Supplementary Online Content

Mason KJ, Barker J, Smith CH, et al. Comparison of drug discontinuation, effectiveness, and safety between clinical trial eligible and ineligible patients in BADBIR [published online March 28, 2018]. *JAMA Derm*. doi:10.1001/jamadermatol.2018.0183

This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary Materials

Figure S1 Flowchart of included patients

There were 8533 registrations to the biologic cohort of BADBIR up to 1st December, 2016; 7408 (87%) of those registrations had completed at least one follow-up visit after baseline with 1509 (18%) registering on etanercept, 4000 (47%) registering on adalimumab and 1627 (19%) registering on ustekinumab.

Figure S1 Flowchart of included patients

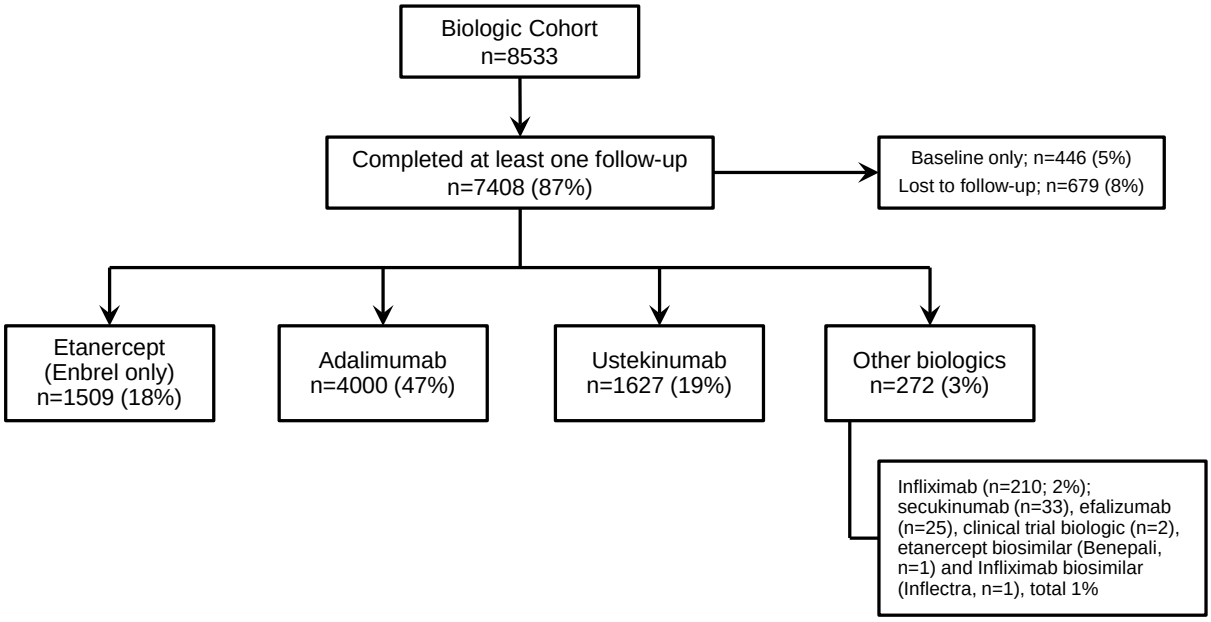

Table S1 **Data extracted from licensing trial manuscripts**

		Etanercept			Adalimumab		Ustekinumab	
	Criteria	Leonardi et al.[5]	Papp et al.[6]	Tyring et al.[7]	Gordon et al.[8]	Menter et al. [9]	Leonardi et al.[10]	Papp et al. [11]
	Clinical Trials ID	---	20021642 †	20030117 †	NCT00235820	NCT00237887	NCT00267969	NCT00307437
Inclusions	Age≥18 years	✓	✓	✓	✓	✓	✓	✓
	Chronic plaque diagnosis	✓	✓	✓	≥1 year	≥6 months	≥6 months	
	Washout periods	Topical 2 weeks; systemics 4 weeks; biologics not specified			Topical 2 weeks; systemics 4 weeks; biologics 12 weeks; Raptiva 6 weeks		Topical 2 weeks; systemics 4 weeks; IP/biologics 12 weeks or 5 half-lives	
	PASI	≥10	≥10	≥10	---	≥12	≥12	
	BSA	≥10%	≥10%	≥10%	≥5%	≥10%	≥10%	
	PGA	---	---	---	---	Moderate ≥4	---	---
	Prior systemic exposures	≥1 UV / systemic		---	---	---	---	---
Exclusions	Prior biologic exposures	TNFi-antagonists			TNFi-antagonists	TNFi-antagonists		IL-12/23 antagonists
	Comorbidities	---		Psychiatric; suicidal ideation	Demyelinating disease		Severe, progressive, or uncontrolled: renal, hepatic, haematological, gastrointestinal, endocrine, pulmonary, cardiac, neurologic, cerebral, or psychiatric disease	
		Uncontrolled hypertension; MI (past year); demyelinating disease; unstable angina pectoris; uncompensated congestive heart failure; severe pulmonary disease; diabetes mellitus			Gastrointestinal; haematological; significant abnormal laboratory test results; immunocompromised			
	Infections	Antibiotics in past week; infection in past 4 weeks			Untreated latent TB; listeriosis; recent serious local or systemic infection		Untreated latent TB; recent serious local or systemic infection; HIV, Hepatitis B or C	
	Cancer	Previous 5 years **			Ever *		Previous 5 years **	
	Females	Pregnant or breast-feeding females			No contraception		No contraception, pregnant or breast-feeding	
Outcomes	Efficacy (PASI 75) ‡	12 weeks (49%[1]; 49%[2]; 47%[3]) and 24 weeks (59%[1]; 54%[2])			12 (53%), 24 (64%), & 60 (56%) weeks	16 (71%) weeks	12 weeks (66%[6] and 79%[7]) and 28 weeks (71%[6] and 79%[7])	
	Safety (total events)	12 & 24 weeks		12 weeks	12 & 60 weeks	16 weeks	12, 40 & 76 weeks	12, 28 & 52 weeks
Eligibility criteria identified from additional sources (text		Papp et al. (2012) [12] - specimen criteria (NCT00121615; 20040216 †); summarises findings			AbbVie report M02-529	AbbVie report M03-656	clinicaltrials.gov using clinical trials ID	

in red)	from all three studies above and details additional eligibility criteria.	Specimen criteria (NCT00646191) [13]	

--- = not reported; ✓ = reported as inclusion criterion; ID = identifier; IP = investigational product; PASI = Psoriasis Area and Severity Index; BSA = Body Surface Area; PGA = Physician's Global assessment; UV = ultraviolet; TNFi = tumour necrosis factor inhibitors; IL = interleukin; TB = tuberculosis; † www.amgentrials.com identifier; * "other than successfully treated NMSC or localized carcinoma in situ of the cervix"; ** except treated NMSC; ‡ doses reported are etanercept 50mg weekly, adalimumab 40mg fortnightly and ustekinumab 90mg 12 weekly after loading schedules were complete.

Table S2 Effectiveness outcome measures by biologic, eligibility and time point

	Etanercept; n=568 (42%)			Adalimumab; n=1437 (39%)			Ustekinumab; n=566 (37%)		
PASI 75, N (%); Chi^2-test †	Eligible n=284	Ineligible n=137	i-PASI n=145	Eligible n=910	Ineligible n=57	i-PASI n=470	Eligible n=284	Ineligible n=137	i-PASI n=145
PASI 75, 6 months	119 (42%)	**30 (22%)**	**12 (8%)**	461 (51%)	**20 (35%)**	**212 (45%)**	159 (56%)	**47 (34%)**	**59 (41%)**
PASI 75, 12 months	130 (46%)	**36 (26%)**	15 (10%)	453 (50%)	23 (40%)	216 (46%)	155 (55%)	**50 (36%)**	**63 (43%)**
PASI 75, 6 & 12 months	83 (29%)	**23 (17%)**	9 (6%)	404 (44%)	18 (32%)	**174 (37%)**	141 (50%)	**41 (30%)**	**53 (37%)**

i-PASI = insufficient baseline Psoriasis Area and Severity Index; † Eligible group vs Ineligible or i-PASI group; $p<0.05$ if bold.

Table S3 Selection Bias in Effectiveness Outcomes

	Complete baseline, 6 & 12 month PASI	Missing 6 month PASI	Missing 12 month PASI	Missing 6 & 12 month PASI	P-value
Etanercept (n=1364)	**568 (42%)**	**263 (19%)**	**238 (17%)**	**295 (22%)**	
Baseline PASI; Mean (±SD) *	15.4 (±7.6)	15.4 (±7.8)	15.9 (±8.7)	16.2 (±7.7)	0.303
Age, years; Mean (±SD) *	45.7 (±12.9)	45.2 (±12.9)	44.9 (±13.8)	45.7 (±13.4)	0.828
Female Sex; n (%) **	228 (40%)	122 (46%)	97 (41%)	136 (46%)	0.192
Adalimumab (n=3667)	**1437 (39%)**	**748 (20%)**	**661 (18%)**	**821 (22%)**	
Baseline PASI; Mean (±SD) *	15.9 (±7.9)	15.3 (±7.5)	15.5 (±7.8)	15.7 (±8.0)	0.518
Age, years; Mean (±SD) *	44.7 (±12.8)	44.8 (±12.5)	44.5 (±12.9)	44.4 (±12.9)	0.785
Female Sex; n (%) **	596 (41%)	316 (42%)	286 (43%)	327 (40%)	0.594
Ustekinumab (n=1518)	**566 (37%)**	**303 (20%)**	**302 (20%)**	**347 (23%)**	
Baseline PASI; Mean (±SD) *	16.0 (±8.0)	16.5 (±7.9)	15.3 (±8.6)	16.6 (±8.5)	**0.033**
Age, years; Mean (±SD) *	46.8 (±13.3)	46.8 (±13.0)	45.5 (±13.3)	46.5 (±13.1)	0.489
Female Sex; n (%) **	217 (38%)	126 (42%)	122 (40%)	127 (37%)	0.564

PASI = Psoriasis Area and Severity Index; * Kruskal-Wallis test; ** Chi2 test; $p<0.05$ in bold.

Table S4 **Incidence rates of serious adverse events by biologic, eligibility and MedDRA System Organ Class**

	Etanercept						Adalimumab						Ustekinumab					
	Eligible		Ineligible		i-PASI		Eligible		Ineligible		i-PASI		Eligible		Ineligible		i-PASI	
MedDRA SOC *	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)	n	IR (95% CI)
All SAEs	42	226 (167, 305)	36	386 (279, 536)	9	249 (130, 479)	131	269 (227, 319)	34	514 (367, 719)	65	271 (213, 346)	40	282 (207, 384)	61	630 (490, 809)	18	237 (149, 375)
Blood	0	---	1	15 (2, 105)	0	---	0	---	0	---	1	5 (1, 34)	0	---	0	---	0	---
Cardiac	3	19 (6, 59)	0	---	1	28 (4, 199)	4	10 (4, 27)	2	56 (14, 224)	3	14 (5, 44)	0	---	1	19 (3, 136)	1	11 (2, 79)
Ear	0	---	0	---	1	28 (4, 199)	1	3 (0, 18)	0	---	0	---	0	---	0	---	0	---
Endocrine	0	---	0	---	0	---	1	3 (0, 18)	0	---	0	---	0	---	0	---	0	---
Eye	1	6 (1, 45)	0	---	0	---	1	3 (0, 18)	0	---	0	---	0	---	0	---	0	---
Gastrointestinal	3	19 (6, 59)	3	44 (14, 138)	1	28 (4, 199)	4	10 (4, 27)	0	---	8	38 (19, 76)	3	26 (8, 79)	4	77 (29, 204)	2	22 (6, 89)
General	0	---	1	15 (2, 105)	0	---	8	20 (10, 40)	0	---	5	24 (10, 57)	1	9 (1, 60)	2	38 (10, 153)	0	---
Hepatic	1	6 (1, 45)	2	30 (7, 118)	0	---	2	5 (1, 20)	0	---	1	5 (1, 34)	0	---	0	---	0	---
Immune	0	---	0	---	0	---	2	5 (1, 20)	0	---	1	5 (1, 34)	0	---	0	---	0	---
Infection	5	32 (13, 76)	4	59 (22, 158)	1	28 (4, 199)	25	63 (43, 94)	0	---	7	33 (16, 70)	2	17 (4, 68)	7	134 (64, 281)	4	45 (17, 119)
Injury	2	13 (3, 51)	0	---	0	---	5	13 (5, 30)	2	56 (14, 224)	1	5 (1, 34)	3	26 (8, 79)	0	---	2	22 (6, 89)
Investigations	0	---	2	30 (7, 118)	1	28 (4, 199)	11	28 (15, 50)	1	28 (4, 199)	9	43 (22, 82)	0	---	6	115 (52, 256)	2	22 (6, 89)
Metabolism	2	13 (3, 51)	0	---	0	---	1	3 (0, 18)	0	---	1	5 (1, 34)	0	---	1	19 (3, 136)	0	---
Musculoskeletal	0	---	1	15 (2, 105)	1	28 (4, 199)	0	---	2	56 (14, 224)	3	14 (5, 44)	3	26 (8, 79)	2	38 (10, 153)	0	---
Neoplasms	2	13 (3, 51)	4	59 (22, 158)	1	28 (4, 199)	6	15 (7, 34)	1	28 (4, 199)	4	19 (7, 51)	4	34 (13, 91)	5	96 (40, 230)	4	45 (17, 119)
Nervous	2	13 (3, 51)	0	---	2	56 (14, 224)	2	5 (1, 20)	1	28 (4, 199)	5	24 (10, 57)	2	17 (4, 68)	1	19 (3, 136)	2	22 (6, 89)

Pregnancy	1	6 (1, 45)	0	---	1	28 (4, 199)	5	13 (5, 30)	0	---	4	19 (7, 51)	1	9 (1, 60)	0	---	1	11 (2, 79)
Psychiatric	0	---	0	---	0	---	3	8 (2, 24)	0	---	3	14 (5, 44)	1	9 (1, 60)	1	19 (3, 136)	0	---
Renal	0	---	1	15 (2, 105)	0	---	3	8 (2, 24)	0	---	1	5 (1, 34)	0	---	0	---	1	11 (2, 79)
Reproductive	0	---	0	---	0	---	2	5 (1, 20)	0	---	1	5 (1, 34)	0	---	0	---	0	---
Respiratory	0	---	0	---	0	---	11	28 (15, 50)	0	---	2	10 (2, 38)	0	---	2	38 (10, 153)	0	---
Skin	2	13 (3, 51)	2	30 (7, 118)	1	28 (4, 199)	13	33 (19, 57)	0	---	6	28 (13, 63)	2	17 (4, 68)	3	57 (19, 178)	1	11 (2, 79)
Social	0	'---	0	---	0	---	1	3 (0, 18)	0	---	0	---	0	---	0	---	0	---
Surgical	8	51 (25, 101)	6	89 (40, 198)	1	28 (4, 199)	20	51 (33, 78)	2	56 (14, 224)	7	33 (16, 70)	6	51 (23, 114)	7	134 (64, 281)	7	78 (37, 164)
Vascular	0	---	1	15 (2, 105)	0	---	0	---	0	---	4	19 (7, 51)	0	---	1	19 (3, 136)	0	---

i-PASI = insufficient baseline Psoriasis Area and Severity Index; n = number of events; IR = incidence rate; CI = confidence interval; MedDRA = Medical Dictionary for Regulatory Activities; SOC = System Organ Class; * no congenital events reported.