UNIVERSITY OF MIAMI

IL-17 Medications for Psoriasis

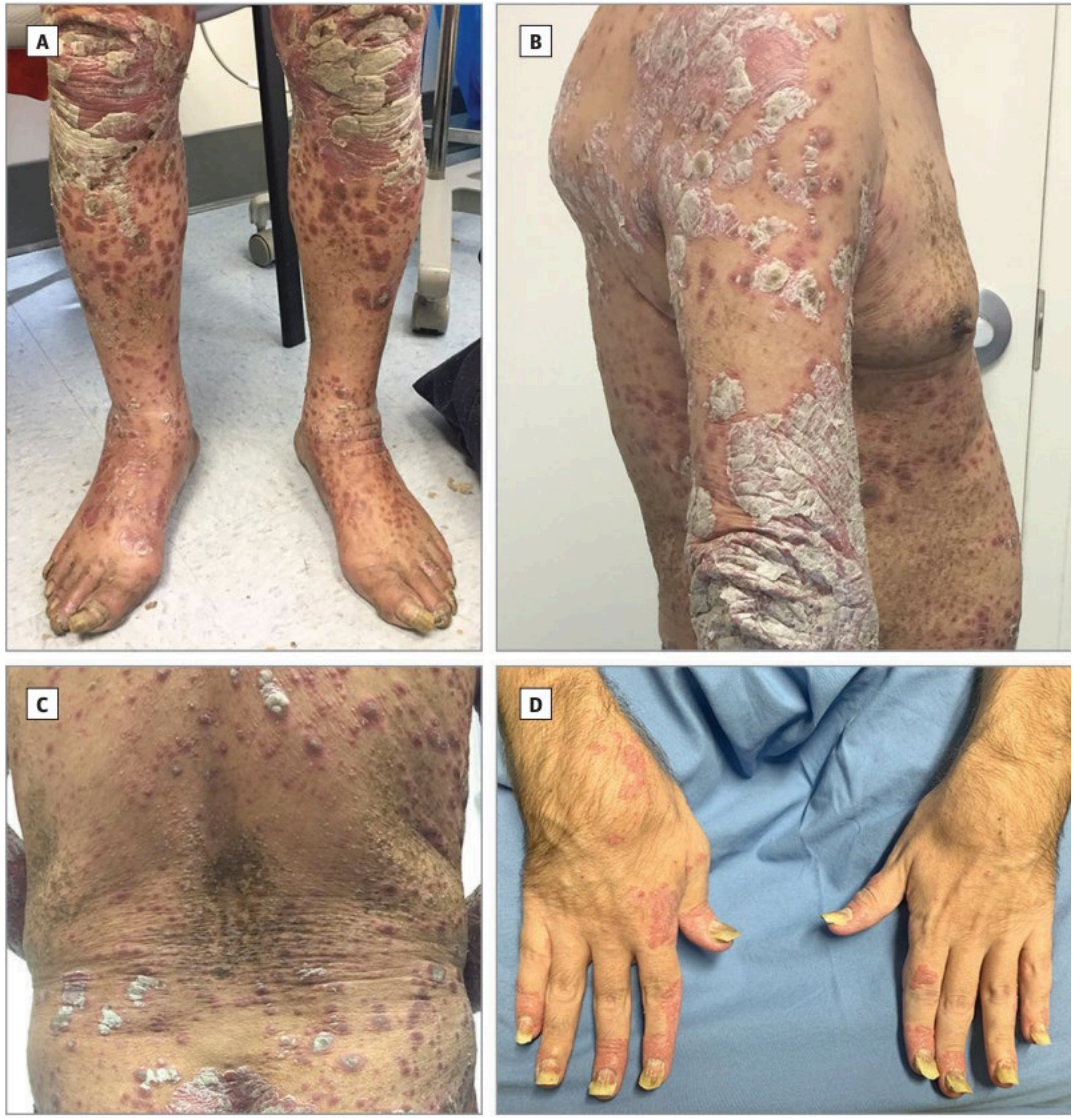
Paolo Romanelli, MD
Professor of Dermatology
Director of ACGME Dermatopathology Fellowship
Director of Psoriasis Clinic at UM/JHS

Review > JAMA. 2020 May 19;323(19):1945-1960. doi: 10.1001/jama.2020.4006.

Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review

April W Armstrong [1], Charlotte Read [1 2]

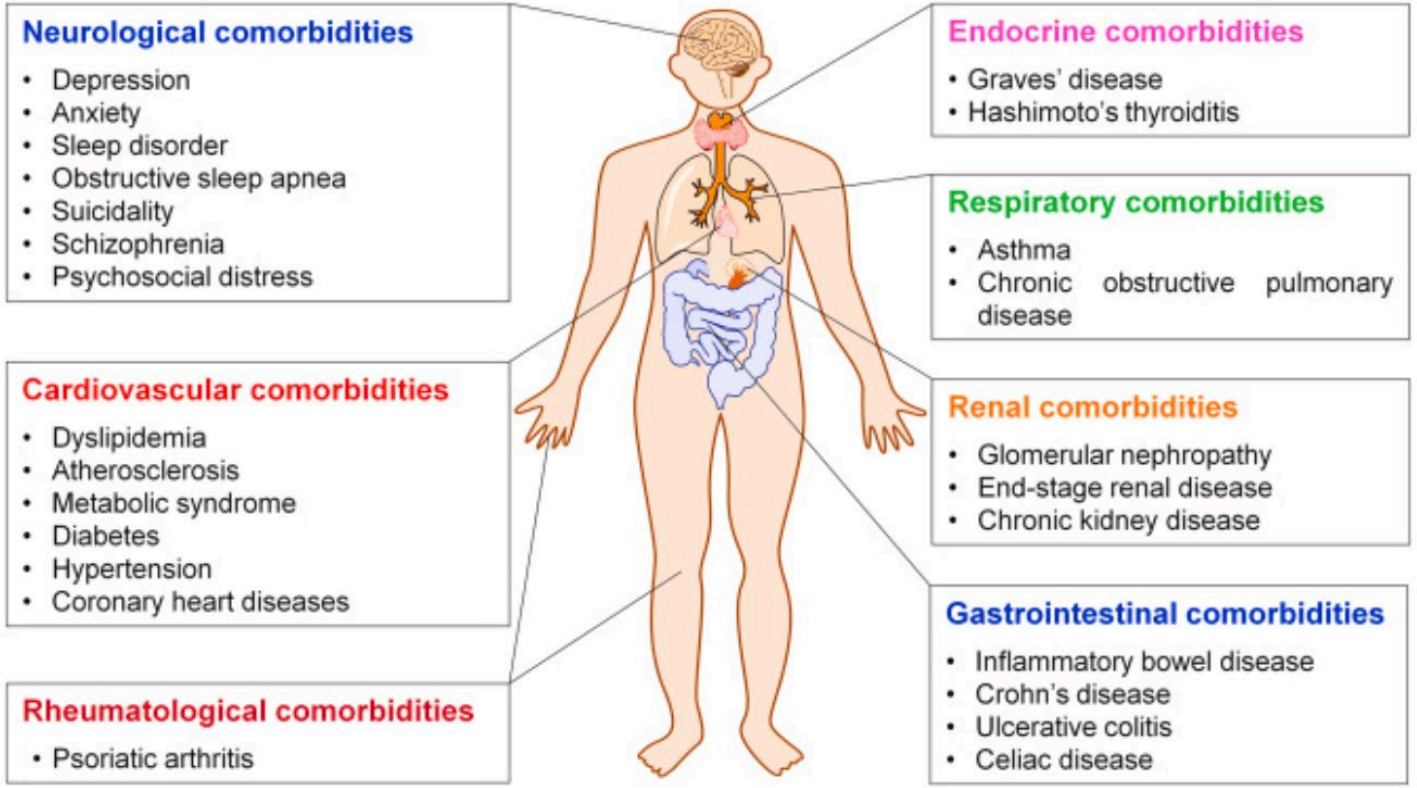
United States prevalence- psoriasis affects approximately 3.2% of adults and 0.13% of children.
US Incidence- approximately 80 new cases per 100,000 person-years.
Worldwide prevalence- approximately 125 million people



Armstrong AW. *et al. JAMA* (2020).

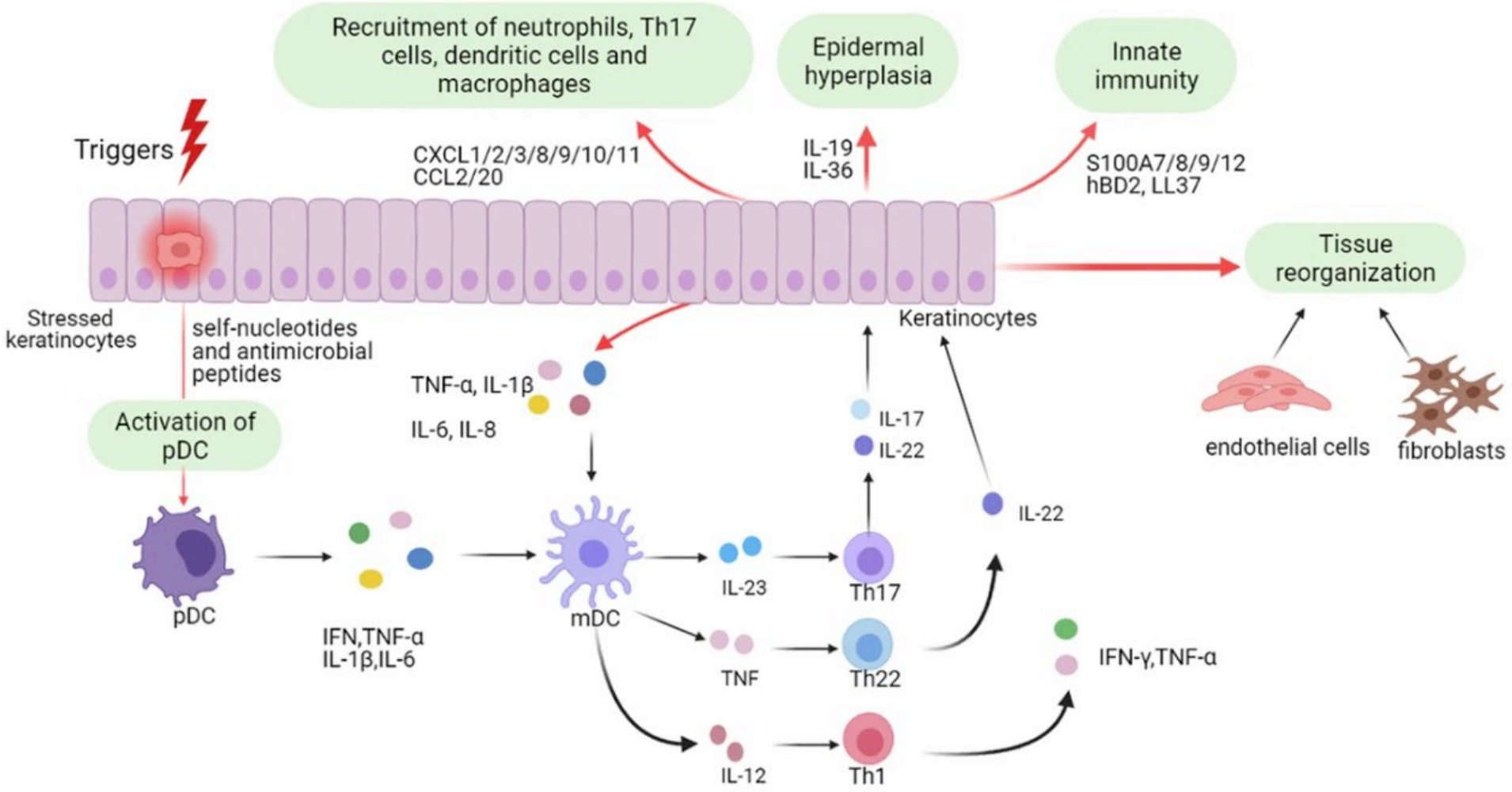
Insights into interplay of immunopathophysiological events and molecular mechanistic cascades in psoriasis and its associated comorbidities

Amit Kumar Srivastava [1], Tara Chand Yadav [1], Harvinder Kour Khera [2], Purusottam Mishra [1], Navdeep Raghuwanshi [3], Vikas Pruthi [1], Ramasare Prasad [4]



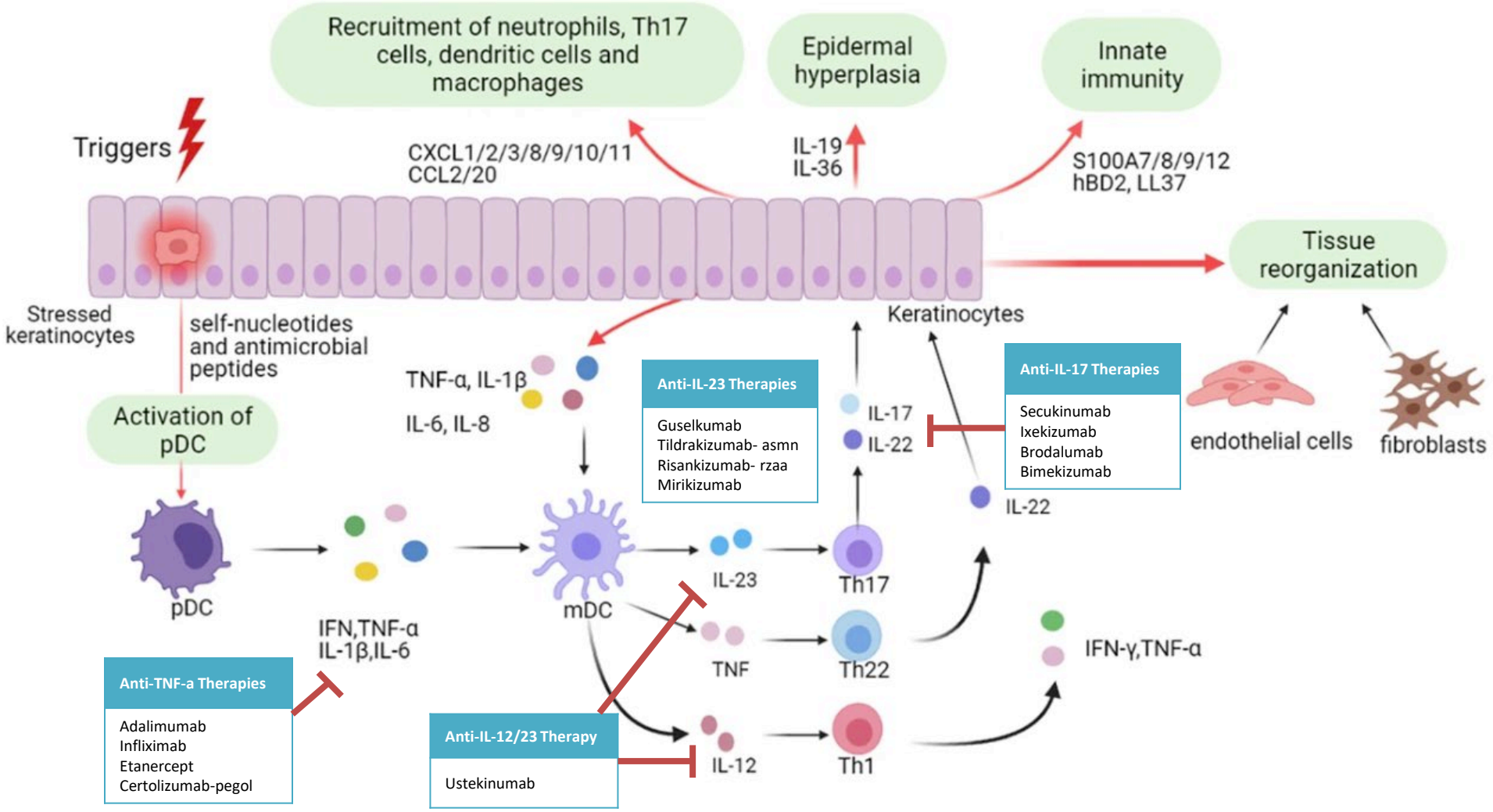
UNIVERSITY OF MIAMI

Srivastava A. *et al. Journal of Autoimmunity* (2021).



Zhou, X. *et al. Cell Death Dis* (2022).

PATHOGENESIS



UNIVERSITY OF MIAMI

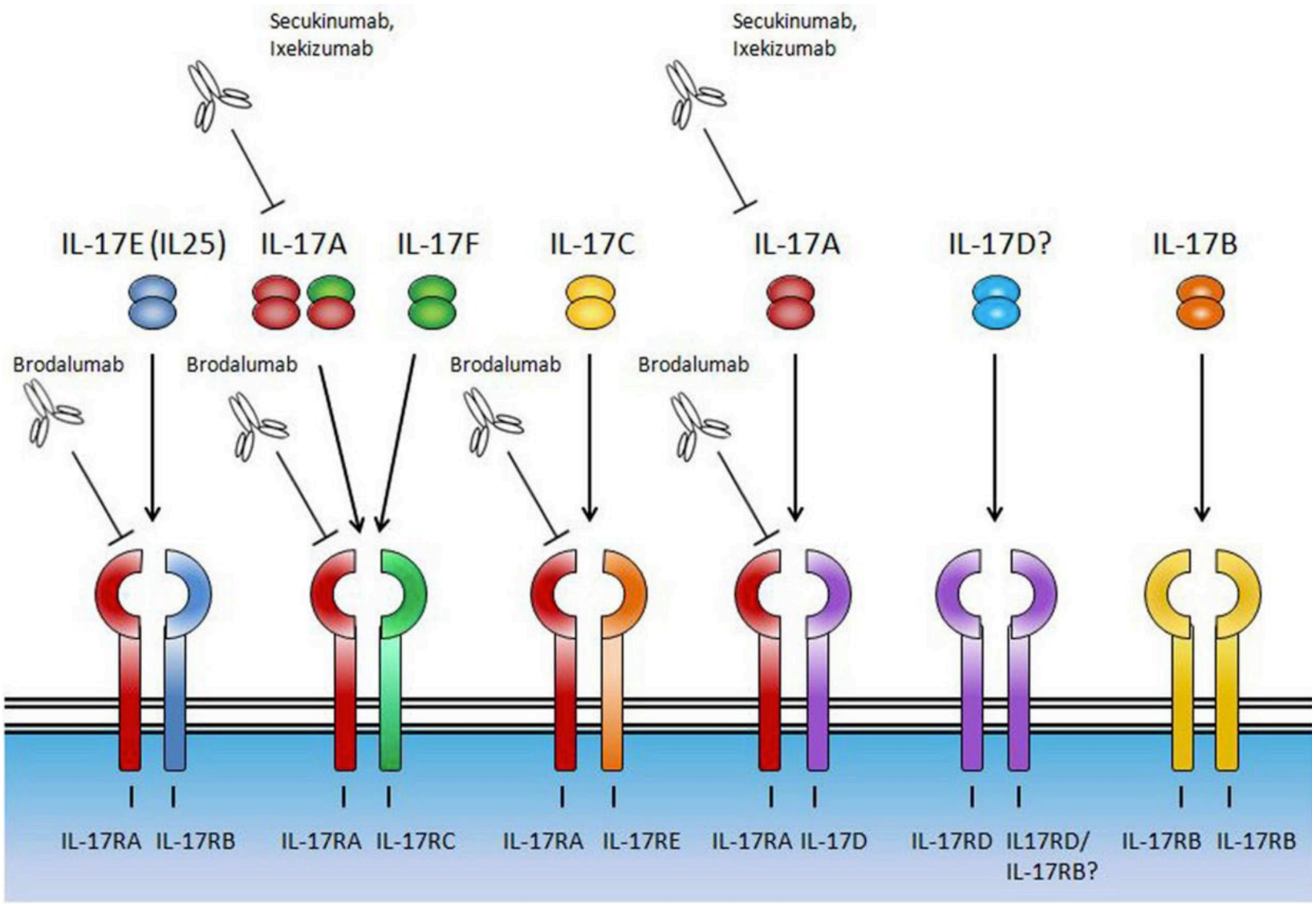
Zhou, X. *et al. Cell Death Dis* (2022).

UNIVERSITY
OF MIAMI

IL-17 Blockers

SECUKINUMAB
IXEKIZUMAB
BRODALUMAB
BIMEKIZUMAB

MECHANISM OF ACTION OF IL-17 INHIBITORS



UNIVERSITY
OF MIAMI

Facheris, P. *et al. Dermatologic Therapy* (2020).

SECUKINUMAB- INDICATIONS

Human IgG1 monoclonal antibody that binds IL-17A

- Adult Chronic Plaque Psoriasis
- Pediatric Chronic Plaque Psoriasis >6 years old
- Psoriatic Arthritis
- Juvenile Psoriatic Arthritis >2 years old
- Ankylosing Spondylitis
- Non-radiographic Axial Spondyloarthritis
- Enthesitis-related Arthritis >4 years old

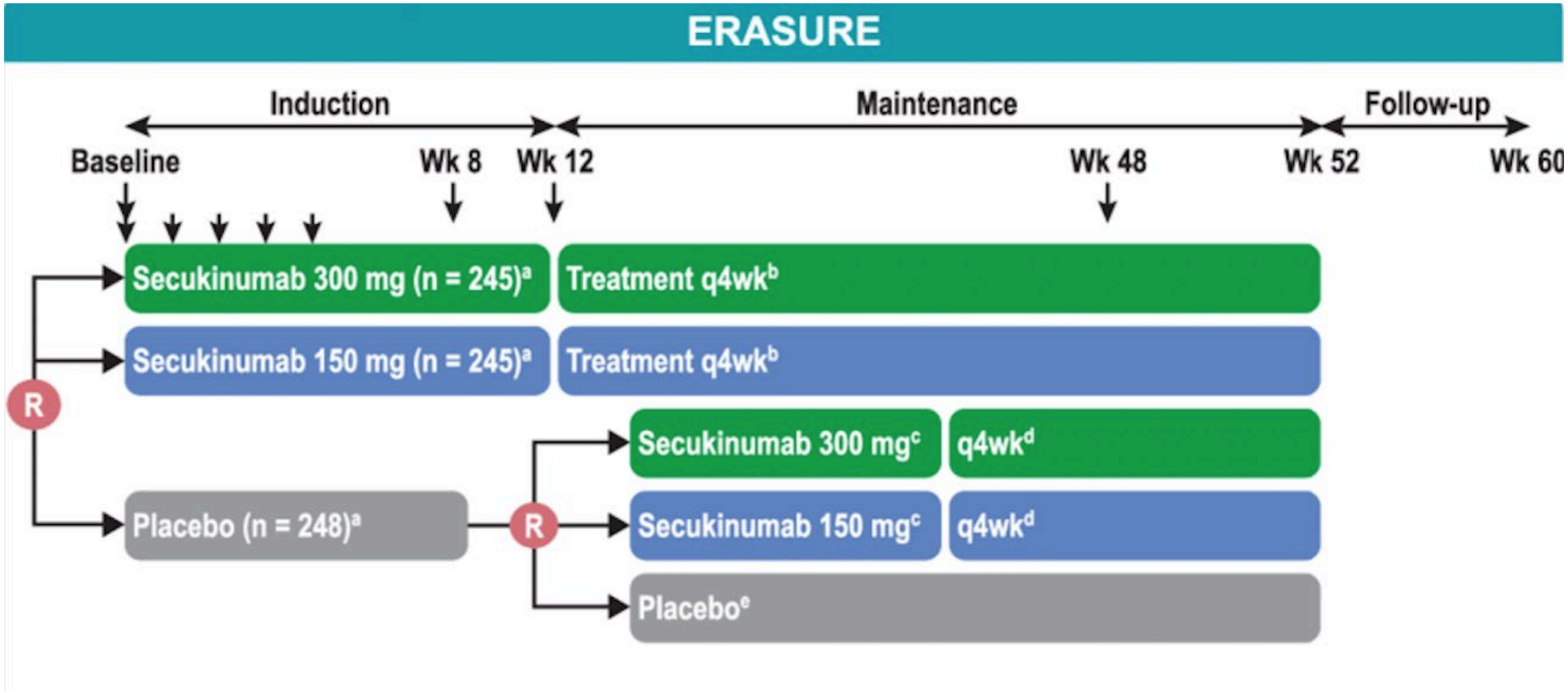
Psoriasis					PsA	AS
GESTURE NCT01806597 N=199 *vs PBO*	FIXTURE NCT01358578 N=936 *vs ETN and PBO*	JUNCTURE NCT01636687 N=177 *vs PBO*	CARIMA NCT02559622 N=150 *vs PBO*	PRIME NCT02474082 N=105 *vs Fumaderm*	FUTURE 1 NCT01392326 N=587 *vs PBO*	MEASURE 1 NCT01358175 N=360 *vs PBO*
TRANSFIGURE NCT01807520 N=190 *vs PBO*	SCULPTURE NCT01406938 N=966 *Fixed regimen vs Re-treatment*	CLEAR NCT02074982 N=335 *vs UST*	PSORITUS NCT02362789 N=130 *vs PBO*	AJP01 NCT02547714 N=34 -	FUTURE 2 NCT01752634 N=387 *vs PBO*	MEASURE 2 NCT01649375 N=211 *vs PBO*
ERASURE NCT01365455 N=702 *vs PBO*	FEATURE NCT01555125 N=174 *vs PBO*	2PRECISE NCT02008890 N=214 *vs PBO*	GAIN NCT02474069 N=772 *Dose optimization*	SCALP NCT02267135 N=97 *vs PBO*	FUTURE 3 NCT01989468 N=406 *vs PBO*	MEASURE 3 NCT02008916 N=223 *vs PBO*

Studies included in the pooled analysis. *ETN* etanercept, *PBO* placebo, *UST* ustekinumab

Gottlieb AB. *et al. Acta Derm Venereol* (2022).

SECUKINUMAB PIVOTAL TRIALS- ERASURE STUDY DESIGN

Phase 3, double-blind, 52-week study comparing Efficacy of Response and Safety of Two Fixed Secukinumab Regimens in Psoriasis



UNIVERSITY OF MIAMI

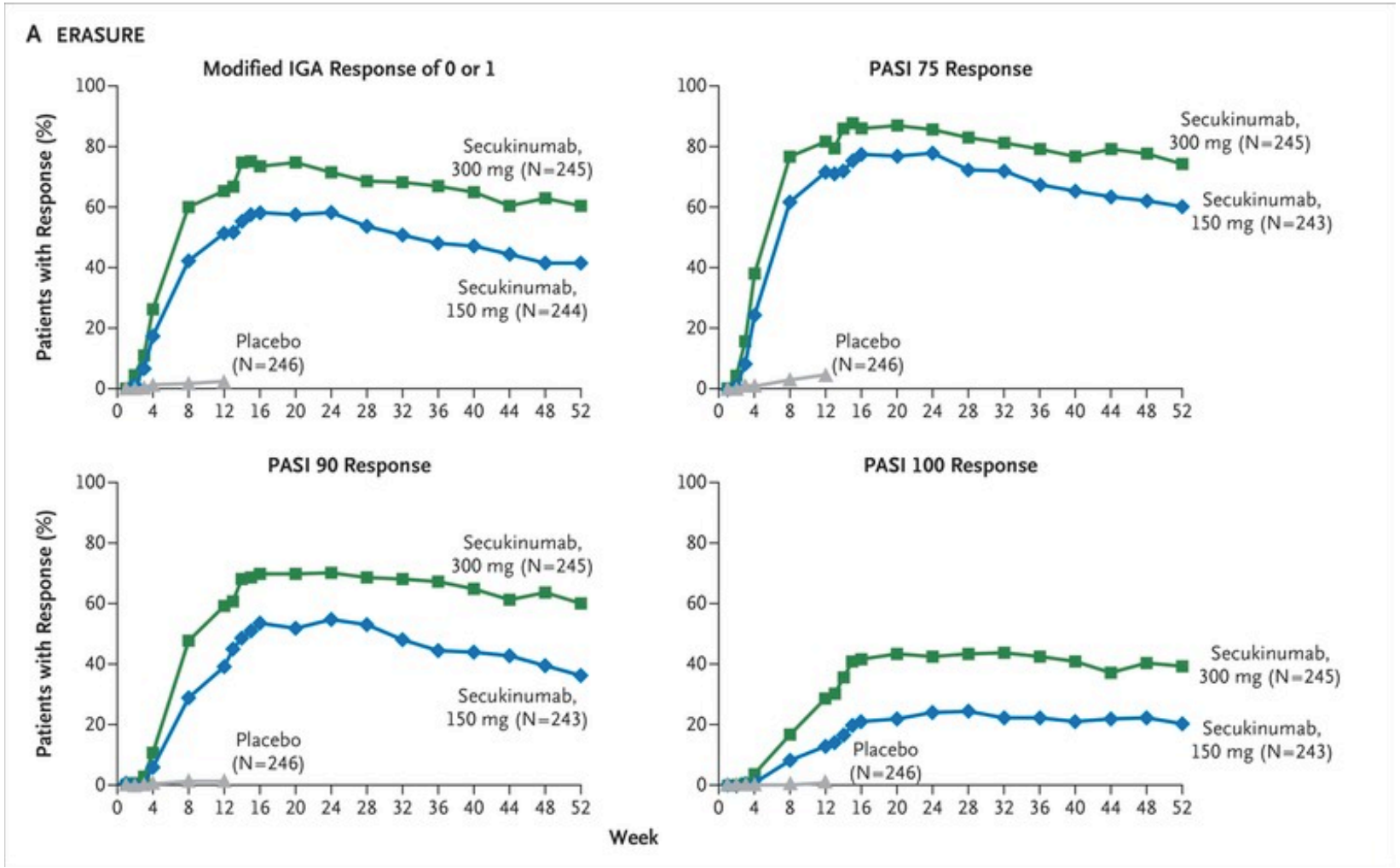
Korman, N. *et al. Journal of Dermatological Treatment (2016).*

SECUKINUMAB- ERASURE RESULTS

Phase 3, double-blind, 52-week study comparing Efficacy of Response and Safety of Two Fixed Secukinumab Regimens in Psoriasis

Secukinumab at the 300-mg and 150-mg doses was shown to be superior to placebo with respect to the key secondary end point of PASI 90 response at week 12 (P<0.001 for both comparisons)

Rates of response on the PASI and the modified IGA increased during week 12 to week 16 and then stabilized after week 16

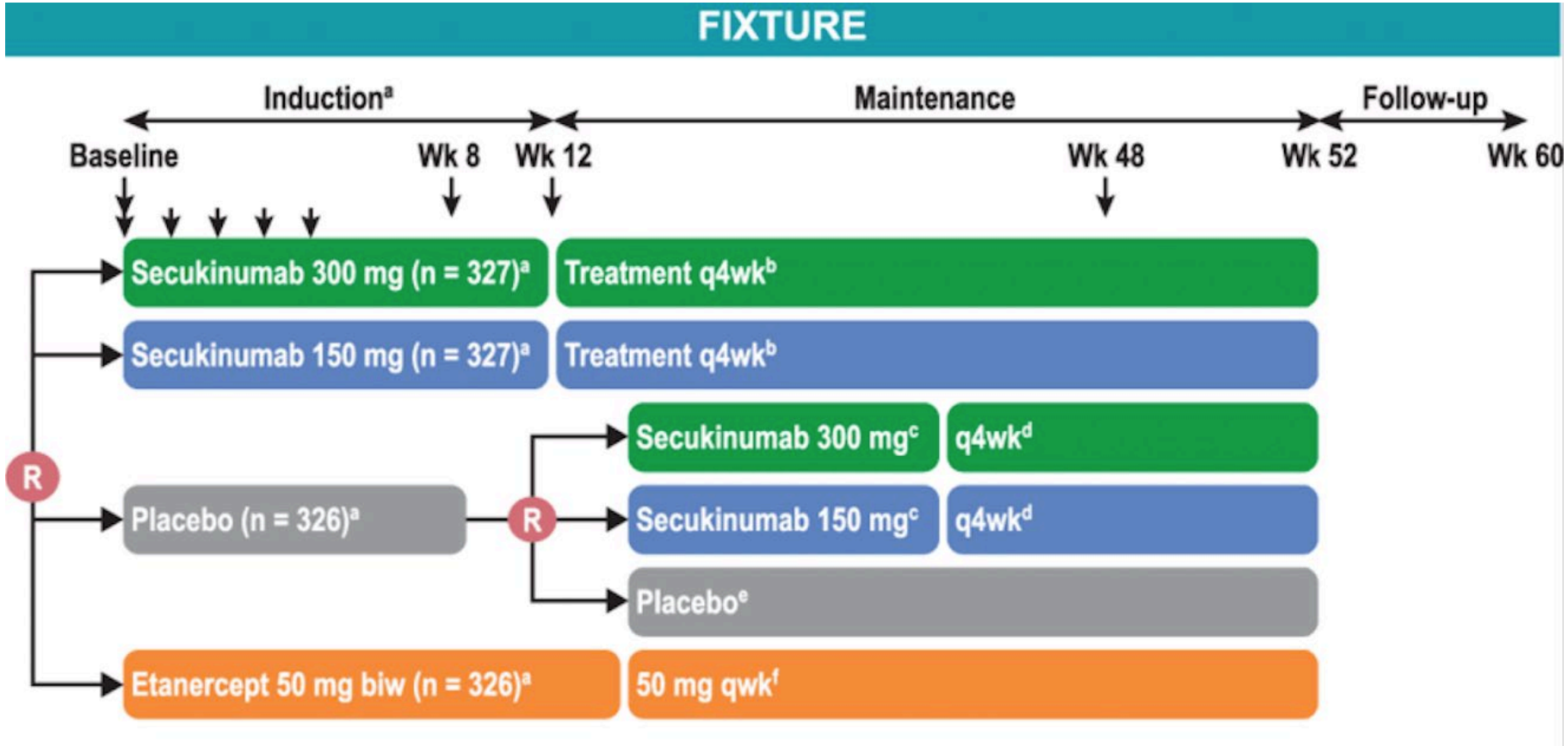


UNIVERSITY OF MIAMI

Langley, R. *et al. New England Journal of Medicine* (2014)

SECUKINUMAB PIVOTAL TRIALS- FIXTURE STUDY DESIGN

Phase 3, double-blind, 52-week study Full Year Investigative Examination of Secukinumab vs. Etanercept Using Two Dosing Regimens to Determine Efficacy in Psoriasis



UNIVERSITY OF MIAMI

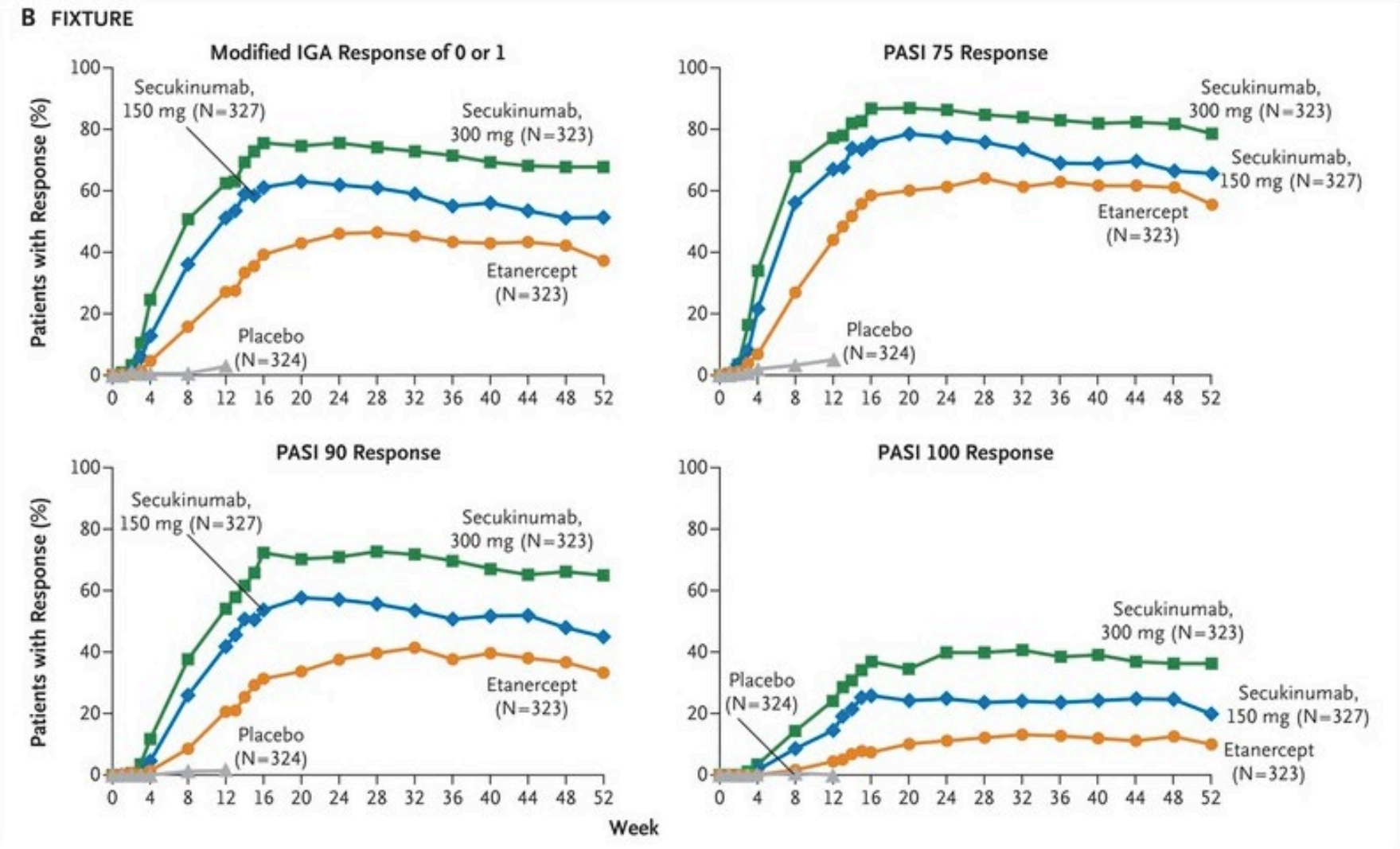
Korman, N. *et al. Journal of Dermatological Treatment (2016).*

SECUKINUMAB- FIXTURE RESULTS

Phase 3, double-blind, 52-week study Full Year Investigative Examination of Secukinumab vs. Etanercept Using Two Dosing Regimens to Determine Efficacy in Psoriasis

Secukinumab was superior to etanercept and placebo with respect to all key secondary end points.

Rates of response according to PASI 75, PASI 90, PASI 100, and a score of 0 or 1 on the modified investigator's global assessment were higher with secukinumab than with etanercept through week 52



UNIVERSITY OF MIAMI

Langley, R. *et al. New England Journal of Medicine* (2014)

SECUKINUMAB- SAFETY DATA

Table 4. Adverse Events during the Induction Period and the Entire 52-Week Study Period in FIXTURE.*

Variable	Induction Period				Entire Study Period†			
	Secukinumab, 300 mg (N=326)	Secukinumab, 150 mg (N=327)	Etanercept (N=323)	Placebo (N=327)	Any Secukinumab, 300 mg (N=467)	Any Secukinumab, 150 mg (N=469)	Etanercept (N=323)	Placebo (N=327)
Exposure to study treatment — days	82.8±9.8	83.3±11.6	82.6±9.4	81.7±11.4	320.7±75.3	317.5±75.4	331.9±89.7	95.3±61.0
	no. of patients with event (percent)				*no. of patients with event (no. of cases per 100 patient-yr)*			
Any adverse event	181 (55.5)	191 (58.4)	186 (57.6)	163 (49.8)	376 (252.0)	364 (236.4)	253 (243.4)	168 (329.7)
Death	0	0	0	0	0	0	0	0
Nonfatal serious adverse event	4 (1.2)	7 (2.1)	3 (0.9)	6 (1.8)	27 (6.8)	24 (6.0)	20 (7.0)	7 (8.3)
Discontinuation due to adverse event‡	4 (1.2)	2 (0.6)	6 (1.9)	3 (0.9)	14	10	12	3
Infection or infestation	87 (26.7)	101 (30.9)	79 (24.5)	63 (19.3)	269 (105.4)	240 (91.9)	170 (91.4)	65 (89.5)
Common adverse event§								
Nasopharyngitis	35 (10.7)	45 (13.8)	36 (11.1)	26 (8.0)	122 (35.2)	108 (31.4)	86 (35.7)	26 (32.8)
Headache	30 (9.2)	16 (4.9)	23 (7.1)	23 (7.0)	58 (15.7)	47 (12.4)	40 (15.2)	24 (29.6)
Diarrhea	17 (5.2)	12 (3.7)	11 (3.4)	6 (1.8)	38 (9.9)	36 (9.3)	22 (7.9)	7 (8.4)
Pruritus	8 (2.5)	12 (3.7)	8 (2.5)	11 (3.4)	16 (4.0)	21 (5.3)	16 (5.7)	11 (13.2)
Arthralgia	5 (1.5)	14 (4.3)	12 (3.7)	10 (3.1)	24 (6.0)	33 (8.5)	23 (8.2)	10 (12.1)
Upper respiratory tract infection	7 (2.1)	10 (3.1)	7 (2.2)	3 (0.9)	26 (6.6)	26 (6.6)	18 (6.4)	3 (3.5)
Back pain	8 (2.5)	8 (2.4)	9 (2.8)	6 (1.8)	31 (7.9)	20 (5.1)	26 (9.3)	6 (7.1)
Cough	11 (3.4)	5 (1.5)	4 (1.2)	4 (1.2)	30 (7.6)	15 (3.7)	12 (4.2)	4 (4.8)
Hypertension	5 (1.5)	10 (3.1)	5 (1.5)	4 (1.2)	20 (5.0)	22 (5.6)	14 (4.9)	4 (4.7)
Nausea	8 (2.5)	6 (1.8)	4 (1.2)	7 (2.1)	11 (2.7)	10 (2.5)	7 (2.4)	7 (8.3)
Oropharyngeal pain	9 (2.8)	5 (1.5)	4 (1.2)	7 (2.1)	25 (6.3)	20 (5.0)	10 (3.5)	7 (8.3)

Langley, R. *et al. New England Journal of Medicine* (2014)

SECUKINUMAB- WHAT ABOUT KIDS?

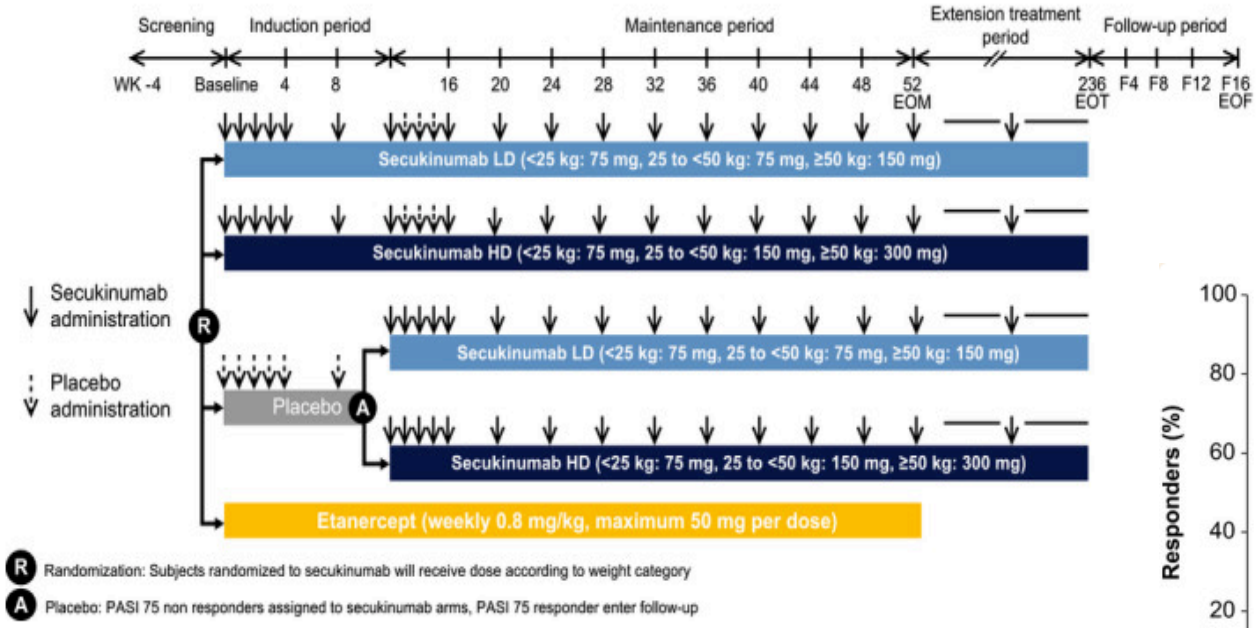
Randomized Controlled Trial > J Eur Acad Dermatol Venereol. 2021 Apr;35(4):938-947.
doi: 10.1111/jdv.17002. Epub 2021 Jan 19.

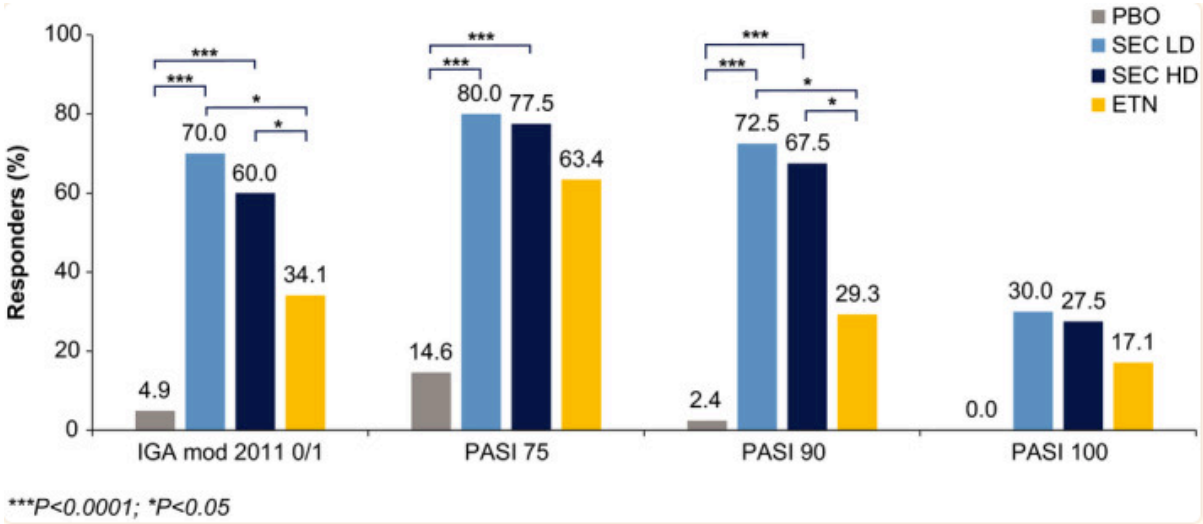
Secukinumab demonstrates high efficacy and a favourable safety profile in paediatric patients with severe chronic plaque psoriasis: 52-week results from a Phase 3 double-blind randomized, controlled trial

C Bodemer [1], A Kaszuba [2], K Kingo [3], A Tsianakas [4], A Morita [5], E Rivas [6], P Papanastasiou [7], D Keefe [8], M Patekar [7], P Charef [7], L Zhang [8], S Cafoncelli [8], C Papavassilis [7]

Phase 3 RCT evaluating Secukinumab in low dose (75mg or 150mg) vs high dose (150mg or 300mg) vs placebo vs Etanercept in pediatric populations 6-18 years old

At week 12, both doses of Secukinumab were superior to placebo and etanercept with respect to IGA 0/1; PASI 75; and PASI 90.



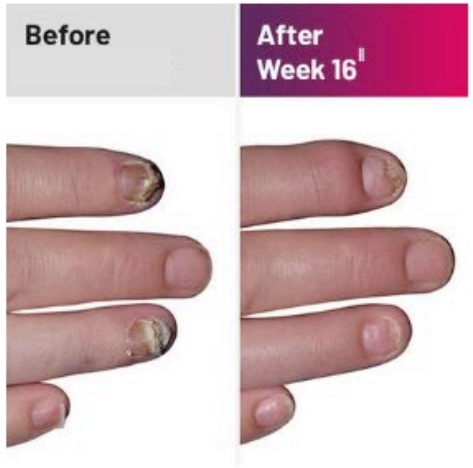


UNIVERSITY OF MIAMI

Bodemer C. *et al. J Eur Acad Dermatol Venereol* (2021).

SECUKINUMAB- HARD AREAS

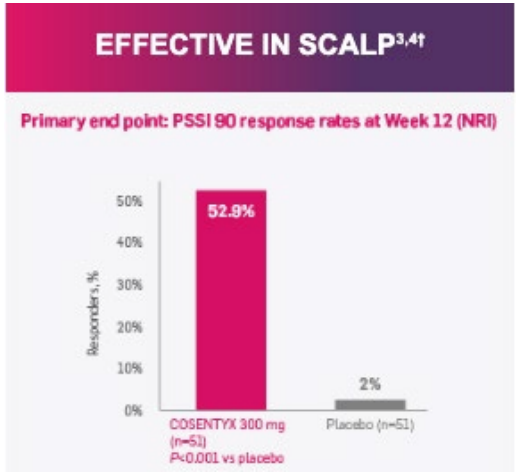
Scalp

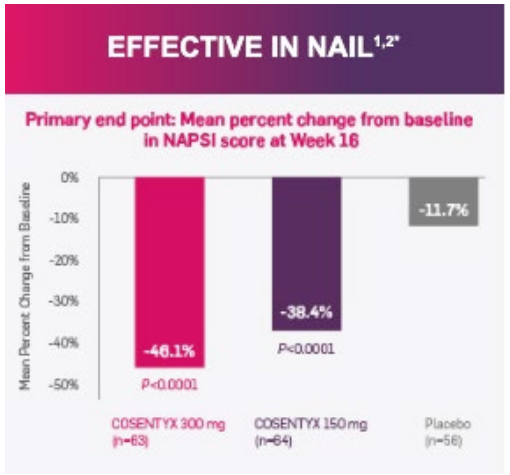


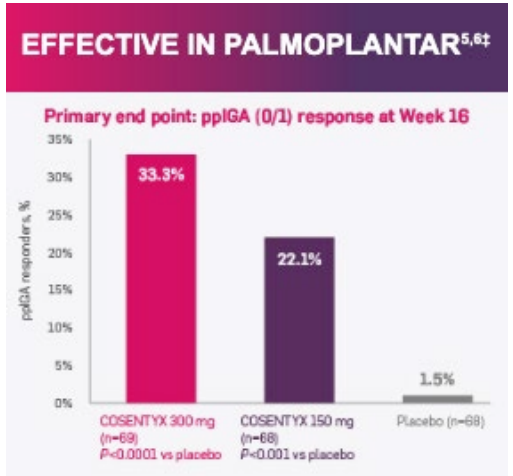
Nails

Palms

Bottoms of feet







UNIVERSITY OF MIAMI

*SCALP Study.

*TRANSFIGURE Study.

*Palmoplantar Investigator's Global Assessment (ppIGA)

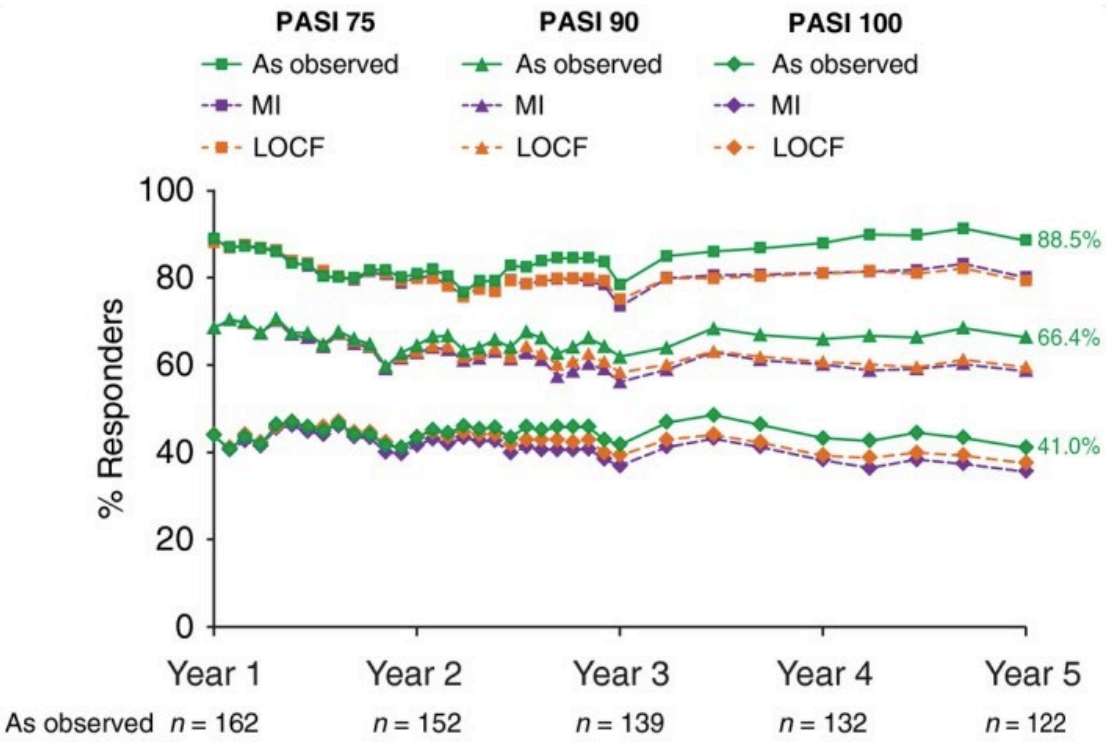
SECUKINUMAB- SCULPTURE TRIAL 5 YEAR DATA

Long- term improvement responses with Secukinumab 300mg q4wks followed for 5 years

	Year 1			Year 5		
	As observed (n=162)	MI (n=168)	LOCF (n=168)	As observed (n=122)	MI (n=168)	LOCF (n=168)
PASI 75 (Mean [95% CI])	88.9% [82.8, 93.1]	88.6% [82.8, 93.0]	88.1% [82.0, 92.4]	88.5% [81.2, 93.4]	80.1% [72.6, 86.5]	79.2% [72.1, 84.9]
PASI 90 (Mean [95% CI])	68.5% [60.7, 75.5]	68.6% [61.0, 75.5]	68.5% [60.8, 75.3]	66.4% [57.2, 74.5]	58.6% [50.3, 66.7]	59.5% [51.7, 66.9]
PASI 100 (Mean [95% CI])	43.8% [36.1, 51.8]	43.9% [36.1, 51.8]	44.0% [36.5, 51.9]	41.0% [32.3, 50.3]	35.6% [27.9, 43.9]	37.5% [30.3, 45.3]

LOCF, last observation carried forward; MI, multiple imputation; n, number of evaluable patients; PASI, Psoriasis Area and Severity Index score.

*Percentage of patients with PASI 75, PASI 90, PASI 100 response at Year 1 and Year 5.



UNIVERSITY OF MIAMI

Bissonnette R. *et al. J Eur Acad Dermatol Venereol* (2018).

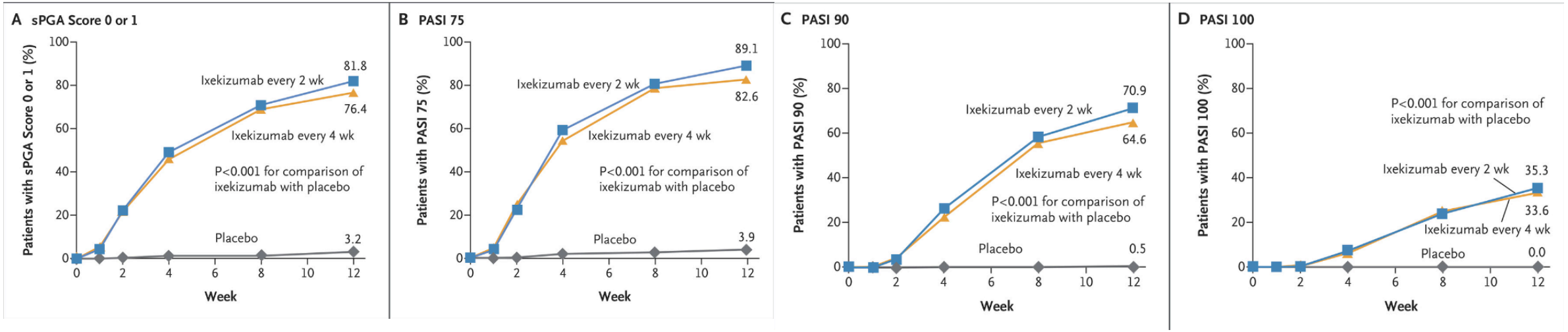
IXEKIZUMAB- INDICATIONS

Human IgG4 monoclonal antibody that binds IL-17A

- Adult Chronic Plaque Psoriasis
- Pediatric Chronic Plaque Psoriasis >6 years old
- Psoriatic Arthritis
- Ankylosing Spondylitis
- Non-radiographic Axial Spondyloarthritis

IXEKIZUMAB- EFFICACY AT 12 WEEKS FROM PHASE III UNCOVER-1,2,3 TRIALS

UNCOVER-1- Randomized, double-blind study evaluating ixekizumab q 2wks vs q 4wks vs placebo
UNCOVER-2- Randomized, double-blind study evaluating ixekizumab q 2wks vs q 4wks vs placebo vs etanercept
UNCOVER-3- Randomized, double-blind study evaluating ixekizumab q 2wks vs q 4wks vs placebo vs etanercept with long-term extension



*UNCOVER-1 Study Data

	UNCOVER-1			UNCOVER-2				UNCOVER-3			
	Ixe q2wks	Ixe q4wks	Placebo	Ixe q2wks	Ixe q4wks	Etanercept	Placebo	Ixe q2wks	Ixe q4wks	Etanercept	Placebo
sPGA 0/1	81.8	76.4	3.2	83.2	72.9	36.0	2.4	80.5	75.4	41.6	6.7
PASI 75 (%)	89.1	82.6	3.9	89.7	77.5	41.6	2.4	87.3	84.2	53.4	7.3
PASI 90 (%)	70.9	64.6	0.5	70.7	59.7	18.7	0.6	68.1	65.3	25.7	3.1
PASI 100 (%)	35.3	33.6	0.0	40.5	30.8	5.3	0.6	37.7	35.0	7.3	0.0

UNIVERSITY OF MIAMI

Griffiths, C. *et al. The Lancet.* 2015
Gordon K. *et al. New England Journal of Medicine.* 2016

IXEKIZUMAB- ADVERSE EVENTS POOLED DATA

Table 2. Adverse Events during the Induction Periods and the Total Ixekizumab Exposure in the Three UNCOVER Trials.*

Adverse Event	Weeks 0–12						Weeks 0–60	
	Placebo (N=791)		Ixekizumab Every 4 wk (N=1161)		Ixekizumab Every 2 wk (N=1167)		All Patients with Ixekizumab Exposure (N=3736)	
	no. of patients (%)	*incidence rate/100 patient-yr*	*no. of patients (%)*	*incidence rate/100 patient-yr*	*no. of patients (%)*	*incidence rate/100 patient-yr*	*no. of patients (%)*	*incidence rate/100 patient-yr*
Any adverse event†	370 (46.8)	205.5	683 (58.8)	256.8	681 (58.4)	253.6	3021 (80.9)	87.4
Serious adverse event	12 (1.5)	6.7	26 (2.2)	9.8	20 (1.7)	7.4	250 (6.7)	7.2
Discontinuation of study regimen because of an adverse event	9 (1.1)	5.0	24 (2.1)	9.0	25 (2.1)	9.3	165 (4.4)	4.8
Death	0	0.0	0	0.0	0	0.0	3 (0.1)	0.1
Common adverse events‡								
Nasopharyngitis	69 (8.7)	38.3	104 (9.0)	39.1	111 (9.5)	41.3	733 (19.6)	21.2
Upper respiratory tract infection	28 (3.5)	15.6	45 (3.9)	16.9	51 (4.4)	19.0	372 (10.0)	10.8
Injection-site reaction	9 (1.1)	5.0	89 (7.7)	33.5	117 (10.0)	43.6	387 (10.4)	11.2
Arthralgia	17 (2.1)	9.4	22 (1.9)	8.3	29 (2.5)	10.8	196 (5.2)	5.7
Headache	23 (2.9)	12.8	50 (4.3)	18.8	51 (4.4)	19.0	243 (6.5)	7.0
Selected adverse events of special interest								
Infection or infestation	181 (22.9)	100.5	318 (27.4)	119.6	315 (27.0)	117.3	2064 (55.2)	59.7
Candidal§	4 (0.5)	2.2	7 (0.6)	2.6	16 (1.4)	6.0	128 (3.4)	3.7
Oral	0	0.0	2 (0.2)	0.8	9 (0.8)	3.4	63 (1.7)	1.8
Vulvovaginal¶	3 (1.3)	1.7	5 (1.3)	1.9	3 (0.7)	1.1	40 (3.3)	3.6
Skin	1 (0.1)	0.6	0	0.0	2 (0.2)	0.7	20 (0.5)	0.6
Esophageal	0	0.0	0	0.0	1 (0.1)	0.4	2 (0.1)	0.1
Nail	0	0.0	0	0.0	0	0.0	1 (<0.1)	0.0
Unspecified	0	0.0	0	0.0	0	0.0	9 (0.2)	0.3
Major adverse cardiovascular and cerebrovascular events‖	1 (0.1)	0.6	2 (0.2)	0.8	0	0.0	23 (0.6)	0.7
Crohn's disease	0	0.0	1 (0.1)	0.4	1 (0.1)	0.4	4 (0.1)	0.1
Ulcerative colitis	0	0.0	0	0.0	2 (0.2)	0.7	7 (0.2)	0.2
Cancer, excluding nonmelanoma skin cancer	1 (0.1)	0.6	2 (0.2)	0.8	1 (0.1)	0.4	14 (0.4)	0.4
Nonmelanoma skin cancer	1 (0.1)	0.6	1 (0.1)	0.4	2 (0.2)	0.7	20 (0.5)	0.6
Selected serious adverse events of special interest								
Infection	3 (0.4)	1.7	8 (0.7)	3.0	5 (0.4)	1.9	51 (1.4)	1.5
Major adverse cardiovascular and cerebrovascular events‖	1 (0.1)	0.6	2 (0.2)	0.8	0	0.0	22 (0.6)	0.6
Crohn's disease	0	0.0	1 (0.1)	0.4	1 (0.1)	0.4	3 (0.1)	0.1
Ulcerative colitis	0	0.0	0	0.0	0	0.0	1 (<0.1)	0.0
Cancer, excluding nonmelanoma skin cancers	1 (0.1)	0.6	1 (0.1)	0.4	0	0.0	10 (0.3)	0.3
Nonmelanoma skin cancer	0	0.0	0	0.0	0	0.0	2 (0.1)	0.1
Other serious adverse event**	9 (1.1)	5.0	16 (1.4)	6.0	15 (1.3)	5.6	179 (4.8)	5.2
Neutropenia††								
Grade 1	23 (2.9)	–	76 (6.6)	–	81 (7.0)	–	321 (8.6)	–
Grade 2	2 (0.3)	–	22 (1.9)	–	25 (2.1)	–	97 (2.6)	–
Grade 3	1 (0.1)	–	0	–	2 (0.2)	–	8 (0.2)	–
Grade 4	0	–	1 (0.1)	–	0	–	2 (0.1)	

UNIVERSITY OF MIAMI

Gordon K. *et al. New England Journal of Medicine.* 2016

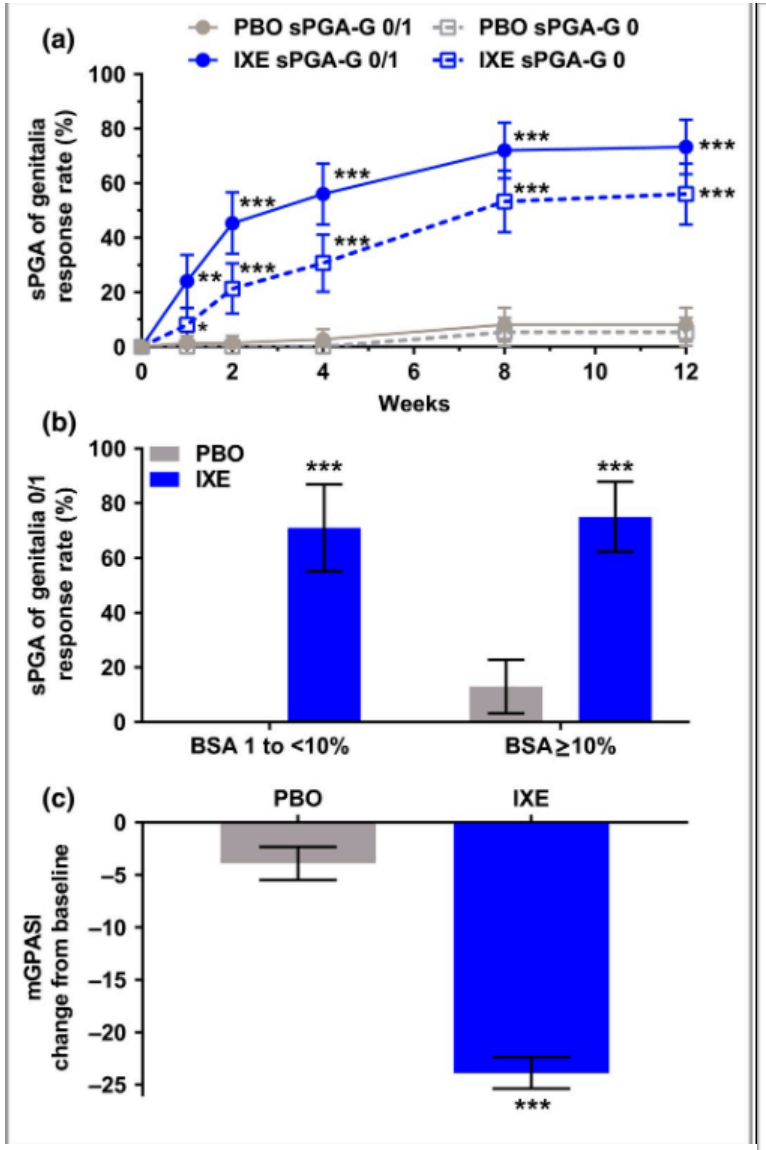
IXEKIZUMAB-GENITAL PSORIASIS IXORA-Q TRIAL

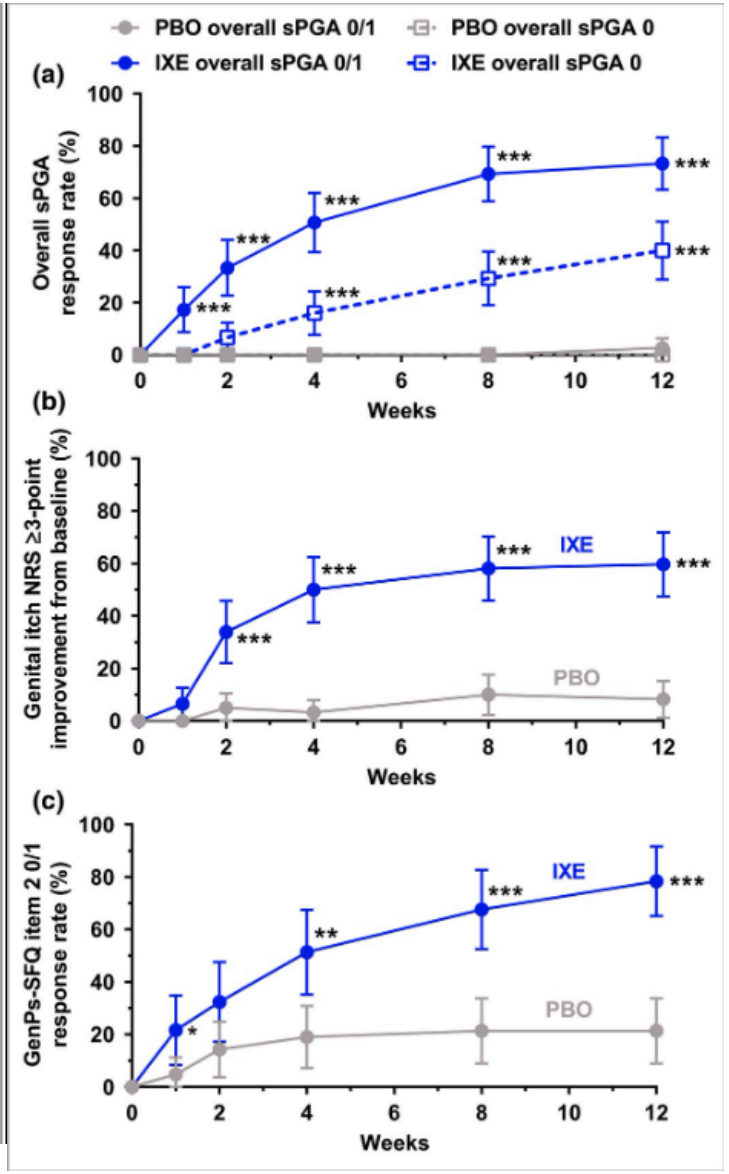
Clinical Trial > Br J Dermatol. 2018 Oct;179(4):844-852. doi: 10.1111/bjd.16736.
Epub 2018 Jul 22.

Efficacy and safety of ixekizumab in a randomized, double-blinded, placebo-controlled phase IIIb study of patients with moderate-to-severe genital psoriasis

C Ryan [1], A Menter [2], L Guenther [3], A Blauvelt [4], R Bissonnette [5], K Meeuwis [6], J Sullivan [7], J C Cather [8], G Yosipovitch [9], A B Gottlieb [10], J F Merola [11], K Callis Duffin [12], S Fretzin [13], O O Osuntokun [14], R Burge [14], A N Naegeli [14], F E Yang [14], C-Y Lin [14], K Todd [14], A Potts Bleakman [14]; IXORA-Q Study Group

At week 12, ixekizumab was superior to placebo for sPGA-G 0/1, overall sPGA 0/1, GenPs-SFQ item 2 score 0/1; and genital itch





UNIVERSITY OF MIAMI

Ryan C. *et al. British Journal of Dermatology.* 2018.

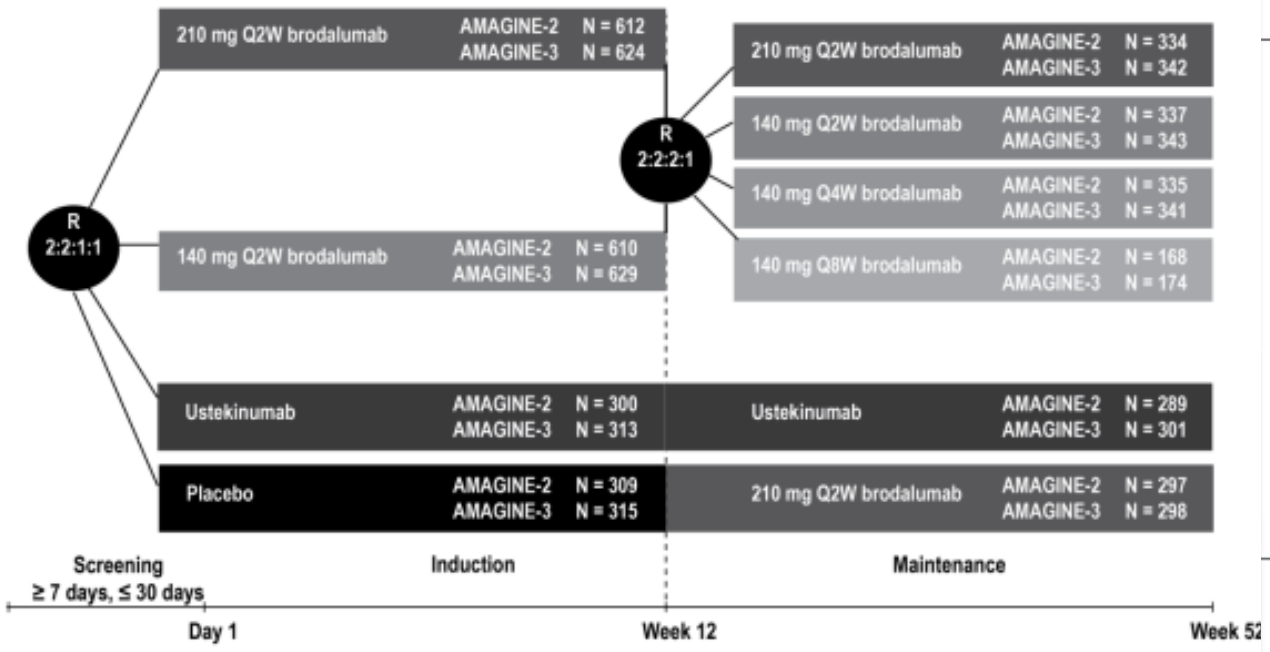
BRODALUMAB- INDICATIONS

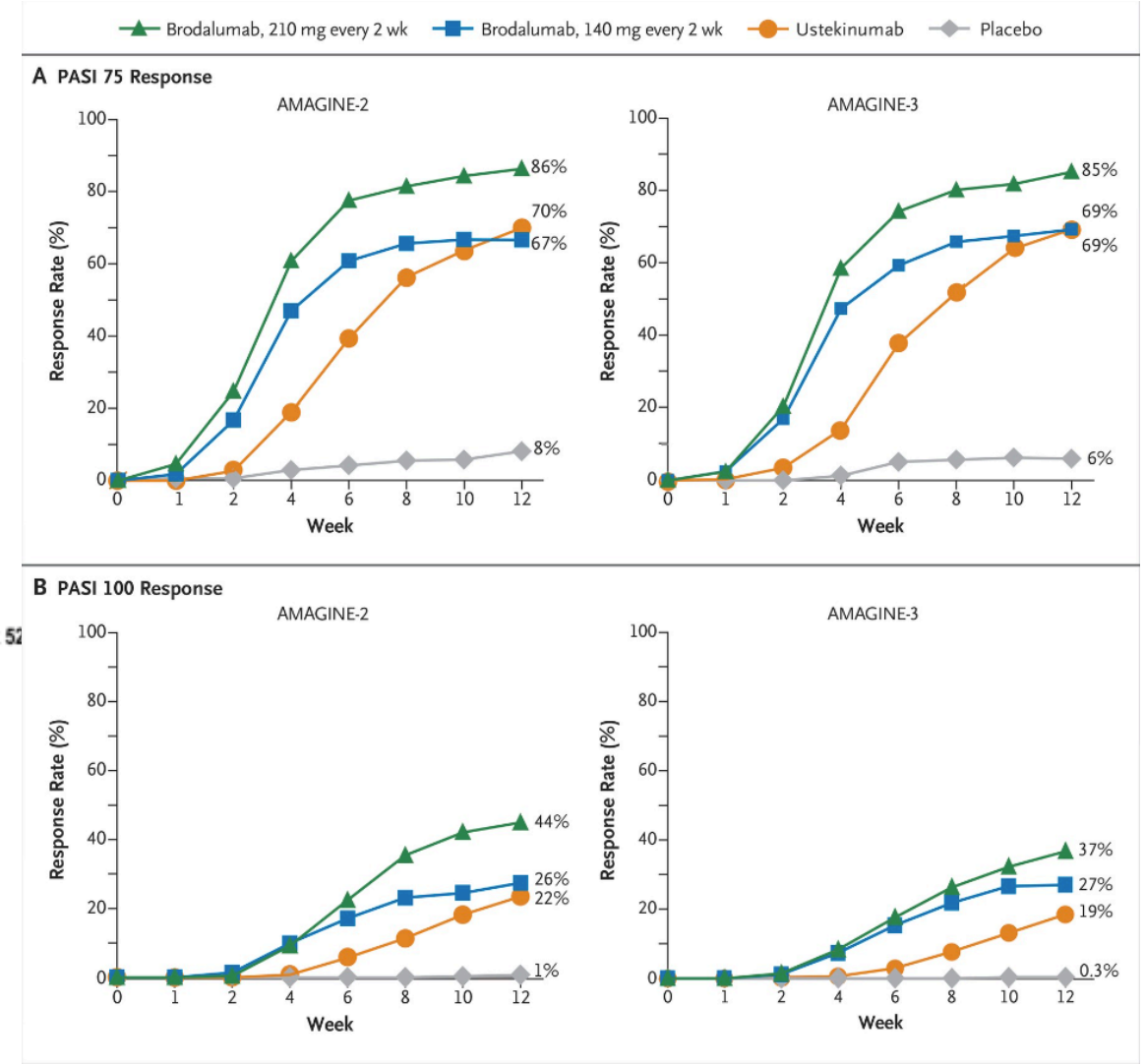
Human monoclonal antibody that blocks the IL-17 receptor A subunit, which blocks biologic activities of IL-17A, IL-17F, IL-17A/F, IL-17C, and IL-17E

Adult Chronic Plaque Psoriasis

BRODALUMAB- AMAGINE-2, 3 TRIALS

Multicenter, randomized, double-blind, placebo-controlled and active comparator–controlled (Ustekinumab), parallel-group, phase 3 trials





At week 12, Brodalumab at the 210mg q2wk dose was superior to brodalumab at the 140mg q2wk dose, ustekinumab, and placebo in PASI 75 and PASI 100.

UNIVERSITY OF MIAMI

Lebwohl M. *et al. New England Journal of Medicine* (2015).

BRODALUMAB- ADVERSE EVENTS

Table S11. Summary of exposure-adjusted event rates of treatment-emergent adverse events through week 52 (AMAGINE-2)

	AMAGINE-2						
		Brodalumab					
		Variable dose			Constant dose		All
	Ustekinumab (Patient-yr = 246.1) (N = 300)	210 mg Q2W after Ustekinumab (Patient-yr = 31.3) (N = 51)	Mixed Dosing (Patient-yr = 478.5) (N = 503)	Combination of 140 mg Q2W / 210 mg Q2W (Patient-yr = 400.7) (N = 423)	140 mg Q2W (Patient-yr = 76.6) (N = 104)	210 mg Q2W (Patient-yr = 379.7) (N = 486)	(Patient-yr = 1366.8) (N = 1567)
	n (r)	n (r)	n (r)	n (r)	n (r)	n (r)	n (r)
Adverse events							
Any	1017 (413.3)	102 (325.9)	2015 (421.1)	1629 (406.5)	316 (412.8)	1531 (403.2)	5593 (409.2)
Serious*	32 (13.0)	1 (3.2)	36 (7.5)	31 (7.7)	8 (10.4)	38 (10.0)	114 (8.3)
Fatal†	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Leading to discontinuation from study	3 (1.2)	0 (0.0)	10 (2.1)	6 (1.5)	5 (6.5)	14 (3.7)	35 (2.6)
Leading to discontinuation of study drug	10 (4.1)	7 (22.4)	19 (4.0)	8 (2.0)	5 (6.5)	18 (4.7)	57 (4.2)
Grade 3, 4, or 5‡	61 (24.8)	1 (3.2)	76 (15.9)	61 (15.2)	12 (15.7)	57 (15.0)	207 (15.1)
Adverse events of interest							
Crohn's disease	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Depression	8 (3.3)	1 (3.2)	13 (2.7)	6 (1.5)	0 (0.0)	3 (0.8)	23 (1.7)
Suicide attempt	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.8)**	3 (0.2)
Suicide ideation	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.1)
Neutropenia	2 (0.8)	0 (0.0)	0 (0.0)	1 (0.2)	1 (1.3)	1 (0.3)	3 (0.2)
Candida infections§	10 (4.1)	2 (6.4)	21 (4.4)	27 (6.7)	5 (6.5)	16 (4.2)	71 (5.2)
Serious infectious episode							
Appendicitis	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)
Cellulitis	0 (0.0)	0 (0.0)	1 (0.2)	3 (0.7)	0 (0.0)	0 (0.0)	4 (0.3)
Gastroenteritis	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Pneumonia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Sepsis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Urinary tract infection	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.1)
Other¶	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)	1 (0.3)	2 (0.1)
Injection site reaction‖	9 (3.7)	3 (9.6)	22 (4.8)	8 (2.0)	4 (5.2)	24 (6.3)	61 (4.5)
Adjudicated MACE	2 (0.8)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	2 (0.5)	5 (0.4)

Table S12. Summary of exposure-adjusted event rates of treatment-emergent adverse events through week 52 (AMAGINE-3)

	AMAGINE-3						
		Brodalumab					
		Variable dose			Constant dose		All
	Ustekinumab (Patient-yr = 248.6) (N = 313)	210 mg Q2W after Ustekinumab (Patient-yr = 44.2) (N = 68)	Mixed Dosing (Patient-yr = 490.1) (N = 515)	Combination of 140 mg Q2W / 210 mg Q2W (Patient-yr = 405.9) (N = 428)	140 mg Q2W (Patient-yr = 87.1) (N = 113)	210 mg Q2W (Patient-yr = 383.5) (N = 489)	(Patient-yr = 1410.8) (N = 1613)
	n (r)	n (r)	n (r)	n (r)	n (r)	n (r)	n (r)
Adverse events							
Any	935 (376.1)	153 (346.1)	1900 (387.7)	1547 (381.2)	352 (404.2)	1522 (396.8)	5474 (388.0)
Serious*	10 (4.0)	3 (6.8)	39 (8.0)	30 (7.4)	8 (9.2)	31 (8.1)	111 (7.9)
Fatal†	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.1)
Leading to discontinuation from study	4 (1.6)	0 (0.0)	3 (0.6)	4 (1.0)	4 (4.6)	12 (3.1)	23 (1.6)
Leading to discontinuation of study drug	7 (2.8)	0 (0.0)	9 (1.8)	16 (3.9)	5 (5.7)	15 (3.9)	45 (3.2)
Grade 3, 4, or 5‡	29 (11.7)	5 (11.3)	57 (11.6)	78 (19.2)	12 (13.8)	59 (15.4)	211 (15.0)
Adverse events of interest							
Crohn's disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutropenia	2 (0.8)	0 (0.0)	8 (1.6)	9 (2.2)	3 (3.4)	1 (0.3)	21 (1.5)
Depression	2 (0.8)	2 (4.5)	8 (1.6)	7 (1.7)	4 (4.6)	4 (1.0)	25 (1.8)
Suicide attempt	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suicidal ideation	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Candida infections§	4 (1.6)	2 (4.5)	21 (4.3)	28 (6.8)	2 (2.3)	27 (7.0)	80 (5.7)
Serious infectious episode							
Appendicitis	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Cellulitis	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	2 (0.1)
Diverticulitis	1 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Gastroenteritis	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)
Pneumonia	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Sepsis	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Urinary tract infection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Other¶	1 (0.4)	1 (2.3)	2 (0.4)	0 (0.0)	1 (1.1)	4 (1.0)	8 (0.6)
Injection site reaction‖	10 (3.8)	3 (6.8)	19 (3.7)	22 (5.7)	3 (3.7)	22 (5.7)	81 (5.7)
Adjudicated MACE	0 (0.0)	0 (0.0)	3 (0.6)	4 (1.0)	2 (2.3)	1 (0.3)	10 (0.7)

UNIVERSITY OF MIAMI

Lebwohl M. *et al. New England Journal of Medicine* (2015).

BRODALUMAB- BLACK BOX WARNING

AMAGINE-2 TRIAL:
† Fatal events were cardiac arrest (constant 210 mg), cardiac arrest (ustekinumab), pancreatic carcinoma (ustekinumab); one additional fatal event occurred after the exposure period: completed suicide (placebo/210 mg; 27 days after last dose)
**Three events of suicide attempt occurred in one individual; the first event occurred during the 12 week induction period

AMAGINE-3 TRIAL:
† Fatal events were cardiac arrest (140mg/210mg), accidental death (motor vehicle (210 mg/140 mg Q2W); two additional fatal events occurred after the exposure period: histiocytosis haematophagic syndrome (140 mg/140 mg Q4W/210 mg rescue; 41 days after the last dose) and cardiomyopathy (210 mg /140 mg Q4W/210 mg rescue; 87 days after the last dose)

WARNING: SUICIDAL IDEATION AND BEHAVIOR

Suicidal ideation and behavior, including completed suicides, have occurred in patients treated with *SILIQ*. Prior to prescribing *SILIQ*, weigh the potential risks and benefits in patients with a history of depression and/or suicidal ideation or behavior. Patients with new or worsening suicidal ideation and behavior should be referred to a mental health professional, as appropriate. Advise patients and caregivers to seek medical attention for manifestations of suicidal ideation or behavior, new onset or worsening depression, anxiety, or other mood changes [see Warnings and Precautions (5.1) in the full Prescribing Information].

Because of the observed suicidal behavior in subjects treated with *SILIQ*, *SILIQ* is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the *SILIQ* REMS Program [see Warnings and Precautions (5.2) in the full Prescribing Information].

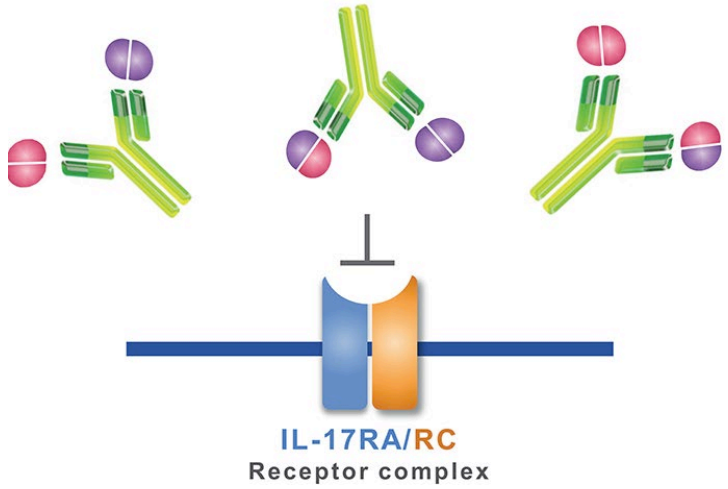
REMS Program Information: https://siliqrems.com/#Main

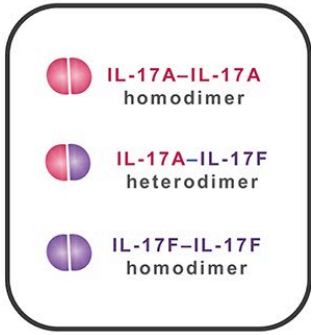
UNIVERSITY OF MIAMI

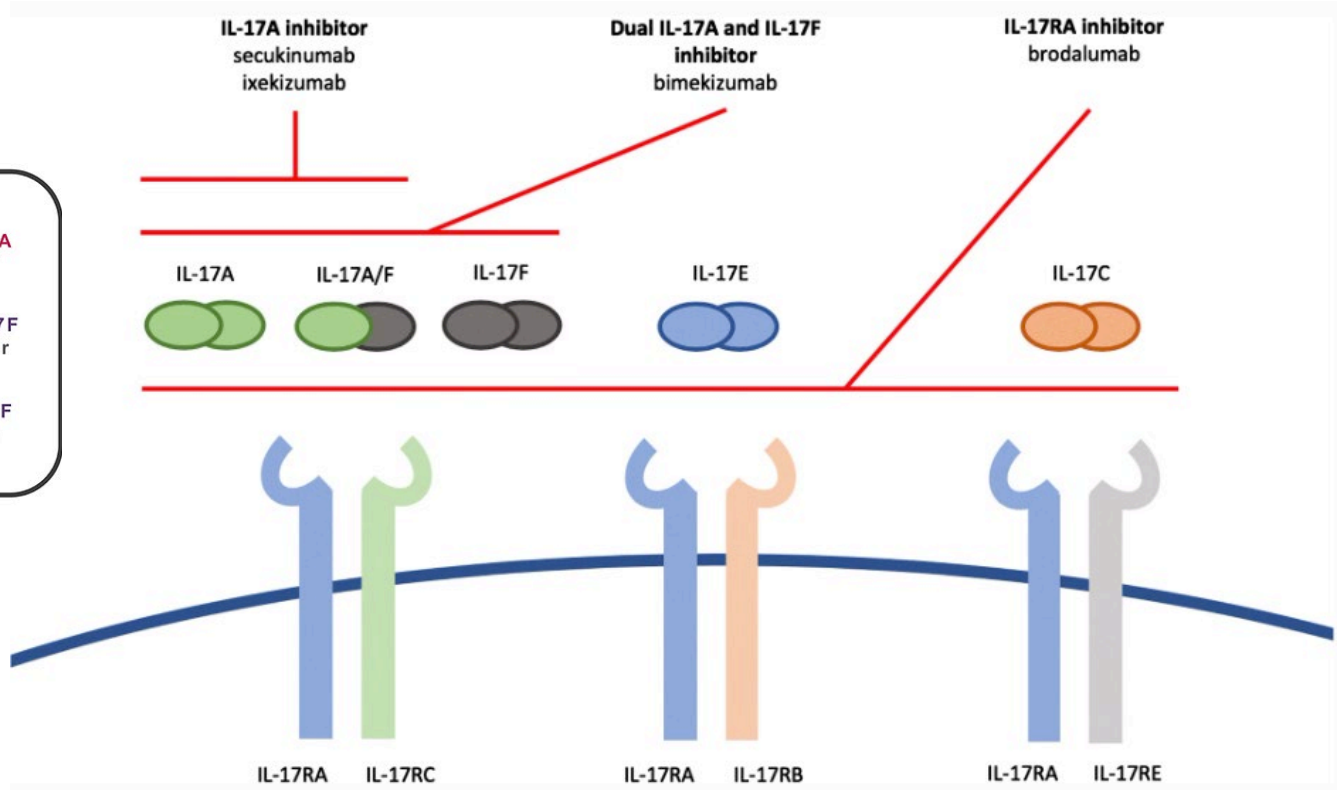
Lebwohl M. *et al. New England Journal of Medicine* (2015).

BIMEKIZUMAB- NEW TREATMENT COMING THIS YEAR

Human IgG1 monoclonal antibody that selectively blocks IL-17A, IL-17F, and IL-17A/F
Currently approved in the European Union/ European Economic Area, Great Britain, Japan, Canada, and Australia





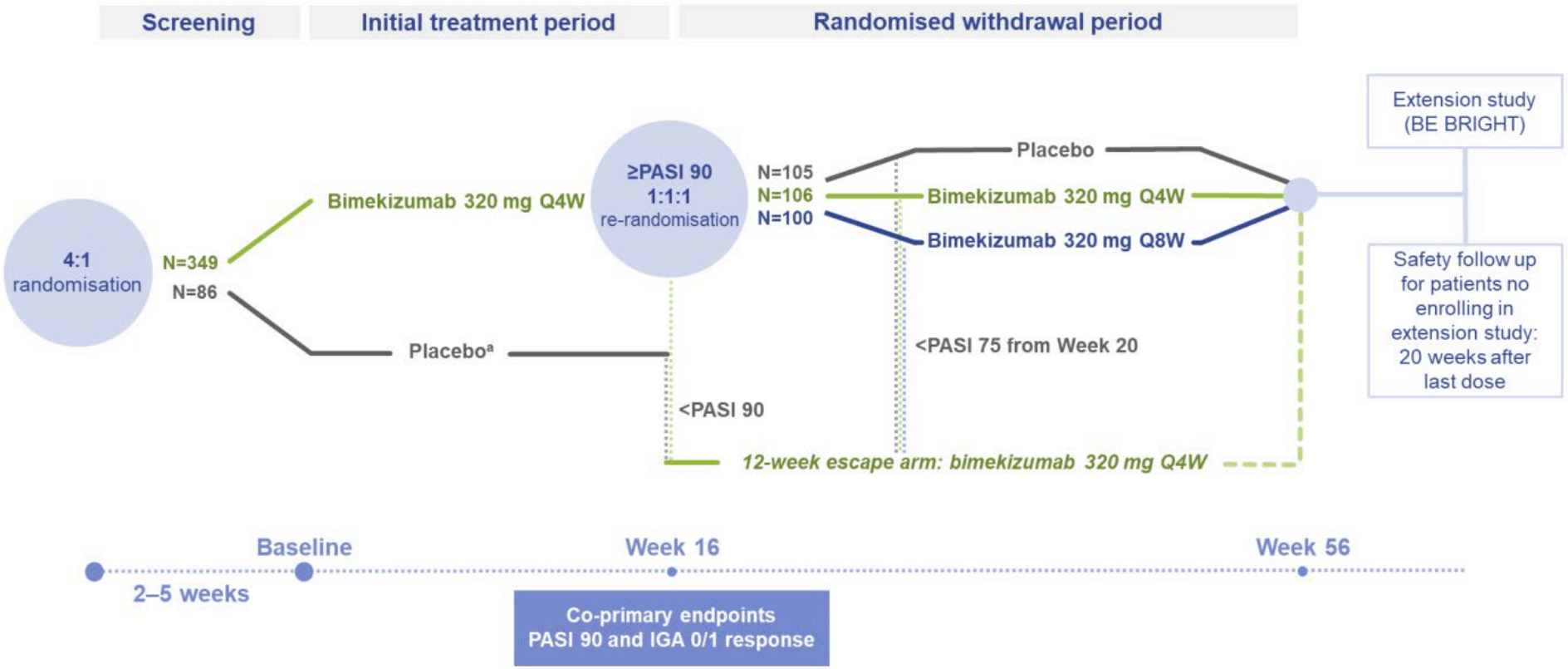


UNIVERSITY
OF MIAMI

Adams R. *et al. Frontiers in Immunology* (2020).
Reis, J. *et al. BioDrugs* (2019).

BIMEKIZUMAB- BE READY PIVOTAL TRIAL STUDY DESIGN

Phase 3, multicenter, randomized, double-blind, placebo-controlled trial

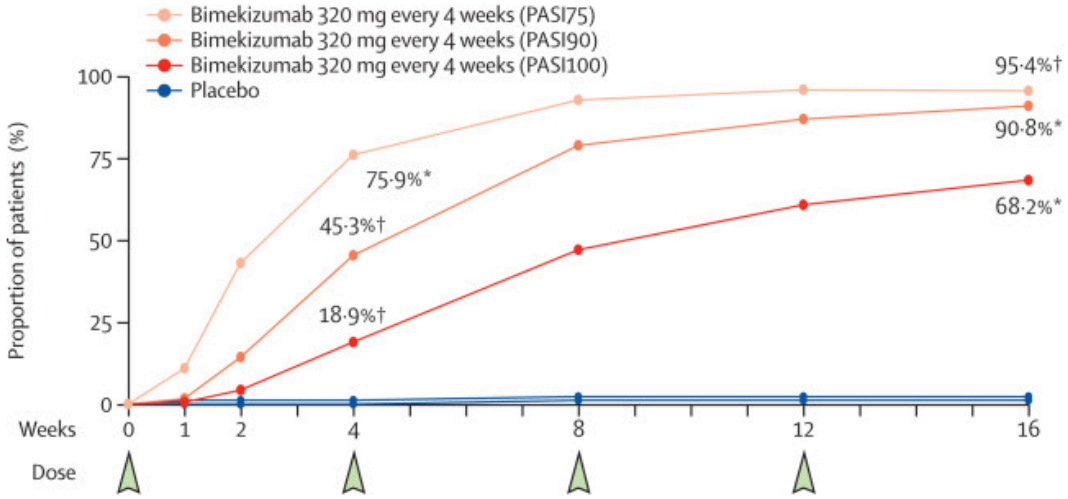


a. One placebo-randomized patient achieved PASI 90 at Week 16 and continued to receive placebo treatment to Week 56. IGA 0/1: score of 0 (clear) or 1 (almost clear) with ≥2-category improvement relative to baseline in Investigator's Global Assessment, scored on a 5-point scale; PASI 75/90: ≥75/90% improvement from baseline in Psoriasis Area and Severity Index; Q4W: every 4 weeks; Q8W: every 8 weeks.

UNIVERSITY OF MIAMI

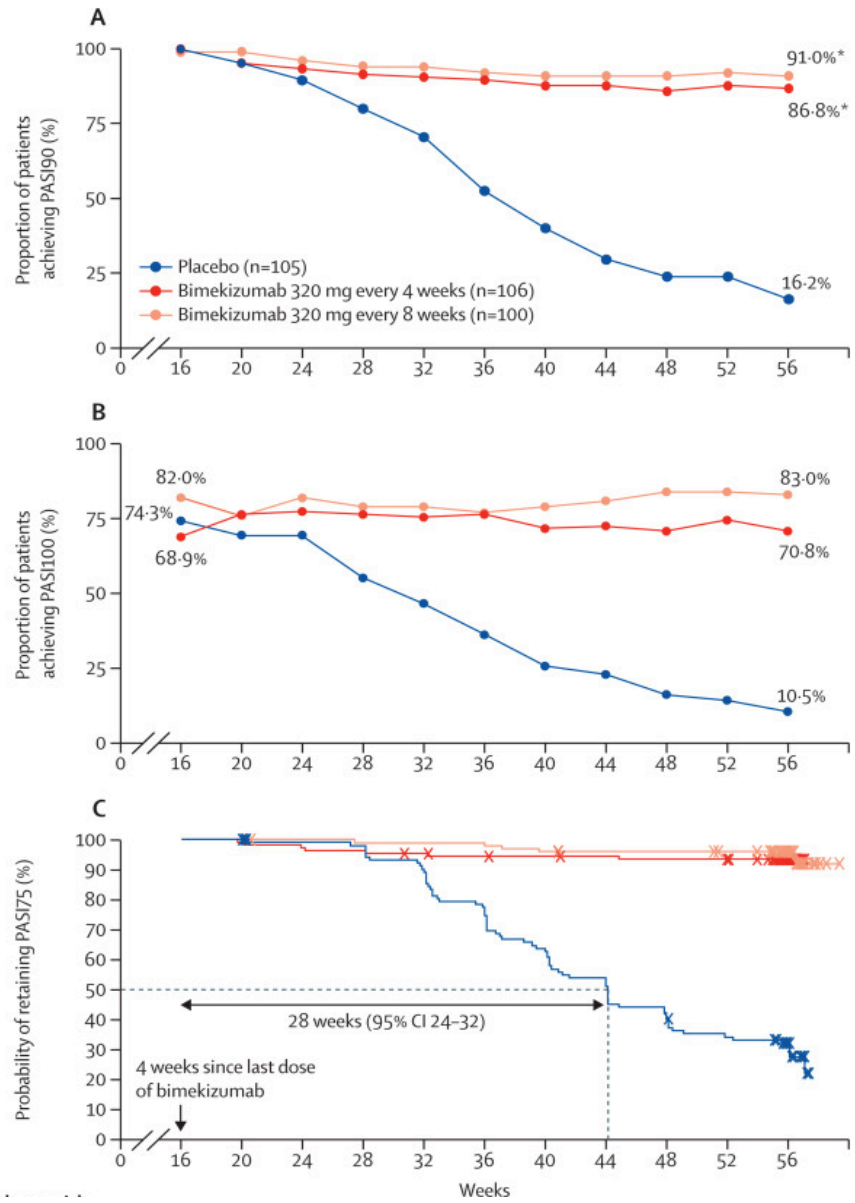
Gordon KB. *et al. Lancet* (2021).

BIMEKIZUMAB- BE READY PIVOTAL TRIAL EFFICACY



At week 16, 95.4% achieved PASI 75, 90.8% achieved PASI 90, and 68.2% achieved PASI 100 in the bimekizumab group.

In the withdrawal period following 16 weeks, 91% and 83% of individuals receiving Bimekizumab q8weeks achieved PASI 90 and PASI 100, respectively. Sustained PASI 90 and PASI 100 were also observed in the Bimekizumab q4week group.



UNIVERSITY OF MIAMI

Gordon KB. *et al. Lancet* (2021).

BIMEKIZUMAB- SAFETY DATA

	Initial treatment period (weeks 0–16)		Randomised withdrawal period (weeks 16–56)		
	Placebo (n=86)	Bimekizumab 320 mg every 4 weeks (n=349)	Placebo (n=105)	Bimekizumab 320 mg every 8 weeks (n=100)	Bimekizumab 320 mg every 4 weeks (n=106)
Any treatment-emergent adverse event	35 (41%)	213 (61%)	72 (69%)	77 (77%)	78 (74%)
Serious treatment-emergent adverse events	2 (2%)	6 (2%)	4 (4%)	3 (3%)	5 (5%)
Discontinuation due to treatment-emergent adverse events	0	3 (1%)	3 (3%)	2 (2%)	0
Severe treatment-emergent adverse events	1 (1%)	3 (1%)	4 (4%)	1 (1%)	4 (4%)
Deaths	0	0	0	0	0
Most common treatment-emergent adverse events					
Nasopharyngitis	4 (5%)	23 (7%)	20 (19%)	23 (23%)	11 (10%)
Oral candidiasis	0	21 (6%)	6 (6%)	9 (9%)	12 (11%)
Upper respiratory tract infection	7 (8%)	14 (4%)	5 (5%)	8 (8%)	12 (11%)
Treatment-emergent adverse events of interest					
Serious infections	0	2 (1%)*	0	0	1 (1%)†
Active tuberculosis	0	0	0	0	0
Latent tuberculosis	0	0	0	0	1 (1%)
Inflammatory bowel disease	0	0	0	0	0
Adjudicated suicidal ideation and behaviour	0	0	0	0	0
Malignancies	0	1 (<1%)‡	1 (1%)§	0	0
Non-melanoma skin cancer	0	1 (<1%)‡	0	0	0
Serious hypersensitivity reactions	0	0	0	0	0
Adjudicated major adverse cardiac events¶	0	0	0	1 (1%)	0
Hepatic events‖	1 (1%)	10 (3%)	0	3 (3%)	8 (8%)

Data are n (%). In the randomised withdrawal period, patients who were initially on bimekizumab 320 mg every 4 weeks and achieved PASI90 at week 16 were re-allocated to receive bimekizumab 320 mg every 4 or 8 weeks, or placebo. PASI90=90% or greater improvement from baseline in Psoriasis Area and Severity Index. *One case of enterovirus infection and one case of pneumonia. †One case of otitis media chronic. ‡One case of basal cell carcinoma. §One case of prostate cancer. ¶A non-fatal myocardial infarction in a male patient aged 53 years with six pre-existing cardiovascular risk factors, which was not attributed to the study drug. ‖The majority of hepatic events were elevated liver function tests (including liver transaminases, gamma-glutamyltransferase, alkaline phosphatase, and bilirubin), which were transient and resolved by the end of the study without dose adjustment.

UNIVERSITY OF MIAMI

Gordon KB. *et al. Lancet* (2021).

UNIVERSITY
OF MIAMI

Thank You!
Any Questions?

REFERENCES

1. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072. doi:10.1016/j.jaad.2018.11.057
2. Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. *JAMA*. 2020;323(19):1945-1960. doi:10.1001/jama.2020.4006
3. Srivastava AK, Chand Yadav T, Khera HK, et al. Insights into interplay of immunopathophysiological events and molecular mechanistic cascades in psoriasis and its associated comorbidities. *J Autoimmun*. 2021;118:102614. doi:10.1016/j.jaut.2021.102614
4. Zhou X, Chen Y, Cui L, Shi Y, Guo C. Advances in the pathogenesis of psoriasis: from keratinocyte perspective. *Cell Death Dis*. 2022;13(1):1-13. doi:10.1038/s41419-022-04523-3
5. Facheris P, Valenti M, Pavia G, et al. Brodalumab: A new way to inhibit IL-17 in psoriasis. *Dermatol Ther*. 2020;33(3):e13403. doi:10.1111/dth.13403
6. Gottlieb AB, Deodhar A, Mcinnes IB, et al. Long-term Safety of Secukinumab Over Five Years in Patients with Moderate-to-severe Plaque Psoriasis, Psoriatic Arthritis and Ankylosing Spondylitis: Update on Integrated Pooled Clinical Trial and Post-marketing Surveillance Data. *Acta Derm Venereol*. 2022;102:adv00698. doi:10.2340/actadv.v102.563
7. Korman NJ, Sofen H, Fretzin S, et al. Secukinumab provides better relief from the impact of psoriasis on daily activities and personal relationships than etanercept: results of two phase 3 placebo-controlled randomized clinical trials in moderate-to-severe psoriasis. *J Dermatol Treat*. 2017;28(5):384-389. doi:10.1080/09546634.2016.1255306
8. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in Plaque Psoriasis — Results of Two Phase 3 Trials. *N Engl J Med*. 2014;371(4):326-338. doi:10.1056/NEJMoa1314258
9. Bodemer C, Kaszuba A, Kingo K, et al. Secukinumab demonstrates high efficacy and a favourable safety profile in paediatric patients with severe chronic plaque psoriasis: 52-week results from a Phase 3 double-blind randomized, controlled trial. *J Eur Acad Dermatol Venereol JEADV*. 2021;35(4):938-947. doi:10.1111/jdv.17002
10. Bissonnette R, Luger T, Thaçi D, et al. Secukinumab demonstrates high sustained efficacy and a favourable safety profile in patients with moderate-to-severe psoriasis through 5 years of treatment (SCULPTURE Extension Study). *J Eur Acad Dermatol Venereol*. 2018;32(9):1507-1514. doi:10.1111/jdv.14878
11. Griffiths CEM, Reich K, Lebwohl M, et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. *Lancet Lond Engl*. 2015;386(9993):541-551. doi:10.1016/S0140-6736(15)60125-8
12. Gordon KB, Blauvelt A, Papp KA, et al. Phase 3 Trials of Ixekizumab in Moderate-to-Severe Plaque Psoriasis. *N Engl J Med*. 2016;375(4):345-356. doi:10.1056/NEJMoa1512711
13. Ryan C, Menter A, Guenther L, et al. Efficacy and safety of ixekizumab in a randomized, double-blinded, placebo-controlled phase IIIb study of patients with moderate-to-severe genital psoriasis. *Br J Dermatol*. 2018;179(4):844-852. doi:10.1111/bjd.16736
14. Lebwohl M, Strober B, Menter A, et al. Phase 3 Studies Comparing Brodalumab with Ustekinumab in Psoriasis. *N Engl J Med*. 2015;373(14):1318-1328. doi:10.1056/NEJMoa1503824
15. Adams R, Maroof A, Baker T, et al. Bimekizumab, a Novel Humanized IgG1 Antibody That Neutralizes Both IL-17A and IL-17F. *Front Immunol*. 2020;11. Accessed March 28, 2023.
16. Reis J, Vender R, Torres T. Bimekizumab: The First Dual Inhibitor of Interleukin (IL)-17A and IL-17F for the Treatment of Psoriatic Disease and Ankylosing Spondylitis. *BioDrugs*. 2019;33(4):391-399. doi:10.1007/s40259-019-00361-6
17. Gordon KB, Foley P, Krueger JG, et al. Bimekizumab efficacy and safety in moderate to severe plaque psoriasis (BE READY): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial. *The Lancet*. 2021;397(10273):475-486. doi:10.1016/S0140-6736(21)00126-4