UC	INF: i.v. 3 mg/kg w 0: 2: 6: and then 4 infusions within 24 wks	90	Retrospective cohort study	Single center	NR	Efficacy: pharmacokinetics: discontinuation: &	12[c]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
	cohort						immunogenicity	
Yanai *et al.*: 2012 (CA)	CD or UC cohort	INF: NR	104	Retrospective cohort study	Single center	>52 weeks	Efficacy: pharmacokinetics: & immunogenicity	4[a]
Baert *et al.*: 2014	CD or UC cohort	Treatment holiday then INF: i.v.: 5 mg/kg: w 0: 2: and 6 or at w 0	128	Retrospective cohort study	Single center	14 weeks	Efficacy: pharmacokinetics: & immunogenicity	17[c]
Buurman *et al.*: 2015	CD or UC cohort	INF: i.v.: 5 mg/kg: w 0: 2: and 6 then every 8 wks	42	Retrospective cohort study	Single center	54 weeks	Efficacy & immunogenicity	16[c]
Ungar *et al.*: 2015	CD or UC cohort	INF: NR	174	Retrospective cohort study	Single center	NR	Safety: efficacy: & immunogenicity	16[c]
Vande Casteele *et al.*: 2012c (CA)	CD or UC cohort	INF: NR	52	Retrospective case-control study	NR	NR	Safety: efficacy: discontinuation: & immunogenicity	6[a]
Afif *et al.*: 2010	CD or UC cohort	INF: NR	155	Retrospective chart review	Single center	NR	Safety: clinical response: treatment change: & discontinuation	14[c]
Bar-yoseph *et al.*: 2013 (CA)	CD or UC cohort	INF: NR	36	Retrospective chart review	NR	NR	pharmacokinetics & immunogenicity	5[a]
Chauhan *et al.*:	CD or	INF: NR	36	Retrospective	NR	NR	Pharmacokinetics &	5[a]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
2013 (CA)	UC cohort			chart review			immunogenicity	
Miele *et al.*: 2004	CD or UC cohort	INF: i.v. 5 or 10 mg/kg NR	132	Retrospective chart review	NR	NR	Safety & immunogenicity	18[c]
Vahabnezhad *et al.*: 2014	CD or UC cohort	INF: i.v. 5 mg/kg every 7 or 8 wks: then 10 mg/kg or every 6 wks	259	Retrospective chart review	Single center	NR	Safety: efficacy: & immunogenicity	17[c]
Wilson *et al.*: 2013 (CA)	CD or UC cohort	INF: NR	160	Retrospective chart review	Single center	NR	Immunogenicity	1[a]
Garces *et al.*: 2013 (CA)	RA: PsA: AS: & IBD	INF: i.v. 3–5 mg/kg every 6 or 8 wks	84	Prospective cohort study	Single center	>104 weeks	Safety & immunogenicity	6[a]
Sandborn *et al.*: 2012a	CD	UST: i.v. 1: 3: or 4 mg/kg w 0 and sc 90 mg w 8 and 16	526	RCT	Multicenter International	36 weeks	Safety: efficacy: & immunogenicity	4[b]
Sandborn *et al.*: 2013	CD	VDM: i.v.: 300 mg: w 0 and 2: then every 2 or 4 wks	1115	RCT	Multicenter International	52 weeks	Safety and efficacy	5[b]
Sands *et al.*: 2014	CD	VDM: i.v.: 300 mg: w 0: 2: and 6	207	RCT	Multicenter International	10 weeks	Safety and efficacy	5[b]

Author	Disease	Posology	Sample size	Study design	Setting	Study duration	Study outcomes	Quality assessment score
Feagan *et al.*: 2013	UC	VDM: i.v.: 300 mg: w 0 and 2: then every 2 or 4 wks	895	RCT	Multicenter International	52 weeks	Safety and efficacy	5[b]
Parikh *et al.*: 2013	CD or UC cohort	VDM: i.v.: 2 or 6 mg/kg every 8 wks	72	LTE (Phase II)	Multicenter International	78 weeks	Safety: efficacy: pharmacokinetics: and immunogenicity	16[c]
Yanai *et al.*: 2015	CD or UC cohort	ADA: NR INF: NR	247	Retrospective cohort study	Multicenter	NR	Efficacy	18[c]
Frederiksen *et al.*: 2014 (CA) Frederiksen *et al.*: 2014	CD or UC cohort	ADA: NR INF: NR	482	Retrospective cohort study	Single center	NR	Pharmacokinetics & immunogenicity	18[c]
van Schaik *et al.*: 2014 (CA)	CD or UC cohort	ADA: NR INF: NR	217	Retrospective cohort study	Single center	NR	Immunogenicity	6[a]
Szepes *et al.*: 2013 (CA)	PsO & IBD	ADA: NR INF: NR	99	Prospective cohort study	NR	NR	Safety: efficacy: & immunogenicity	2[a]

[a]Quality scoring of randomized and non-randomized studies from conference proceedings based on the modified Downs and Black checklist.

[b]Quality scoring of RCTs based on the Jadad score.

[c]Quality scoring of non-randomized studies based on the Downs and Black checklist.

(CA): conference abstract; 6-MP: mercaptopurine; ABA: abatacept; ADA: adalimumab; AS: ankylosing spondylitis; AZA: azathioprine; CD: Crohn's disease; CZP: certolizumab pegol; eow: every other week; GLM: golimumab; i.v.: intravenous; IBD: inflammatory bowel disease; INF: infliximab; IS: immunosuppressants; LTE: long-term extension; MTX: methotrexate; N/A: not applicable; NR: not reported; nRCT: non-randomized clinical trial; PsA: psoriatic arthritis; PsO: psoriasis; RA: rheumatic arthritis; RCT: randomized clinical trial sc: subcutaneous; UC: ulcerative colitis; VDM: vedolizumab; UST: ustekinumab; w: week; wks: weeks.

Supplementary Table 5. Studies excluded due to low-quality assessment scores.

Full-text observational study excluded for scoring ≤10 points on the Downs and Black tool
Malickova K: Duricova D: Bortlik M: Janatkova I: Zima T: Lukas M. Phosphatidylserine-dependent anti-prothrombin antibodies (aPS/PT) in infliximab-treated patients with inflammatory bowel diseases. Autoimmunity Highlights 2013;4:27–32. Score = 10
Abstracts excluded for scoring ≤2 points on the modified Downs and Black tool
Leclerc M: Marotte H: Paul S: *et al.* Persistence of antibodies to infliximab for more than two months strongly predicts loss of response to infliximab in inflammatory bowel diseases. J Crohns Colitis 2014;8:S226–S227. Score = 2
Szepes Z: Kunstar E: Farkas K: *et al.* Clinical utility of measuring serum TNF alpha level: anti TNF alpha levels and antibody titers in critical situations in inflammatory bowel disease and in psoriasis. J Crohns Colitis 2013;7:S118–S119. Score = 2
Velayos FS: Sheibani S: Lockton S: *et al.* Prevalence of antibodies to adalimumab (ATA) and correlation between ATA and low serum drug concentration on CRP and clinical symptoms in a prospective sample of IBD patients. Gastroenterol 2013;144:S91. Score = 1
Wilson C: Huffman S: McGoogan K. Common factors among children who developed antibodies to infliximab. Inflamm Bowel Dis 2013;19:S98. Score = 1

Supplementary Table 6. Factors influencing the formation and detection of ADAbs.[1–3]

Treatment-related factors influencing the formation of ADAbs
Structure of biologic agent
Treatment duration
Route of administration
Concomitant medications (e.g. immunosuppressive agents)
Patient-related factors influencing the formation of ADAbs
Age, gender
Disease status
Genetic factors
Prior exposure to biologics
Immunocompetence
Factors influencing the detection of ADAbs
Assay technique
Timing of sampling relative to drug exposure

ADAbs: anti-drug antibodies.

Supplementary Table 7. ADAbs to infliximab and study outcomes.

Dichotomous efficacy outcomes						
Author	**Disease**	**Study design (number of patients assessed)**	**Study outcomes**	**Patients with ADAbs[a]** ***n*** **(%)**	**Patients without ADAbs[b]** ***n*** **(%)**	***p*** **value**
Hanauer *et al.*, 2004[4]	CD	RCT (514)	Episodic: 54 wks: CDAI improvement CDAI remission	 6 (67) 3 (33)	 25 (59) 16 (36)	 - -
Sands *et al.*, 2004[5]	CD	RCT (258)	CDAI responders	14 (32)	25 (31)	-
Colombel *et al.*, 2010[6]	CD	RCT & LTE (219)	Steroid-free remission (26 wks) Steroid-free remission (50 wks)	9 (56.3) 8 (57.1)	12 (66.7) 12 (70.6)	- -
Farrell *et al.*,	CD	Prospective cohort	Continuous responders	0 (0)	21 (61.8)	-

2003[7]		study (53)	Past responders Partial responders Non-responders	11 (57.9) 2 (10.5) 6 (31.6)	4 (11.8) 6 (17.6) 3 (8.8)	- - -
Maser *et al.*, 2006[8]	CD	Prospective cohort study (105)	Endoscopic improvement ADAbs status and undetectable IFX: HBI remission	NR (25) NR (66)	NR (7) NR (67)	$p = 0.43$ $p = 0.62$
Church *et al.*, 2014[9]	CD	Retrospective chart review (195)	Secondary non-responders Partial non-responders	15 (88.2) 2 (11.8)	NR NR	- -
Hukkinen *et al.*, 2014[10]	CD	Retrospective cohort study (13)	Responders	2 (50)	NR	-
Rutgeerts *et al.*, 2005[11] (ACT I)	UC	RCT (229)	Mayo responders	3 (21.4)	3 (8.3)	-
Rutgeerts *et al.*,	UC	RCT (188)	Mayo responders	11 (57.9)	45 (57.0)	-

2005[11] (ACT II)						
Brandse *et al.*, 2015[12] (CA)	UC	Prospective cohort study (20)	Mayo responders	1 (14.3)	10 (50)	
Seow *et al.*, 2010[13]	UC	Prospective cohort study (108)	Mayo responders Endoscopic improvement Colectomy	6 (14) 11 (25) 23 (52)	4 (18) 8 (35) 13 (59)	$p = 0.95$ $p = 0.61$ $p = 0.78$
Hamalainen *et al.*, 2013[14]	CD or UC cohort	Prospective cohort study (28)	IFX poor responders IFX loss of response IFX good responders	1 (20) 2 (40) 1 (20)	NR NR NR	- - -
Kong *et al.*, 2011[15] (CA)	CD or UC cohort	Prospective cohort study (30)	Responders Partial/non-responders	2 (33.3) 4 (66.7)	NR NR	- -
Pallagi-Kunstar *et al.*, 2014[16]	CD or UC cohort	Prospective cohort study (67)	Loss of response	5 (35.7)	NR	-

Rosenthal *et al.*, 2012[17] (CA)	CD or UC cohort	Prospective cohort study (38)	ADAbs prevalence (non-resp.) ADAbs prevalence (resp.: 14 wks) ADAbs prevalence (resp.: 54 wks)	2 (50) 3 (8.8) 7 (20.6)	NR NR NR	- - -
Ungar *et al.*, 2014[18]	CD or UC cohort	Prospective cohort study (125)	Resp. (52 wks: high ADAbs titers) Resp. (104 wks: high ADAbs titers) Resp. (156 wks: high ADAbs titers) Resp. (204 wks: high ADAbs titers)	NR (40.2) NR (30.2) NR (23.1) -	NR (67.5) NR (67.5) NR (67.5) NR (67.5)	- - - -
Hoekman *et al.*, 2015[19]	CD or UC cohort	Prospective cohort study (39)	Clinical remission	2 (50)	NR	-

Schatz *et al.*, 2011[20] (CA)	CD or UC cohort	Retrospective cohort study (50)	Loss of response	10 (52.6)	6 (NR)	-
Pariente *et al.*, 2012[21]	CD or UC cohort	Retrospective cohort study (76)	HBI/SCCAI responders to dose escalation	6 (60)	21 (72)	-
Vande Casteele *et al.*, 2013[22]	CD or UC cohort	Retrospective cohort study (90)	Loss of response Loss of response (persistent) Loss of response (transient) Loss of response & IFX plus IS Loss of response & IFX plus IS (persis.) Loss of response & IFX plus IS (trans.)	43 (81) 30 (78) 13 (87) 12 (28) 10 (26) 2 (13)	17 (50) 17 (50) 17 (50) 6 (35) 6 (35) 6 (35)	- $p = 0.004$ $p = 0.012$ - NS NS
Yanai *et al.*,	CD or	Retrospective cohort	Remission	3 (50)	NR	-

2014[23] (CA)	UC cohort	study (NR)				
Vahabnezhad *et al.*, 2014[24]	CD or UC cohort	Retrospective chart review (40)	Recaptured responders: ADAbs prevalence (CD) ADAbs prevalence (UC) Non-recaptured responders: ADAbs prevalence (CD) ADAbs prevalence (UC)	 5 (22) 0 (0) 11 (73) 1 (50)	 NR NR NR NR	 - - - -
Continuous efficacy outcomes						
Author	**Disease**	**Study design (number of patients assessed)**	**Study outcomes**	**Patients with ADAbs** ***n***	**Patients without ADAbs** ***n***	***p* value**

Imaeda *et al.*, 2012[25]	CD	Prospective cohort study (58)	CDAI score	206	94	$p < 0.001$
Bortlik *et al.*, 2013[26]	CD	Retrospective cohort study (84)	Treatment failure: HR	4.34	0.39	-
Ungar *et al.*, 2014[18]	CD or UC cohort	Prospective cohort study (125)	ADAbs and loss of response: r	0.62	-	$p < 0.001$
Discontinuation of therapy						
Author	**Disease**	**Study design (number of patients assessed)**	**Study outcomes**	**Patients with ADAbs *n* (%)**	**Patients without ADAbs *n* (%)**	***p* value**
Hanauer *et al.*, 2004[4]	CD	RCT (514)	Discontinuation	5 (6)	7 (2)	-
Maser *et al.*,	CD	Prospective cohort	Discontinuation	4 (18.2)	10 (38.5)	-

2006[8]		study (105)				
Hayes *et al.*, 2014[27]	UC	Retrospective chart review (37)	Discontinuation	6 (100)	NR	-
Hamalainen *et al.*, 2013 [14]	CD or UC cohort	Prospective cohort study (28)	Discontinuation	1 (20)	NR	-
Vande Casteele *et al.*, 2013[22]	CD or UC cohort	Retrospective cohort study (90)	Discontinuation: Sust. loss of resp/hypersensitivity Trans loss of resp/hypersensitivity Sust. vs. Trans.: RR	 26 (68) 2 (13) 5.1	 NR NR -	 - - $p = 0.0005$
Vande Castelle *et al.*, 2012[28] (CA)	CD or UC cohort	Retrospective case-control study (52)	Discontinuation (sust.) Discontinuation (trans.)	5 (14) 10 (68)	- -	- -
Afif *et al.*, 2010[29]	CD or UC cohort	Retrospective chart review (149)	Discontinuation	6 (17)	NR	-

[a]For dichotomous outcomes, the number and percentage of ADAbs-positive patients are shown as a proportion of the total number of patients with ADAbs-positive findings.

[b]The number and percentage of ADAbs-negative patients are shown as a proportion of the total number of patients with ADAbs-negative findings.

ADAbs: anti-drug antibodies; CA: conference abstract; CD: Crohn's disease; CDAI: CD activity index; HR: hazard ratio; IFX: infliximab; IS: immunosuppressant; LTE: long-term extension; N: number of patients; NR: not reported; persis.: persistent resp; r: correlation coefficient; RCT: randomized controlled trial; resp: response; RR: relative risk; sust: sustained; trans: transient; UC: ulcerative colitis; wks: weeks.

Supplementary Table 8. ADAbs to adalimumab and study outcomes.

Dichotomous efficacy outcomes						
Author	**Disease**	**Study design (number of patients assessed)**	**Study outcomes**	**Patients with ADAbs[a]** ***n*** **(%)**	**Patients without ADAbs[b]** ***n*** **(%)**	***p*** **value**
Eckert *et al.*, 2013[30]	CD	RCT (182)	Resp. or Remission (Wk 26) Remission (Wk 52)	2 (33.3) 1 (16.7)	NR NR	- -
Sandborn *et al.*, 2007[31]	CD	RCT (269)	CDAI remission (24 wks) CDAI remission (56 wks)	3 (43) 2 (29)	NR NR	- -
Vande Casteele *et al.*, 2015[32] (CA)	CD	Prospective cohort study (23)	Clinical remission	1 (100)	NR	-

West *et al.*, 2008[33]	CD	Retrospective cohort study (25)	Responders	1 (20.0)	NR (90.0)	-
Roblin *et al.*, 2014[34]	CD or UC cohort	Single-arm study (40)	Mucosal healing CDAI remission	1 (11.1) 1 (11.1)	NR NR	- -
Continuous efficacy outcomes						
Author	**Disease**	**Study design (number of patients assessed)**	**Study outcomes**	**Patients with ADAbs** ***n***	**Patients without ADAbs** ***n***	***p* value**
Bodini *et al.*, 2014[35] (CA)	CD	Prospective cohort study (23)	HBI: score	10	5	$p < 0.0001$
Zittan *et al.*, 2015[36] (CA)	CD	Prospective cohort study (91)	CRP: mg/dL	7.9	13.4	-

Steenholdt *et al.*, 2015[37] (CA)	CD or UC cohort	Prospective cohort study (72)	Loss of response: OR	67	-	$p < 0.0001$
Frederiksen *et al.*, 2014a[38] (CA) Frederiksen *et al.*, 2014b[39]	CD or UC cohort	Retrospective cohort study (142)	Secondary failure: OR	28 (3–248)	-	$p < 0.001$
Discontinuation of therapy						
Author	**Disease**	**Study design** **(number of patients assessed)**	**Study outcomes**	**Patients with ADAbs** ***n* (%)**	**Patients without ADAbs** ***n* (%)**	***p* value**
Karmiris *et al.*, 2009[40] Baert *et al.*,	CD	Prospective cohort study (148)	Discontinuation	10 (83.3)	NR	-

2014[41]						

[a]For dichotomous outcomes, the number and percentage of ADAbs-positive patients are shown as a proportion of the total number of patients with ADAbs-positive findings.

[b]The number and percentage of ADAbs-negative patients are shown as a proportion of the total number of patients with ADAbs-negative findings.

ADAbs: anti-drug antibodies; ADM: adalimumab; CA: conference abstract; CD: Crohn's disease; CDAI: CD Activity Index; conc.: concentration; CRP: C-reactive protein; detect.: detectable; HBI: Harvey Bradshaw Index; HR: hazard ratio; IS: immunosuppressant; LTE: long-term extension; N: number of patients; NR: not reported; OR: odds ratio; persis.: persistent resp; r: correlation coefficient; RCT: randomized controlled trial; resp: response; RR: relative risk; sust: sustained; trans: transient; UC: ulcerative colitis; undetect.: undetectable; wks: weeks.

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