Atopic Dermatitis & Psoriasis Highlights

Ian McDonald

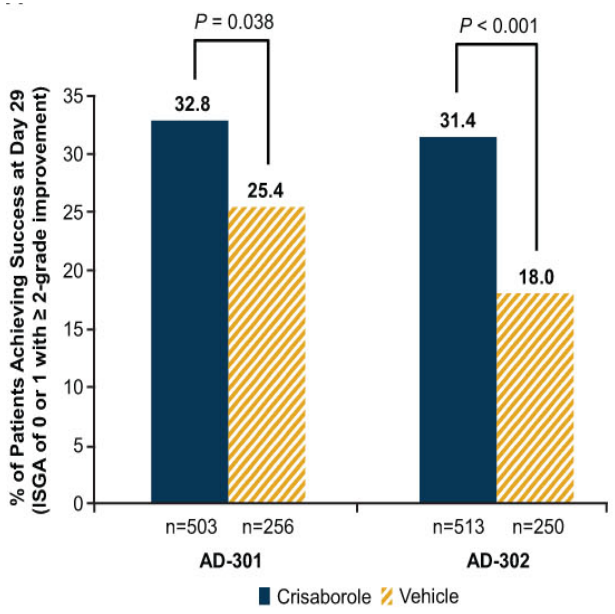
Dermatology SpR

Atopic dermatitis

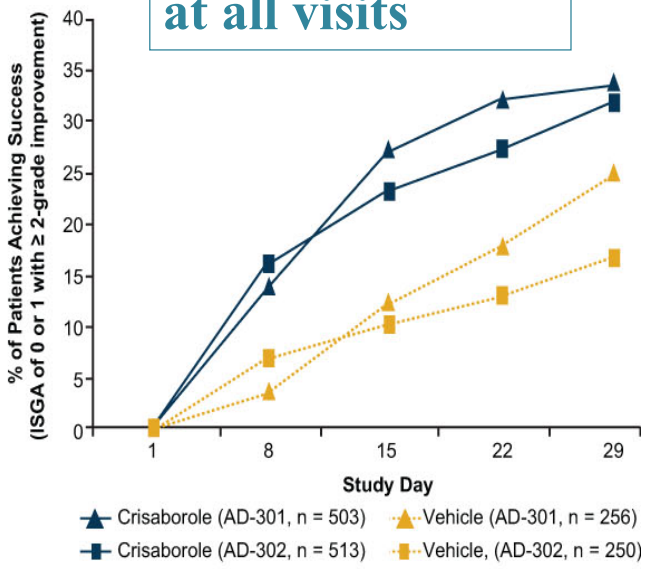
- Pathophysiology
- Associated morbidity
- Topical therapy
- Systemic therapy

Crisaborole PDE4 inhibitor

Primary endpoint: Success in ISGA* at 4 wks



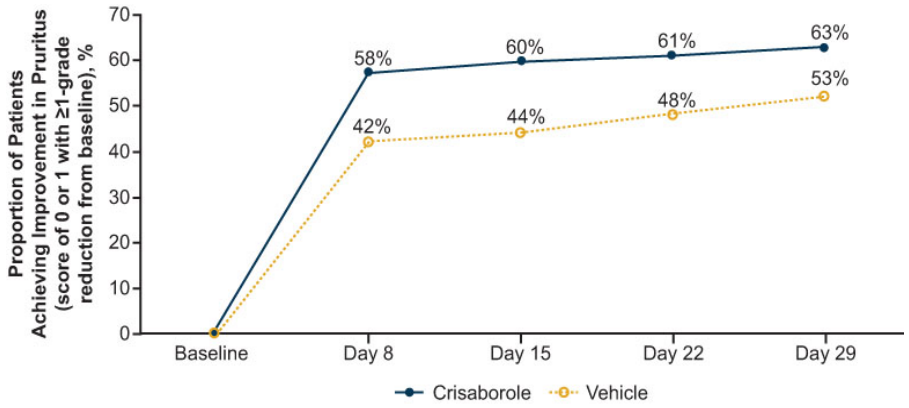
Success in ISGA at all visits



*ISGA = Investigator's Static Global Assessment

Paller et al. JAAD 2016;75:494

Improvement in Pruritus



Paller et al. JAAD 2016;75:494

Minimal or no blood levels after topical application in children and adolescents

- **No clinically important safety signals**

Tom et al. Pediatr Derm 2016;33:150; Zane et al. Pediatr Dermatol 2016;33:380

- **Frew TEAEs in >1% in long-term 48-week open-label safety trial**
  - **Atopic dermatitis flares (3.1%)**
  - **Application site burning or stinging in 2.3%**
  - **Application site infection 1.2%**

Eichenfield et al. JAAD 2017;77:641

Cost!

Roflumilast moderate AD Ph 2a
RVT-501 mild –moderate Ph 2

What's new for topical therapy?

CLINICAL TRIAL

BJD
British Journal of Dermatology

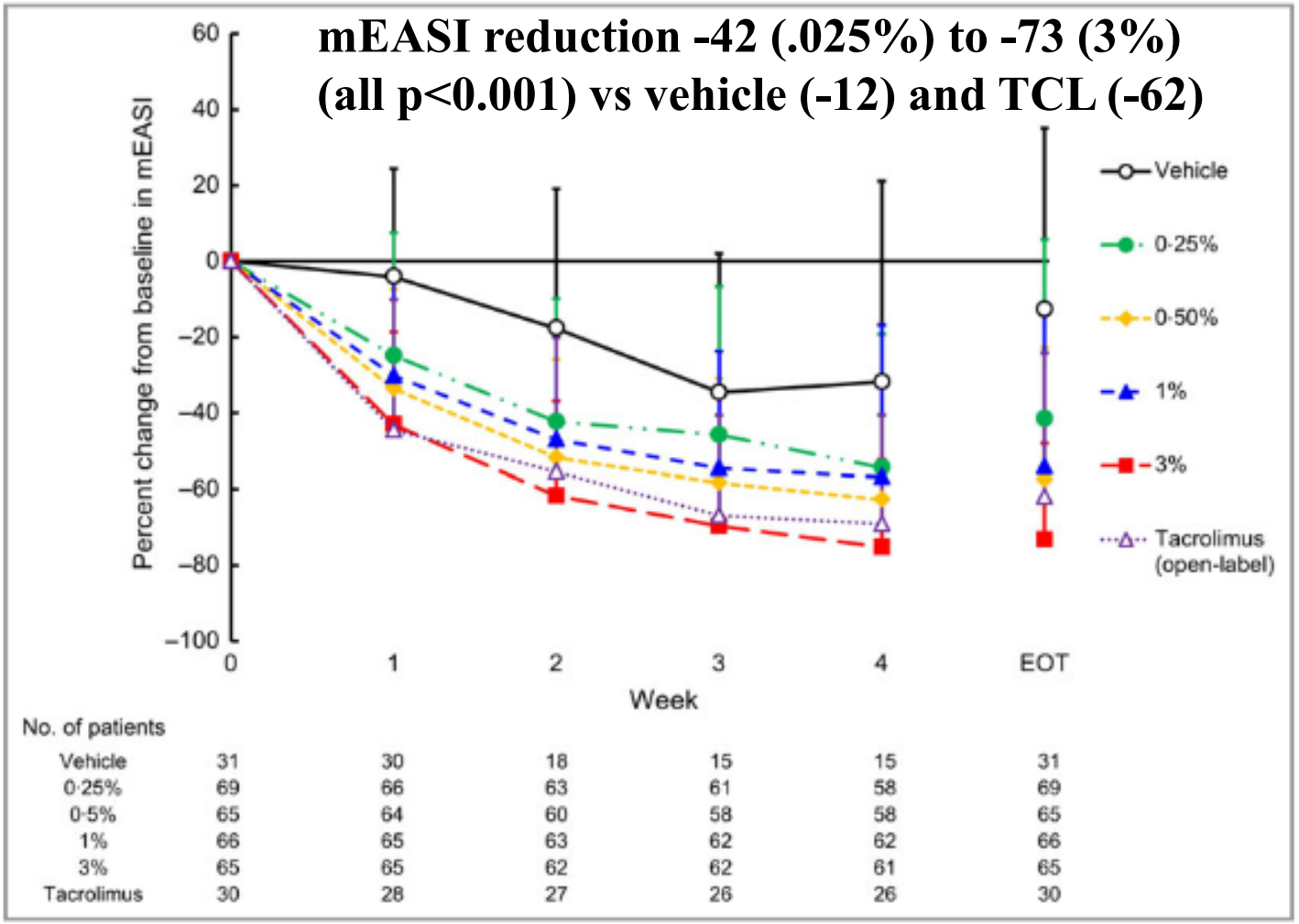
Efficacy and safety of topical JTE-052, a Janus kinase inhibitor, in Japanese adult patients with moderate-to-severe atopic dermatitis: a phase II, multicentre, randomized, vehicle-controlled clinical study*

H. Nakagawa,[1] O. Nemoto,[2] A. Igarashi[3] and T. Nagata[4]

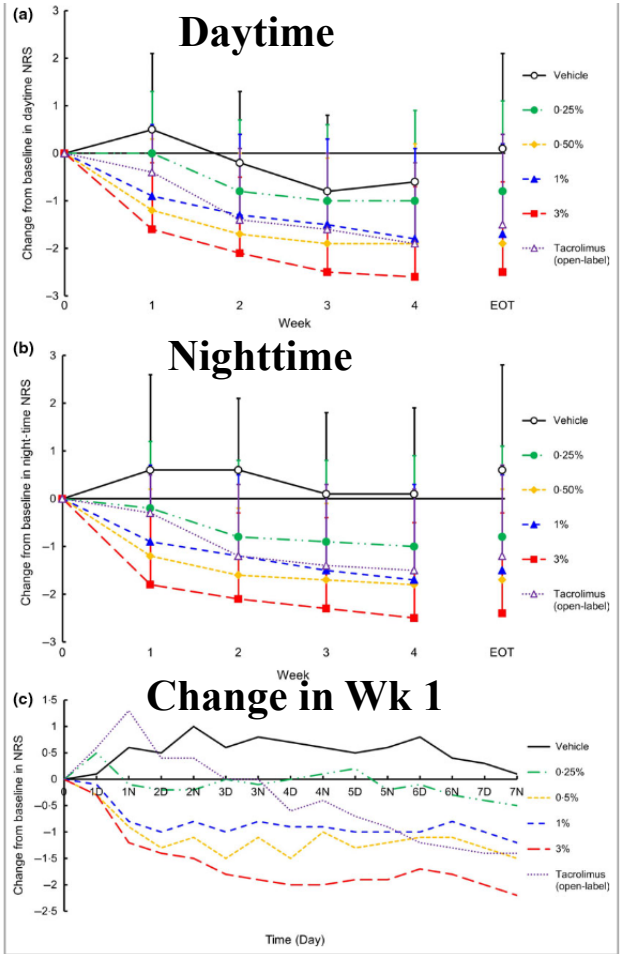
[1]Department of Dermatology, The Jikei University School of Medicine, Tokyo, Japan
[2]Kojinkai Sapporo Skin Clinic, Hokkaido, Japan
[3]Division of Dermatology, NTT Medical Center Tokyo, Tokyo, Japan
[4]Pharmaceutical Division, Japan Tobacco Inc., 4–1, Nihonbashi-Honcho 3-chome, Chuo-ku, Tokyo, Japan

Linked Comment: Bissonnette. *Br J Dermatol* 2018; **178**:321.

mEASI reduction



Itch



Reduction in Itch NRS

- **Both daytime and nighttime pruritus reduction p<0.001 at all concentrations Pruritus with reduction by day 1**
- **Dose-dependent levels detectable in blood (52% with 3%) but far below when given orally (max dose per application 5g)**

Bacteriotherapy

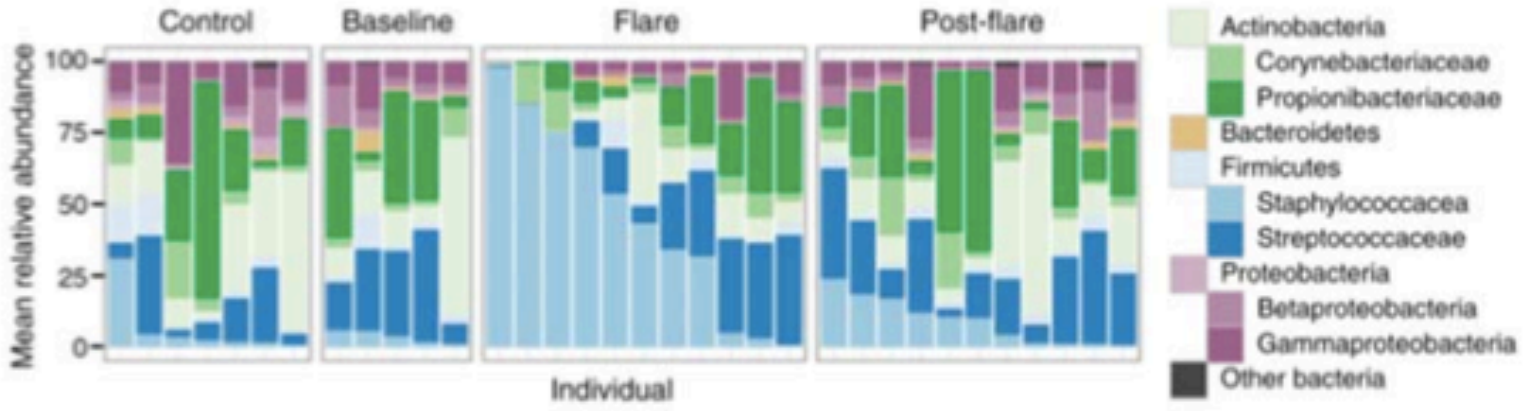
SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

MICROBIOME

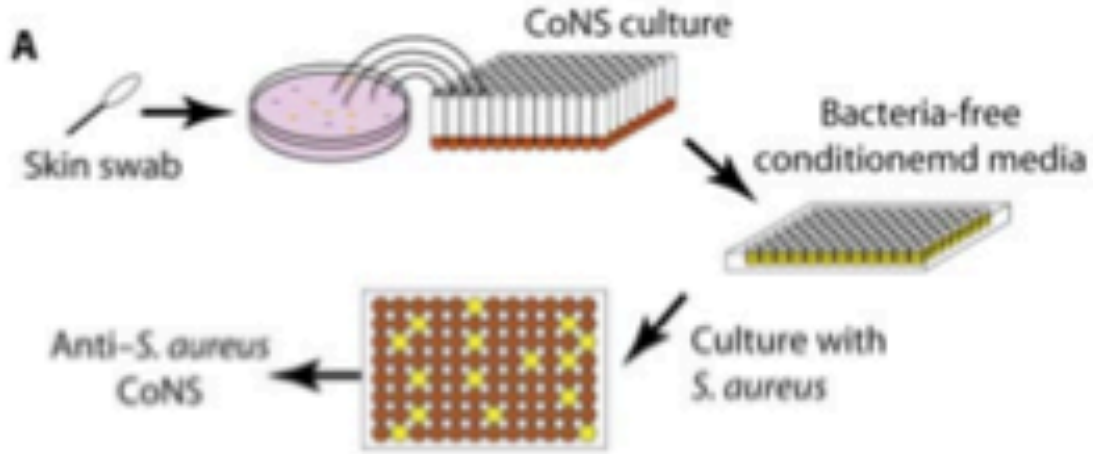
Antimicrobials from human skin commensal bacteria protect against *Staphylococcus aureus* and are deficient in atopic dermatitis

Teruaki Nakatsuji,[1] Tiffany H. Chen,[1] Saisindhu Narala,[1] Kimberly A. Chun,[1] Aimee M. Two,[1] Tong Yun,[1] Faiza Shafiq,[1] Paul F. Kotol,[1] Amina Bouslimani,[2] Alexey V. Melnik,[2] Haythem Latif,[3] Ji-Nu Kim,[3] Alexandre Lockhart,[4] Keli Artis,[4] Gloria David,[4] Patricia Taylor,[5] Joanne Streib,[5] Pieter C. Dorrestein,[2,6] Alex Grier,[7] Steven R. Gill,[7] Karsten Zengler,[3] Tissa R. Hata,[1] Donald Y. M. Leung,[5] Richard L. Gallo[1]*

Staph dominate during flares



Coag negative Staph produce AMPs (functional screen)



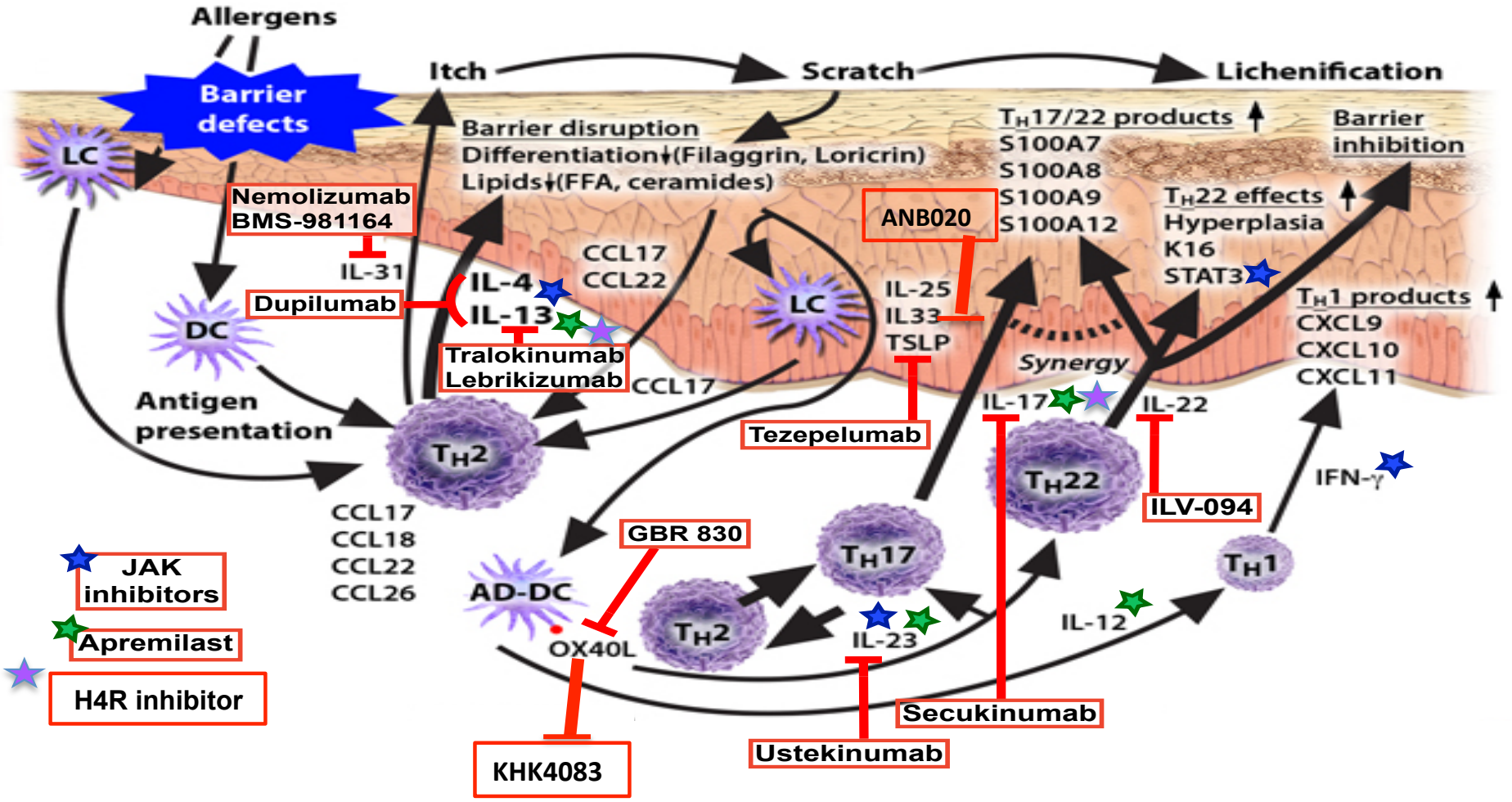
Transplantation of antimicrobial CoNS reduces survival of *S. aureus* on human skin

Subject ID	% Anti–*S. aureus* CoNS	CoNS clones	Species	Antimicrobial class
AMT1	1.2	AMT1-A9	*S. epidermidis*	Lantibiotic
AMT2	0.6	AMT2-A12	*S. hominis*	Lantibiotic
AMT3	1.2	AMT3-A12	*S. hominis*	Lantibiotic
AMT4	15.5	AMT4-C2	*S. hominis*	Lantibiotic
		AMT4-D12	*S. hominis*	Lantibiotic
		AMT4-G1	*S. hominis*	Bacteriocin
AMT5	1.8	AMT5-C5	*S. epidermidis*	Bacteriocin
		AMT5-G6	*S. epidermidis*	Bacteriocin

S. aureus survival was measured by colony c
single applica

Now with AMPs!

Systemic therapy- emerging targets/ therapies

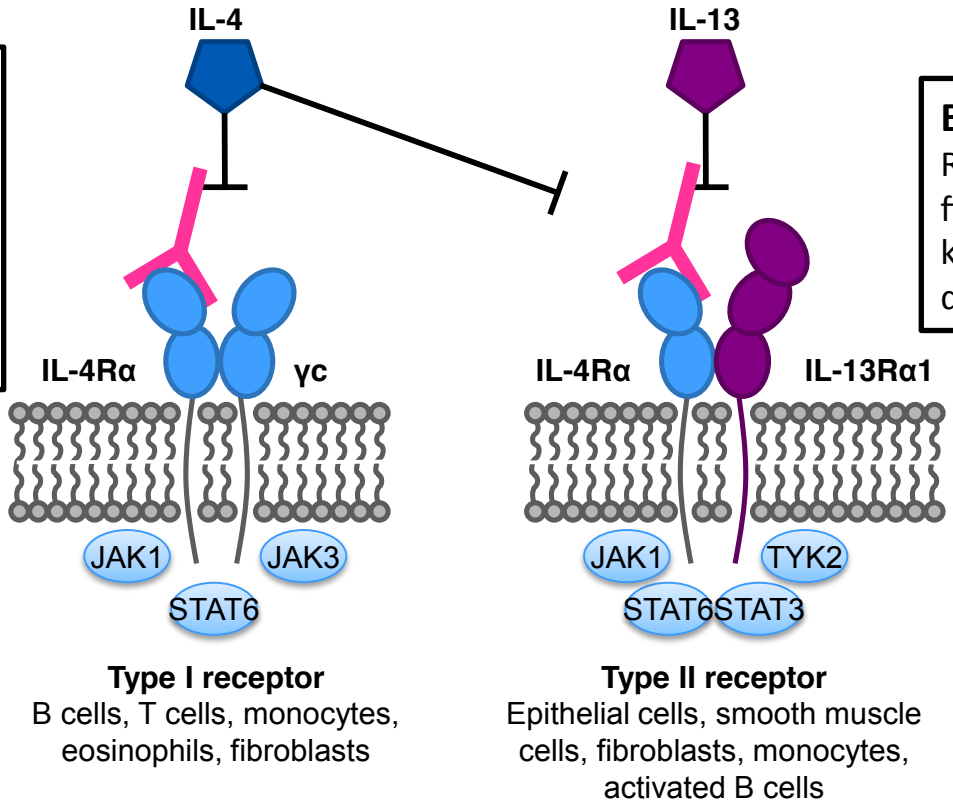


Noda S, Krueger JG, and Guttman-Yassky E. JACI 2015

Dupilumab

Dupilumab blocks the IL-4/IL-13 receptor/ligand system

Immune dysregulation
Promote T cells,
Eosinophils recruitment
inflammatory trafficking,
Mast cell activation and
priming
Il-31 production



Type I receptor
B cells, T cells, monocytes,
eosinophils, fibroblasts

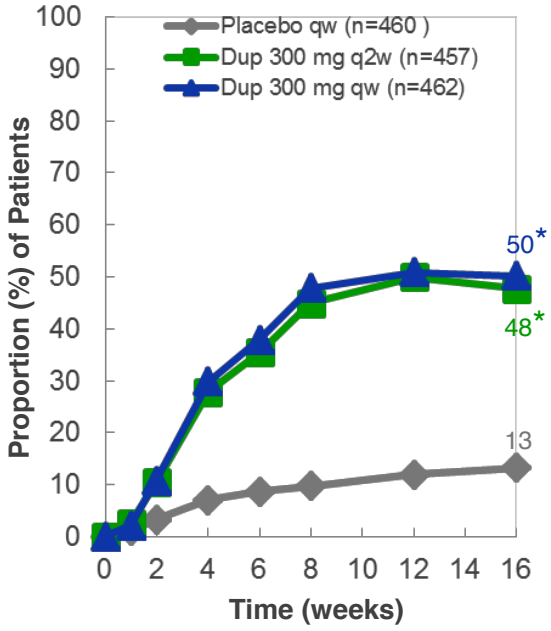
Type II receptor
Epithelial cells, smooth muscle
cells, fibroblasts, monocytes,
activated B cells

Barrier dysregulation
Reduce barrier protiens
fillagrin, AMPs,
keratinocyte terminal
differntiation

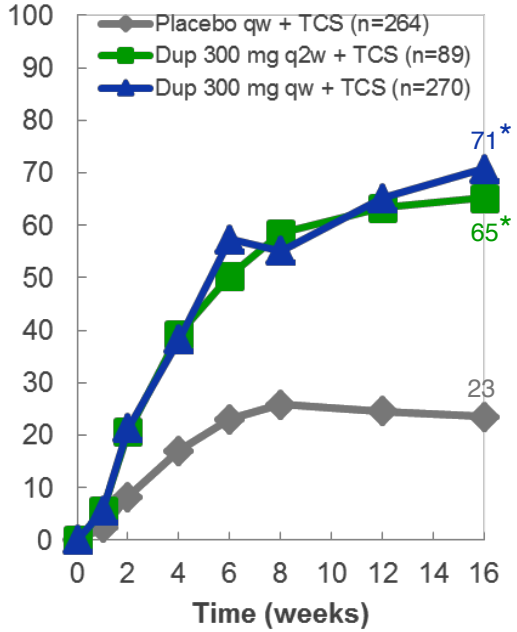
Thaci D, et al. EADV 2013: FC03.3. Sponsored by Regeneron Pharmaceuticals, Inc. and Sanofi

Patients Achieving EASI-75 Through Week 16

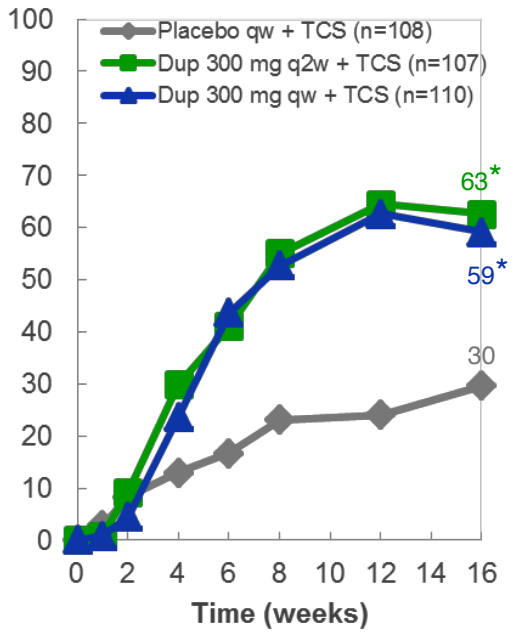
SOLO 1 & 2[1]



CHRONOS[2,†]

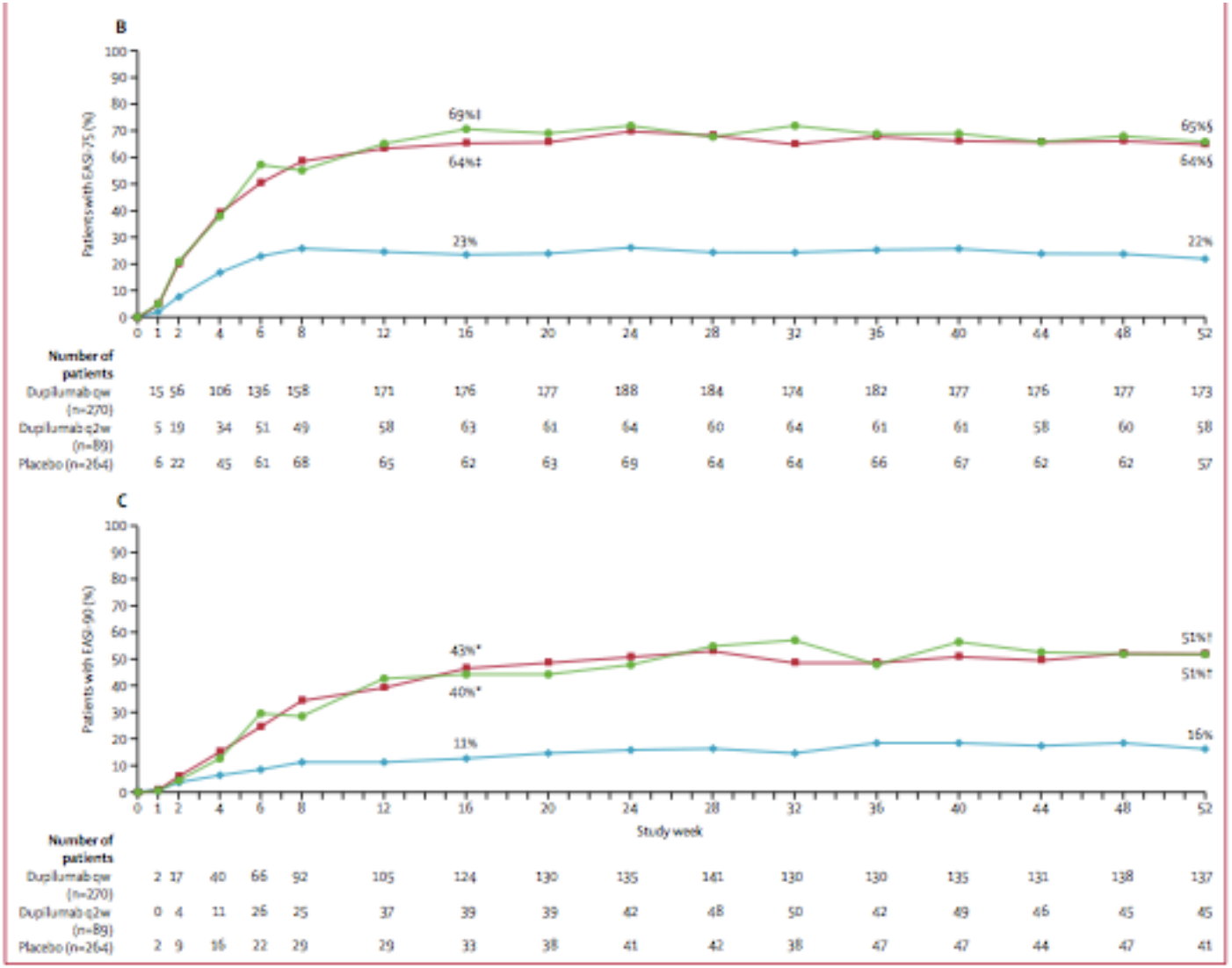


CAFÉ[3]

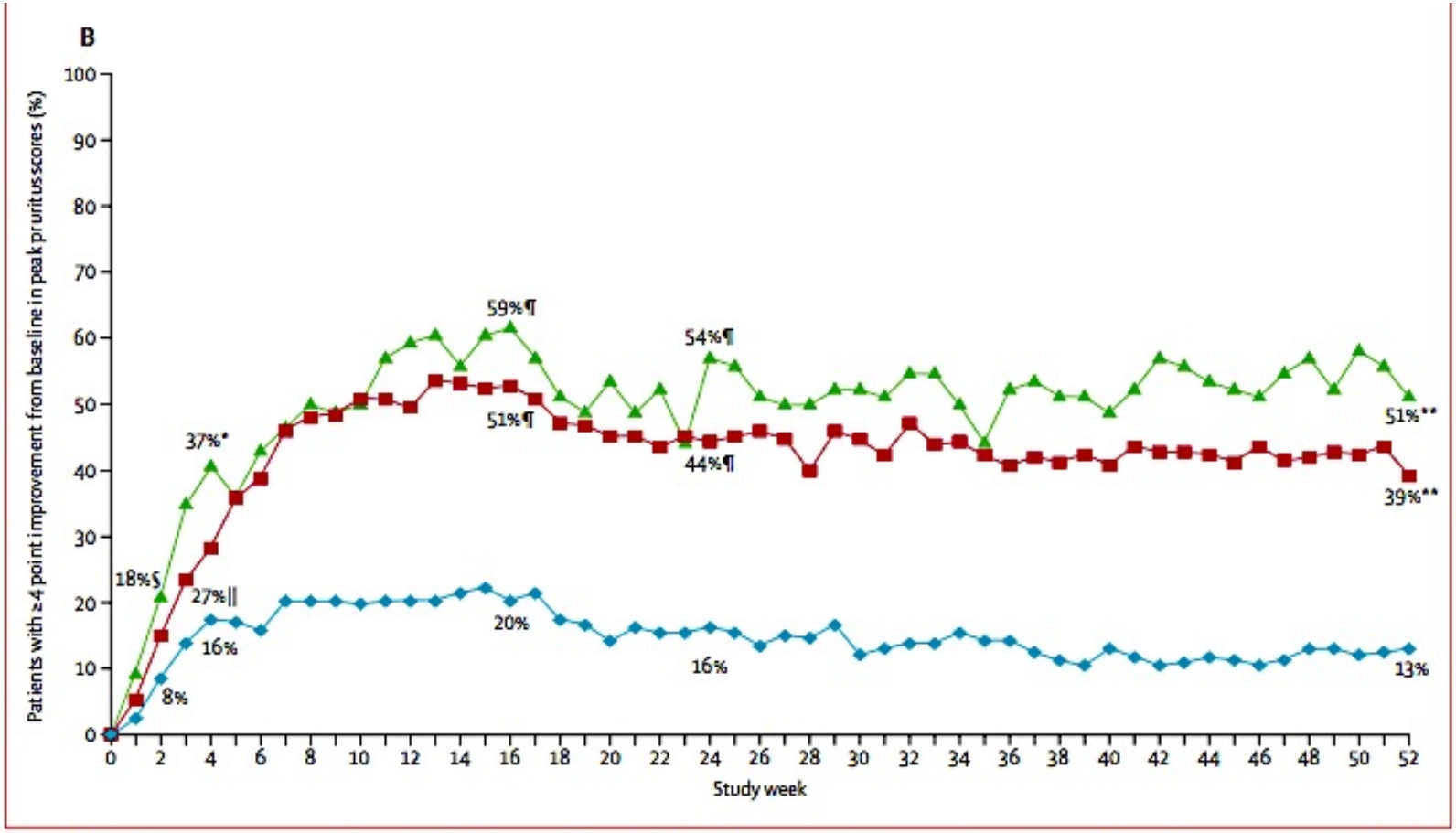


*P<0.0001 vs placebo or placebo + TCS. †Presented data are from the FAS-52 of patients who completed the study before the data cutoff. Week 16 statistics use the FAS.
Patients who used rescue therapy or withdrew from the trial were classified as nonresponders in the statistical analysis. 1. Ferrándiz C *et al.* Presented at: EADV 2017; September 13–17, 2017; Geneva, Switzerland. Abstract FC07.09. 2. Blauvelt A *et al. Lancet* 2017;389:2287–2303. 3. De Bruin-Weller M *et al.* Presented at: EADV 2017; September 13–17, 2017; Geneva, Switzerland. Abstract D3T01.1B.

Efficacy at 1 year

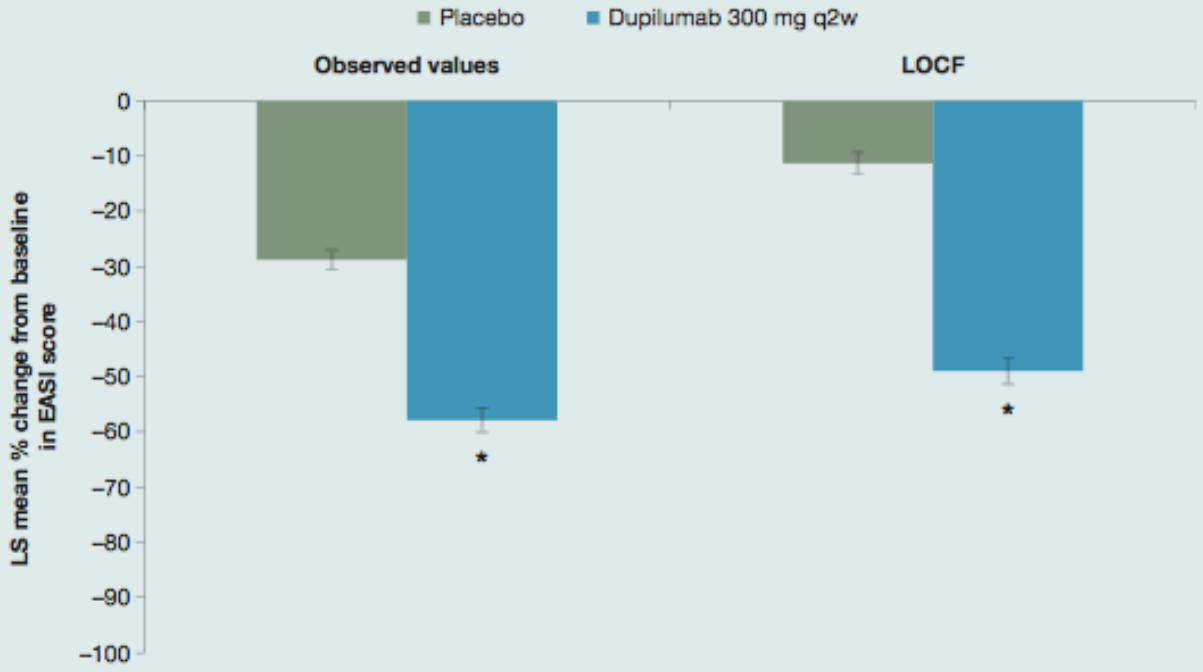


Itch


B
Patients with ≥4 point improvement from baseline in peak pruritus scores (%)
Study week
18%§
27%‖
37%*
59%¶
51%¶
54%¶
44%¶
51%**
39%**
8%
16%
20%
16%
13%

? Non responders

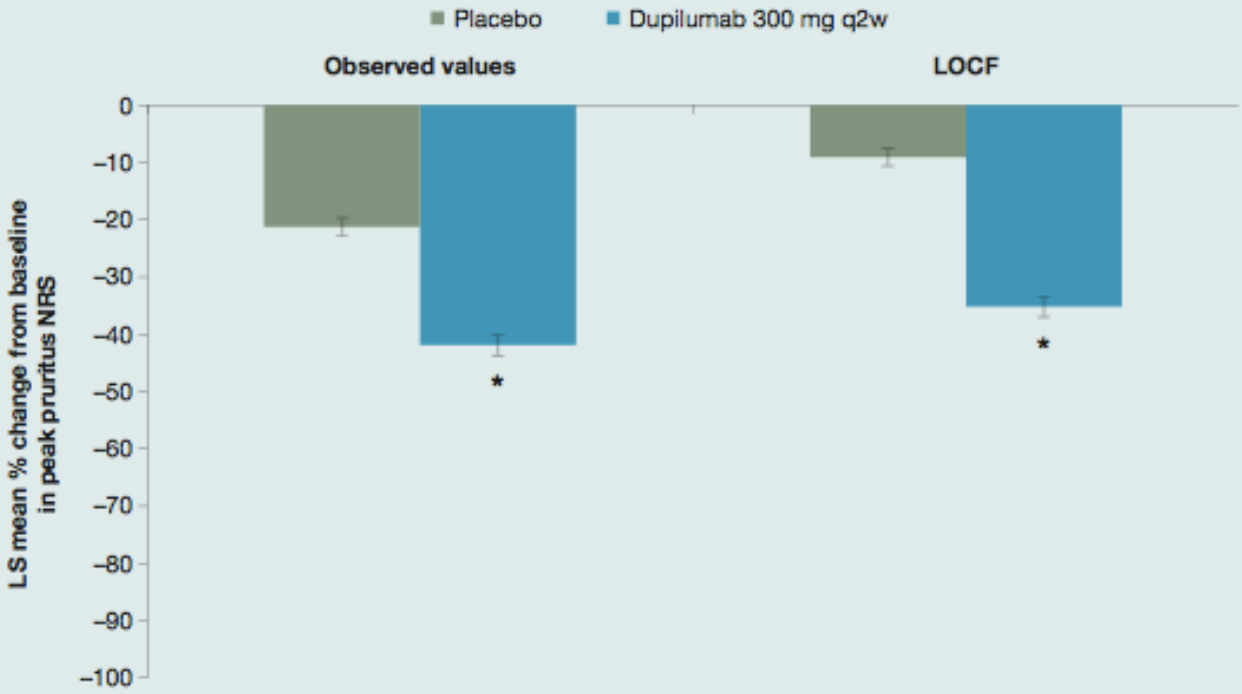
Figure 2. Percent change from baseline in EASI score at Week 16 in patients not achieving IGA 0 or 1.



IGA at Week 16	Placebo (Observed values), N	Dupilumab 300 mg q2w (Observed values), N	Placebo (LOCF), N	Dupilumab 300 mg q2w (LOCF), N
2, 3, or 4	370	262	396	278

Error bars indicate standard error (SE). *$P < 0.0001$ vs placebo.

Figure 4. Percent change from baseline in peak pruritus NRS score at Week 16 in patients not achieving IGA 0 or 1.



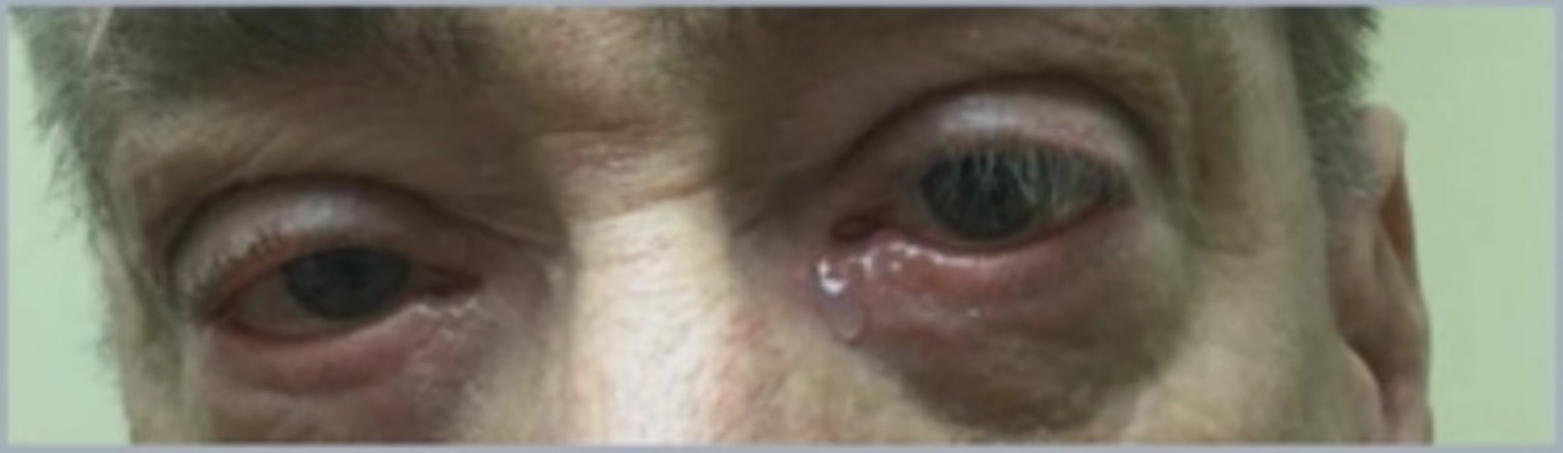
IGA at Week 16	Placebo (Observed values), N	Dupilumab 300 mg q2w (Observed values), N	Placebo (LOCF), N	Dupilumab 300 mg q2w (LOCF), N
2, 3, or 4	360	255	395	275

Error bars indicate SE. *$P < 0.0001$ vs placebo.

	n			n per 100 patient-years		
	Placebo qw plus TCS (n=315)	Dupilumab 300 mg q2w plus TCS (n=110)	Dupilumab 300 mg qw plus TCS (n=315)	Placebo qw plus TCS (n=315)	Dupilumab 300 mg q2w plus TCS (n=110)	Dupilumab 300 mg qw plus TCS (n=315)
Adverse events						
Total number of adverse events	1493	478	1482	532·38	476·23	507·73
Total number of serious adverse events	22	5	10	7·85	4·98	3·43
Patients with adverse events						
≥1 adverse event	84% (266)	88% (97)	83% (261)	321·38	383·68	322·89
Death†	0	0	<1% (1)	0	0	0·34
≥1 serious adverse event	5% (16)	4% (4)	3% (9)	5·86	4·05	3·12
Adverse events leading to treatment discontinuation	8% (24)	2% (2)	3% (9)	8·52	2·70	2·81
Adverse events (SOC‡–PT§)						
Infections and infestations‡	58% (182)	57% (63)	53% (166)	108·08	101·50	94·33
Nasopharyngitis§	19% (61)	23% (25)	19% (60)	24·80	29·23	23·67
Upper respiratory tract infection§	10% (32)	10% (11)	14% (43)	12·27	11·89	16·17
Sinusitis§	3% (9)	2% (2)	6% (18)	3·26	2·00	6·43
Influenza§	5% (17)	4% (4)	3% (9)	6·24	4·06	3·13
Eye disorders‡	15% (46)	31% (34)	32% (102)	17·99	43·63	44·85
Conjunctivitis¶‖	8% (25)	14% (15)	19% (61)	9·42	16·36	23·81
Skin and subcutaneous tissue disorders‡	53% (167)	28% (31)	33% (103)	96·50	38·27	45·84
Atopic dermatitis§	46% (144)	18% (20)	17% (52)	73·37	22·61	19·96
General disorders and administration site conditions‡	16% (50)	26% (29)	26% (81)	20·32	36·24	35·20
Injection site reaction§	8% (24)	15% (16)	19% (60)	9·19	17·94	24·45
Respiratory-thoracic and mediastinal disorders‡	17% (53)	12% (13)	14% (45)	21·35	14·20	16·94
Asthma§	6% (19)	5% (5)	1% (2)	7·06	5·15	0·69
Nervous system disorders‡	12% (38)	9% (10)	12% (38)	14·94	10·80	14·37
Headache§	6% (19)	5% (5)	8% (24)	7·12	5·19	8·78
Non-herpetic skin infections**	18% (56)	11% (12)	8% (26)	59·3	36·1	27·4
Any herpes infections¶	8% (25)	7% (8)	7% (22)	25·6	24·0	22·7
Oral herpes§	3% (9)	4% (4)	5% (15)	3·26	4·10	5·30
Herpes simplex§	1% (2)	3% (3)	2% (5)	0·72	3·03	1·73
Herpes virus infection§	<1% (1)	1% (1)	1% (2)	0·36	1·00	0·69
Herpes zoster§	2% (5)	1% (1)	<1% (1)	1·80	1·00	0·34
Eczema herpeticum§	2% (6)	1% (1)	0	2·17	1·01	0
Genital herpes§	<1% (1)	0	<1% (1)	0·36	0	0·34
Herpes ophthalmic§	1% (2)	0	<1% (1)	0·72	0	0·34
Ophthalmic herpes simplex§	0	0	<1% (1)	0	0	0·34
Ophthalmic herpes zoster§	<1% (1)	0	0	0·36	0	0

MedDRA=Medical Dictionary for Regulatory Activities. PT=preferred term. q2w=every 2 weeks. qw=once weekly. SOC=system organ class. TCS=topical corticosteroids. *Safety analyses were done with the safety analysis set, which included all randomised patients who received a dose of any study drug (appendix p 13). The adverse events included here that are listed as number of patients (%) according to the PTs in the MedDRA version 18.0 were those that occurred in at least 5% of the patients in any study group, with the exception that all herpesviral PTs are listed. Adverse events were defined as any untoward medical occurrence; serious adverse events as any adverse event that results in death, is life-threatening, requires hospital admission or prolongation of existing hospital admission, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is an important medical event. †One patient died as a result of a motor vehicle accident; this was considered to be not related to study drug. ‡Adverse event reported at the PT level of the MedDRA hierarchy. §Adverse event reported at SOC level of the MedDRA hierarchy. ¶Adverse event reported at the high-level term level of the MedDRA hierarchy. ‖Conjunctivitis (high-level term) includes the PTs conjunctivitis allergic, conjunctivitis bacterial, atopic keratoconjunctivitis, and conjunctivitis. **Adjudicated.

Table 3: **Adverse events reported in patients in any treatment group during the 52-week treatment period (safety analysis set)***



Conjunctivitis at q2week dosing through Week 16:

SOLO Pooled data: 10% vs 2%

CHRONOS: 9% vs 5% (11.8 vs 6% at Week 52)

CAFÉ: 28% vs 11%

Conjunctivitis treatment on Dupilumab

- Lubricating eye drops
- Opthalmology referral
- Steroid eye drops
- Topical Csa 0.05% opthalmic emulsion
- Tacrolimus 0.03% eye ointment compounded

  - ***Wollenberg et al. Conjunctivitis Occuring in Atopic Dermatitis Patients treated with Dupilumab- Clinical Characteristics and Treatment. JACI 2018***

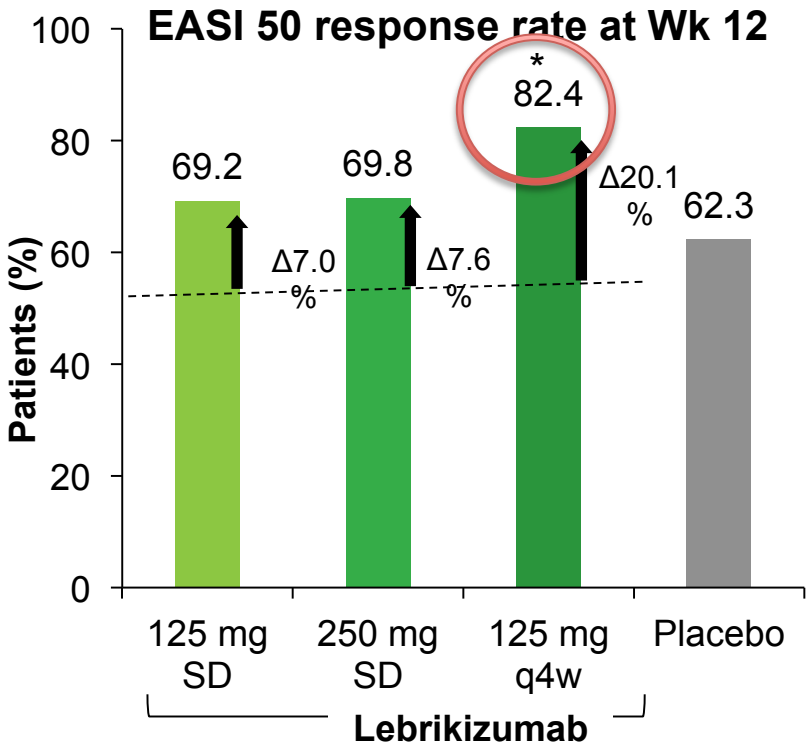
IL-13 inhibition

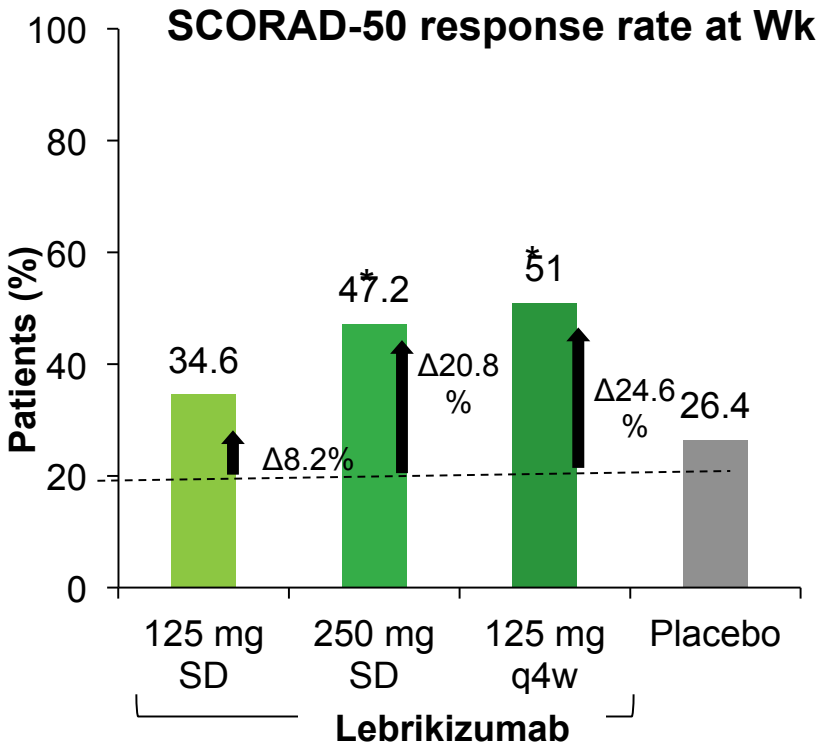
Is IL-13 inhibition enough for controlling AD or do we need dual inhibition

Two Phase 2 trails complete

- Librikizumab
- Tralokinumab

TREBLE: Primary endpoints for lebrikizumab in patients with moderate to severe AD

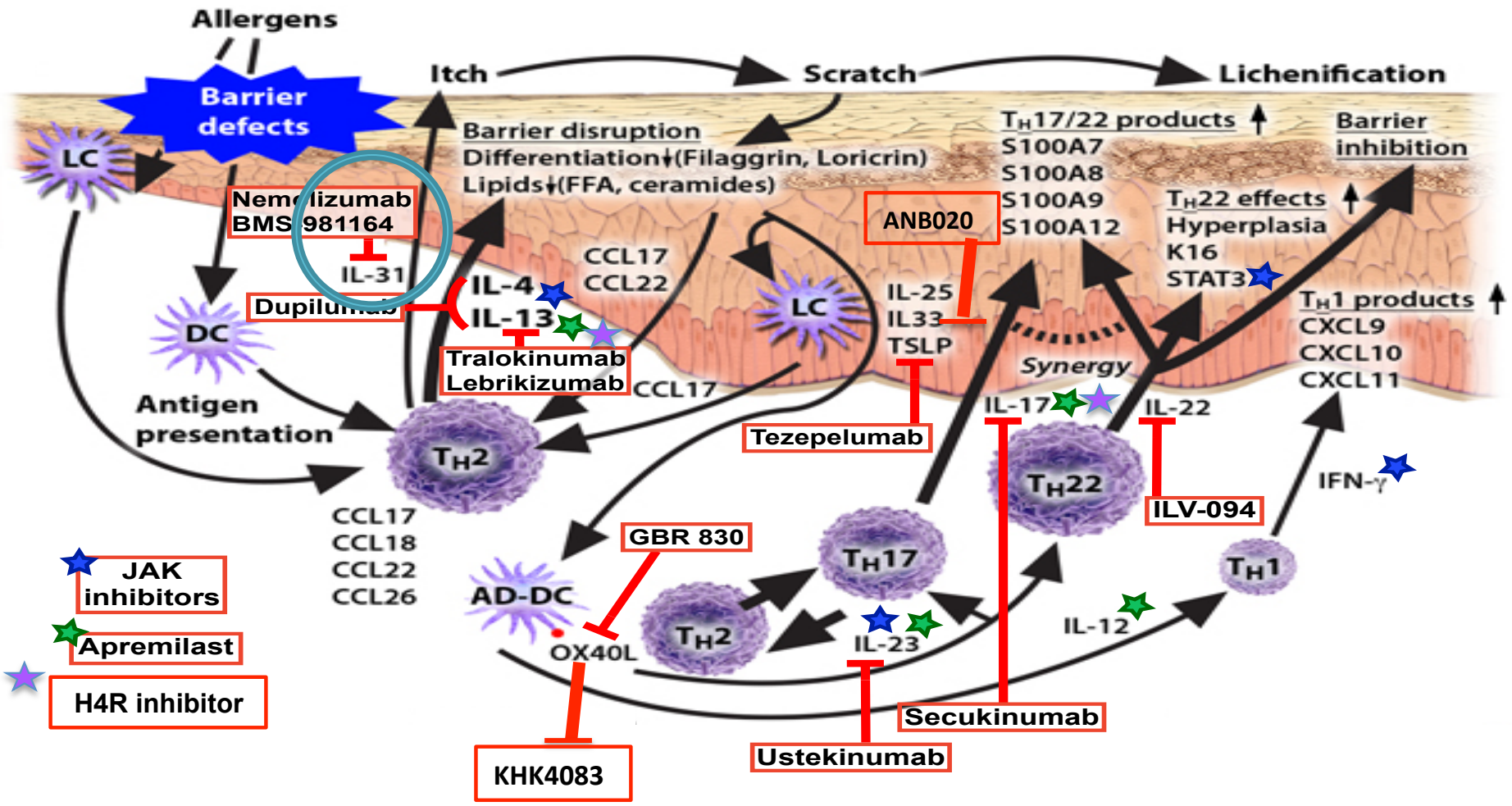




*P<0.05 vs placebo; SD, single dose

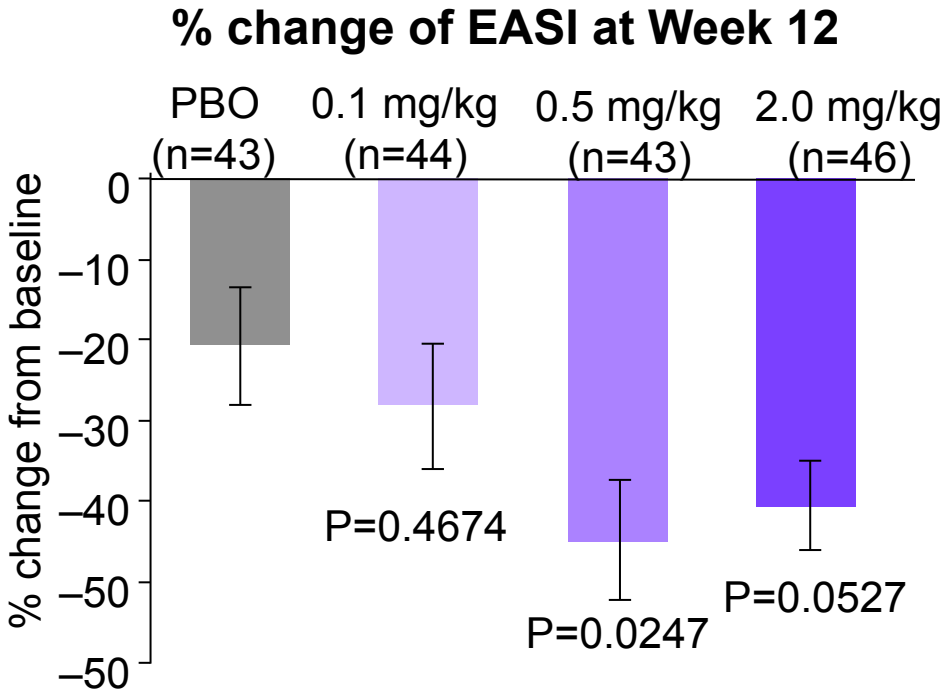
Pruritus VAS
mean change from baseline
-34.9 to -40.7

EADV 2016,



Noda S, Krueger JG, and Guttman-Yassky E. JACI 2015

Phase 2 study of Nemolizumab (anti-IL 31 receptor monoclonal antibody) in patients with moderate to severe AD



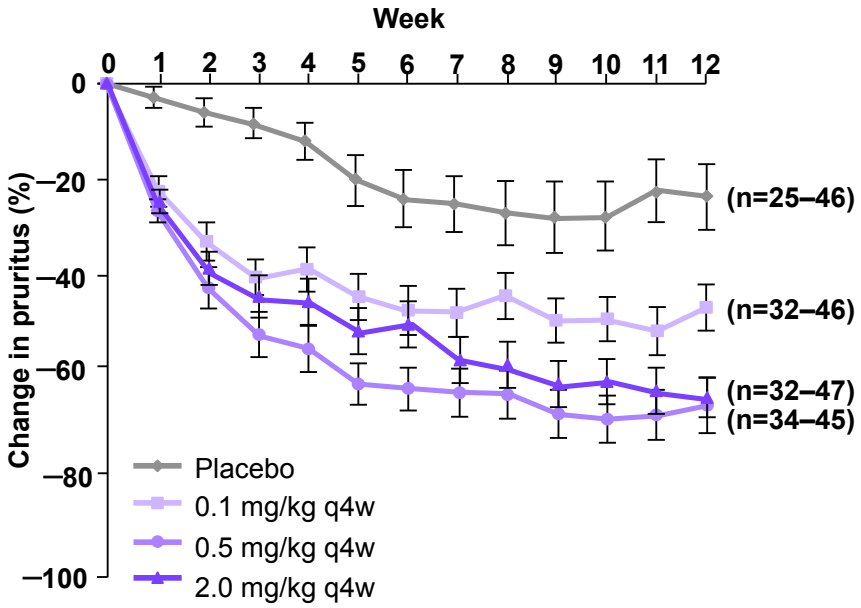
Summary:

- Reduction in pruritus of up to 60%
- Improved quantity and quality of sleep
- Improved QoL
- Improvement in dermatitis

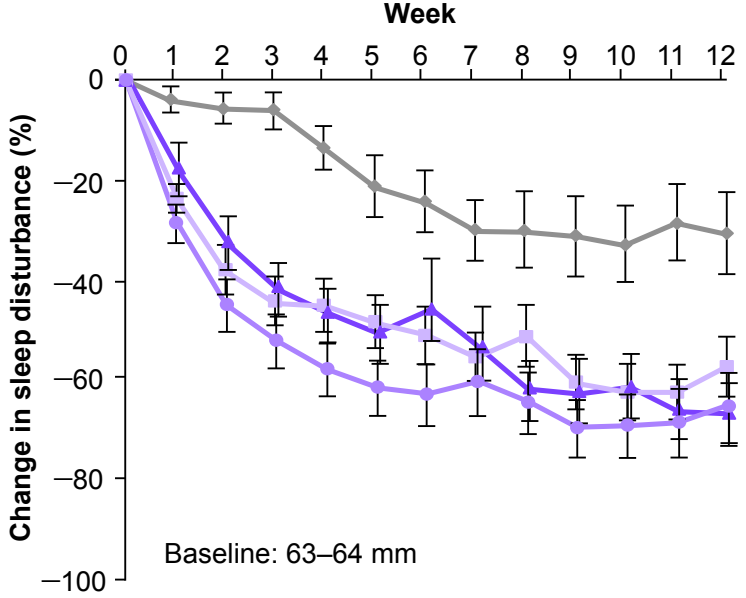
Ruzicka T, et al NEJM 2017

Phase 2 study of nemolizumab in patients with moderate to severe AD: Change in pruritus and sleep disturbance VAS

Time course of percentage change in pruritus VAS



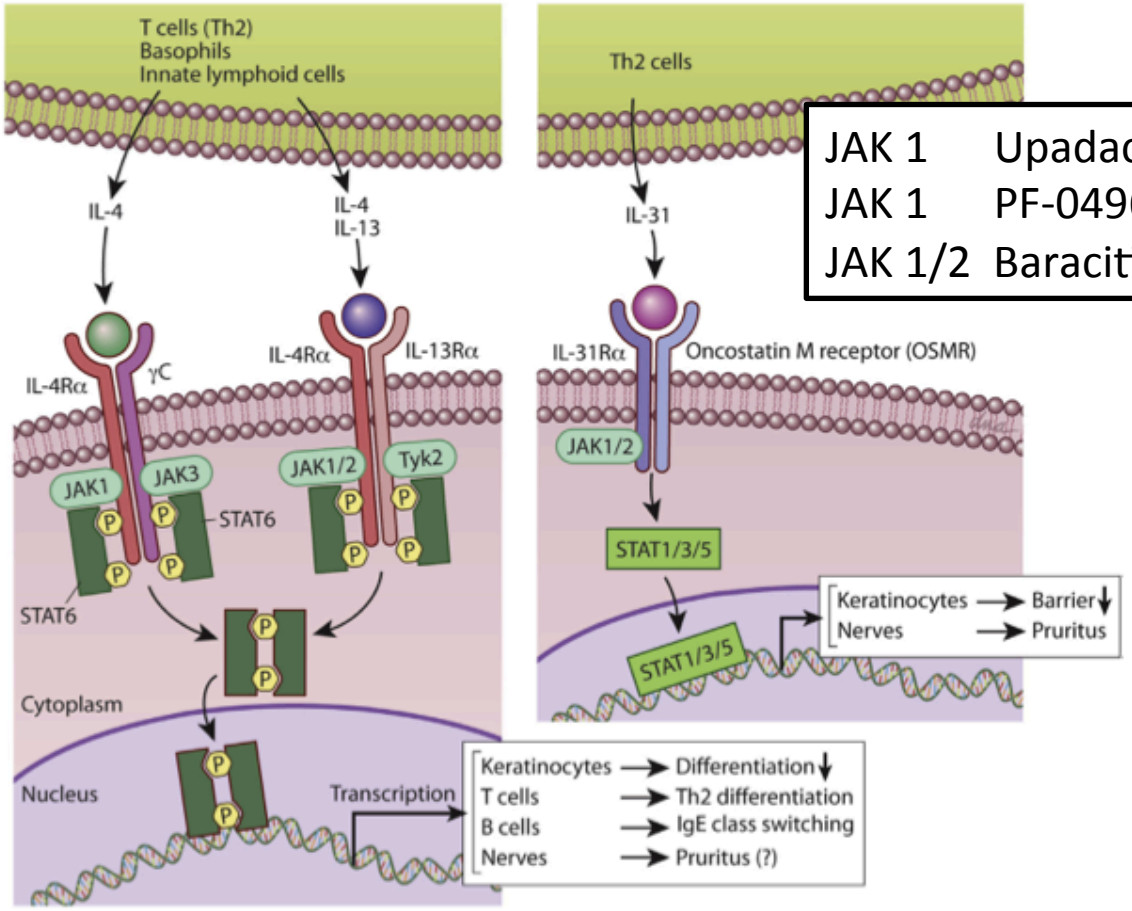
Time course of percentage change in sleep disturbance VAS



Mean ± SE; Per-protocol population, no imputation, excluded data after rescue therapy

Ruzicka T, et al. NEJM 2017.

JAKs



JAK 1	Upadacitinib (AbbVie)
JAK 1	PF-04965842 (Pfizer)
JAK 1/2	Baracitinib (Lily)

FIG 2. JAK-STAT signaling. Schematic diagram of the IL-4/IL-13/STAT6 signaling pathways through IL-4 receptor α and JAK1. γc activates JAK3, whereas IL-13 receptor α1 activates tyrosine kinase 2 *(TYK2)* and JAK2. Activated JAKs then phosphorylate STAT6. Phosphorylated STAT6 dimerizes, migrates to the nucleus, and binds to the promoters of the IL-4– and IL-13–responsive genes, such as those associated with impaired keratinocyte differentiation, T_H2 cell differentiation, IgE class-switching, and possible pruritus. Similarly, IL-31 binds to IL-31 receptor A, activates JAK1/2, and then phosphorylates STAT1/3/5. These signals lead to impaired skin barrier function and pruritus.

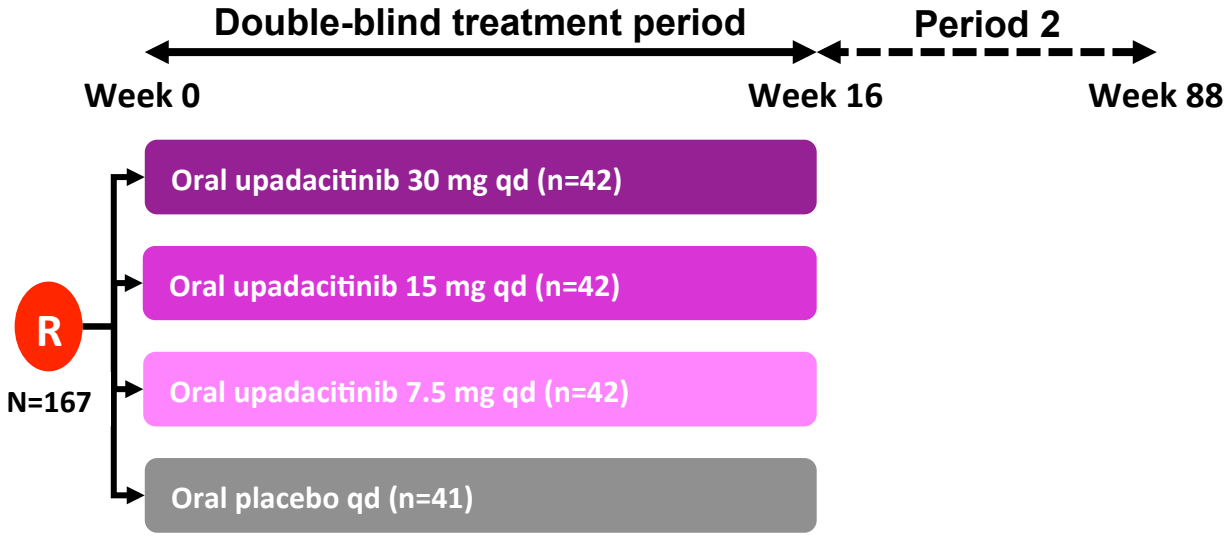
Phase 2b randomized, placebo-controlled, dose-ranging trial of JAK1 inhibitor upadacitinib in moderate to severe AD

Inclusion criteria

- Age: 18–75 years
- EASI score ≥16
- BSA ≥10%
- IGA score ≥3
- Inadequate response to TCS or TCI (or topical treatments medically inadvisable)

Exclusion criteria

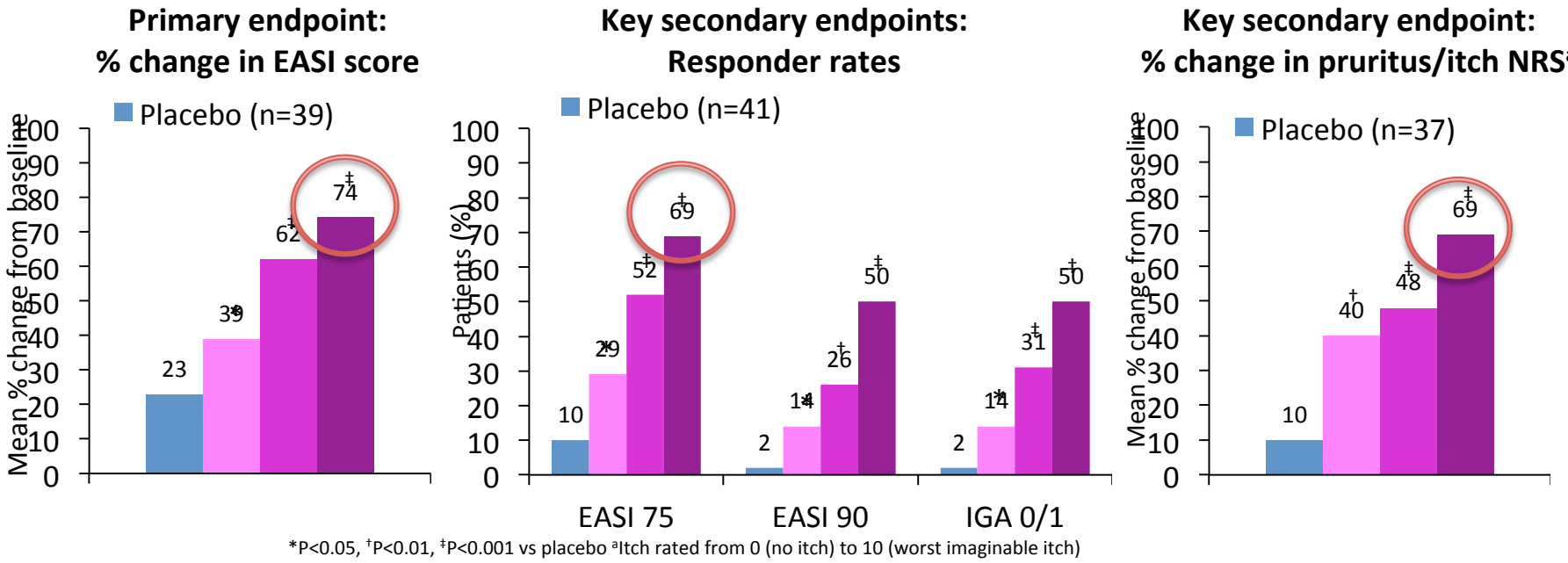
- Prior exposure to a JAK inhibitor or dupilumab



- Primary endpoint: Mean % change in EASI score at Week 16 compared with placebo
- Key secondary endpoints: Proportion of patients achieving EASI 90, EASI 75, IGA 0 or 1 at Week 16, and % change in pruritus/itch NRS from baseline to Week 16, compared with placebo

ClinicalTrials.gov: NCT02925117
AbbVie data on file. Upadacitinib AD Phase 2b press release; available at https://news.abbvie.com/news/press-releases (accessed September 7, 2017)

Dose Response in all primary and secondary endpoints



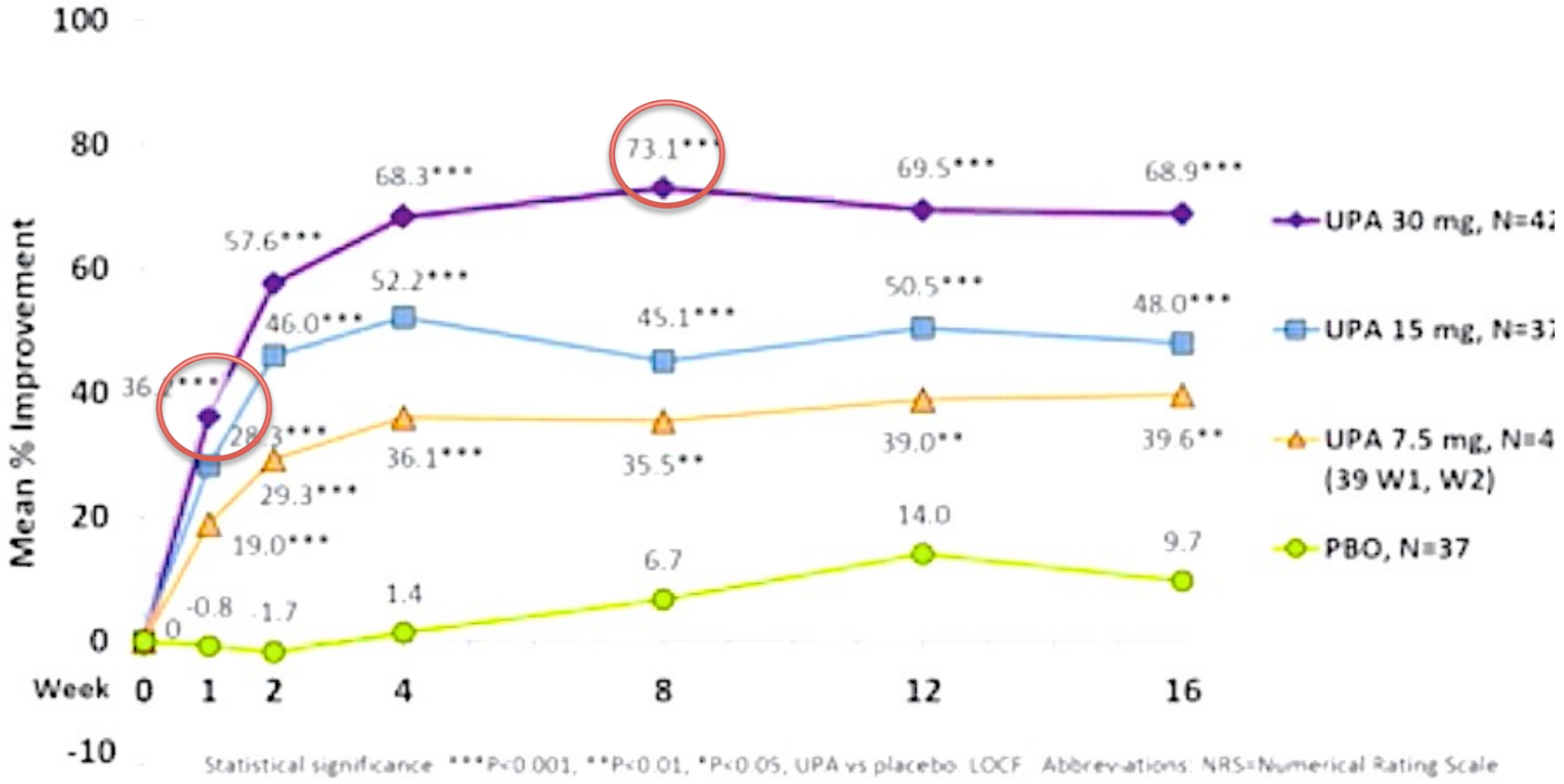
*P<0.05, †P<0.01, ‡P<0.001 vs placebo [a]Itch rated from 0 (no itch) to 10 (worst imaginable itch)

- **JAK Inhibitors seem to have a better safety profile in AD compared to RA and psoriasis**
- **No herpes zoster, malignancies, deaths or cases of pulmonary embolism or deep vein thrombosis were reported**

AbbVie data on file. Upadacitinib AD Phase 2b press release; available at https://news.abbvie.com/news/press-releases (accessed September 7, 2017)

Key Secondary Endpoints (continued):

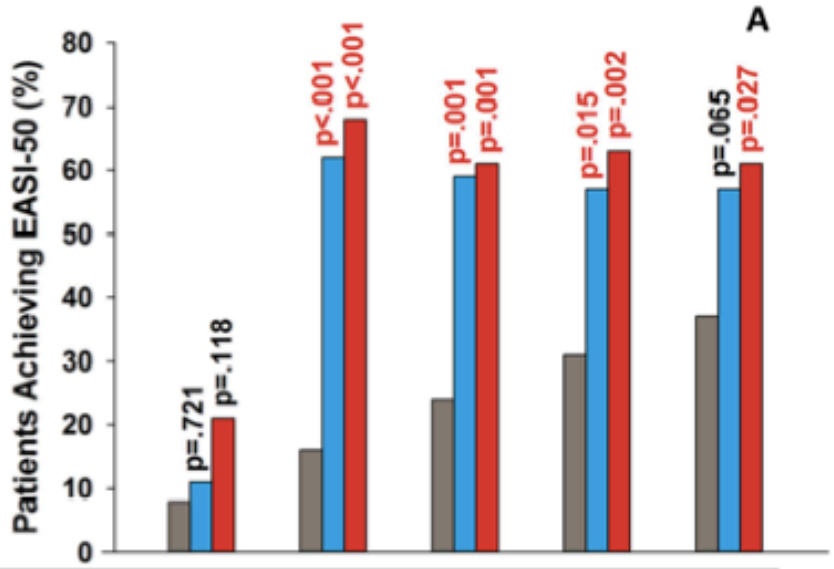
Mean % improvement from baseline in pruritus NRS through week 16



Statistical significance: ***P<0.001, **P<0.01, *P<0.05, UPA vs placebo. LOCF. Abbreviations: NRS=Numerical Rating Scale

Baracitinib in patients with moderate to severe Atopic dermatitis: a phase 2 parallel, double blinded, randomized placebo-controllled multiple dose study

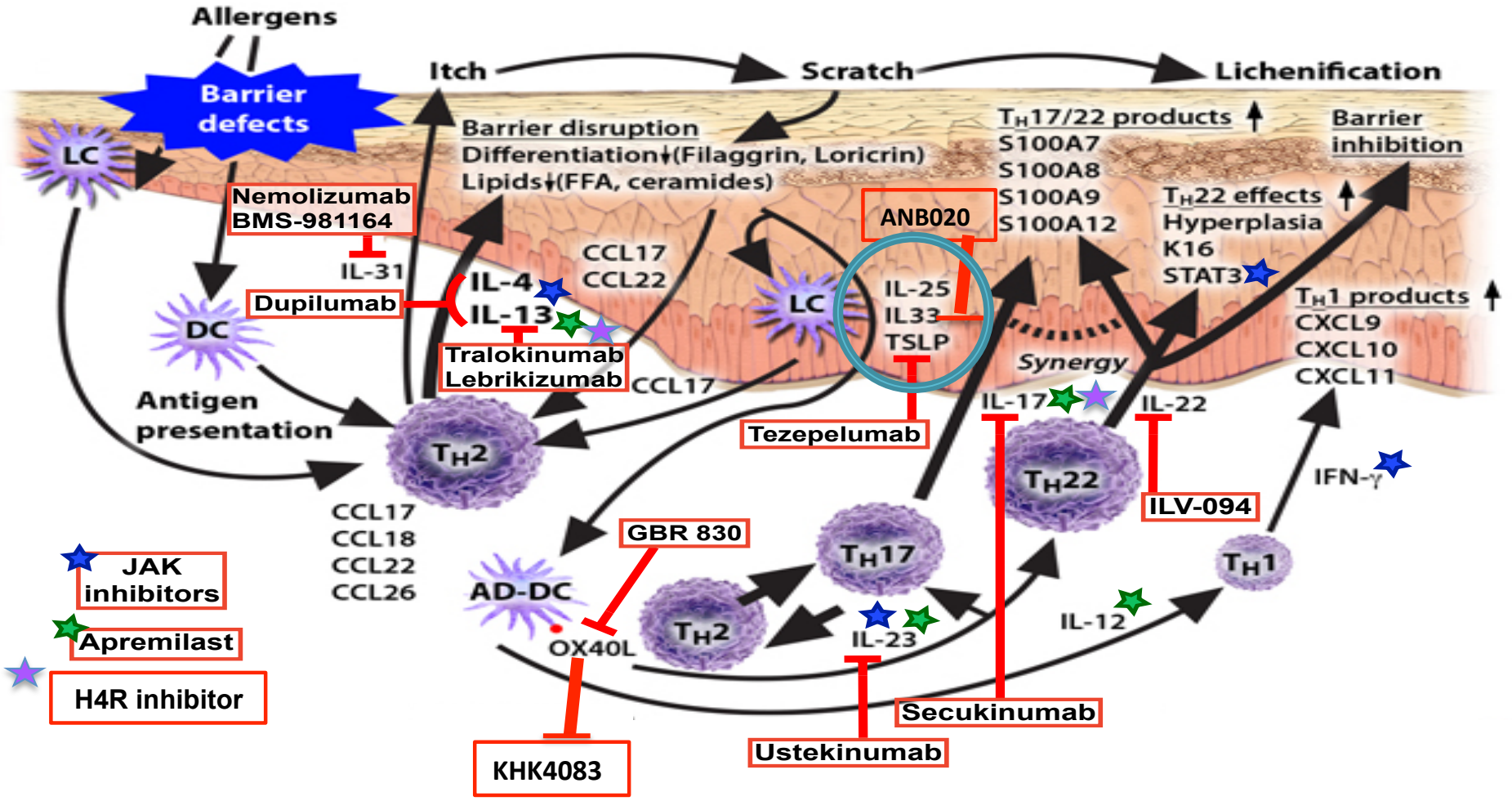
Fig 2. Percentage of patients achieving EASI-50 (A) and percentage change from baseline in EASI score (B).



Weeks	1	4	8	12	16
Placebo + TCS (%)	8	16	24	31	37
Baricitinib 2 mg + TCS (%)	11	62	59	57	57
Baricitinib 4 mg + TCS (%)	21	68	61	63	61

New treatments

IL-33

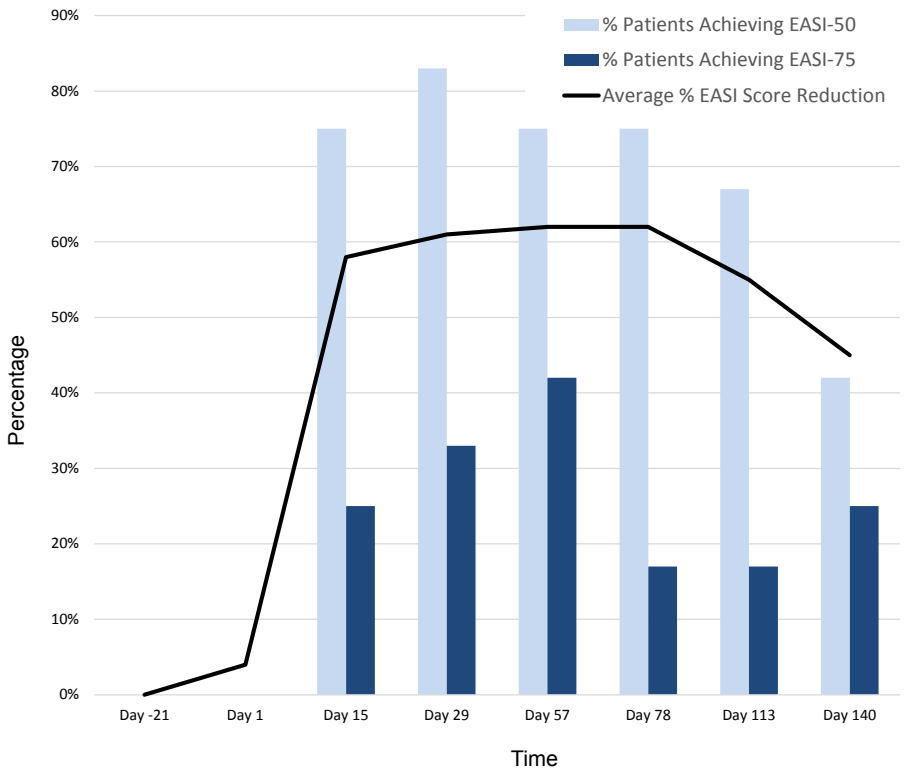


Noda S, Krueger JG, and Guttman-Yassky E. JACI 2015

IL-33

EASI Scores Following Single ANB020 Dose

Rapid response and all patients achieved EASI-50 on or before Day 57



Timepoint	Average % EASI Score Reduction*	% Patients Achieving EASI-50*	% Patients Achieving EASI-75*
Day -21 (Baseline)	0%	0	0
Day 1 (ANB020 Dosing)	4%	0	0
Day 15	58%	9 of 12 (75%)	3 of 12 (25%)
Day 29	61%	10 of 12 (83%)	4 of 12 (33%)
Day 57	62%	9 of 12 (75%)	5 of 12 (42%)
Day 78	62%	9 of 12 (75%)	2 of 12 (17%)
Day 113	55%	8 of 12 (67%)	2 of 12 (17%)
Day 140	45%	5 of 12 (42%)	3 of 12 (25%)

* Relative to baseline upon enrollment at Day -21

- ***MOR106, an Anti-IL-17C mAb, a Potential New Approach for Treatment of Moderate-to-severe Atopic Dermatitis: Phase 1 Study***

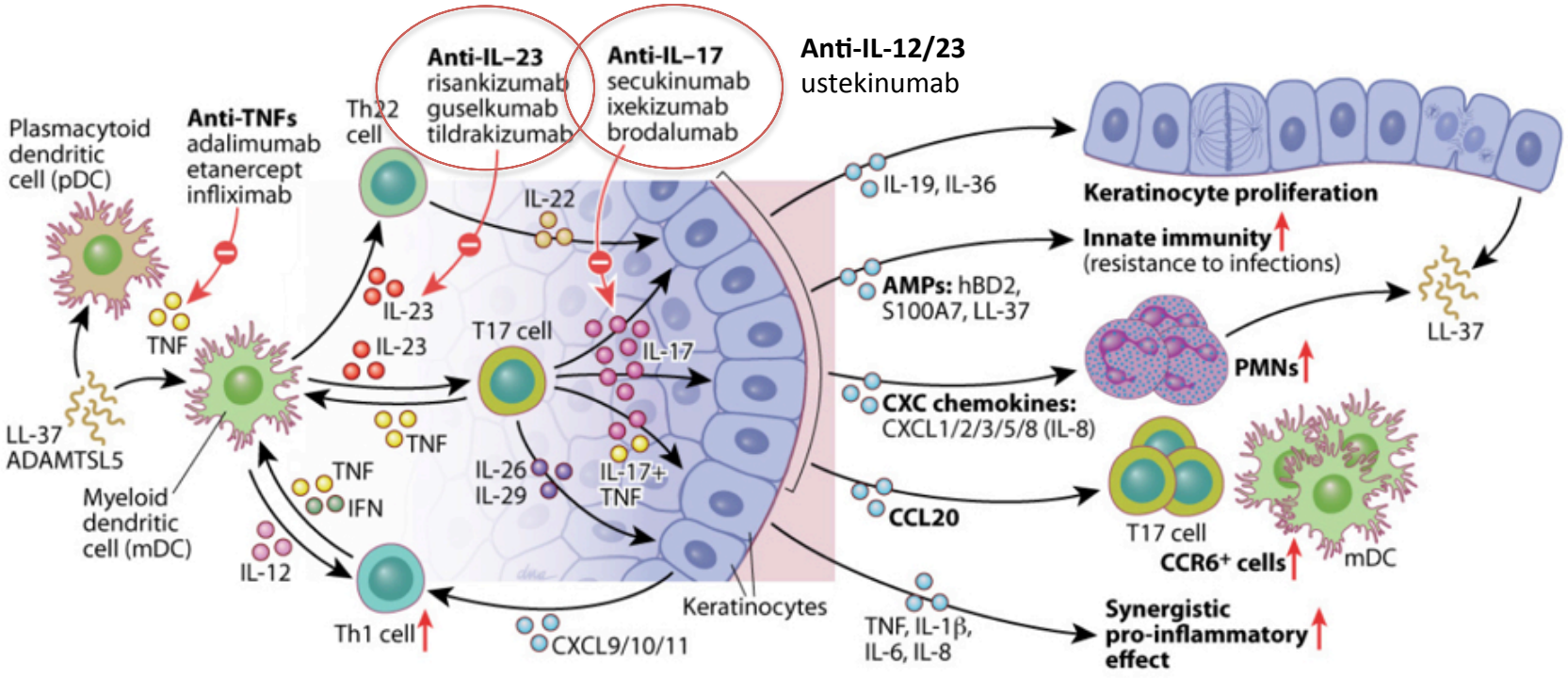
- ***Oral ASN002, a Novel JAK/SYK inhibitor, in Patients with Moderate-to-Severe Atopic Dermatitis: A Randomized, Double-Blind, Placebo-Controlled Clinical Study***

Psoriasis

- PSO updates “late breakers”
  - IL-17
  - IL-23
  - Cardiovascular disease and PSO

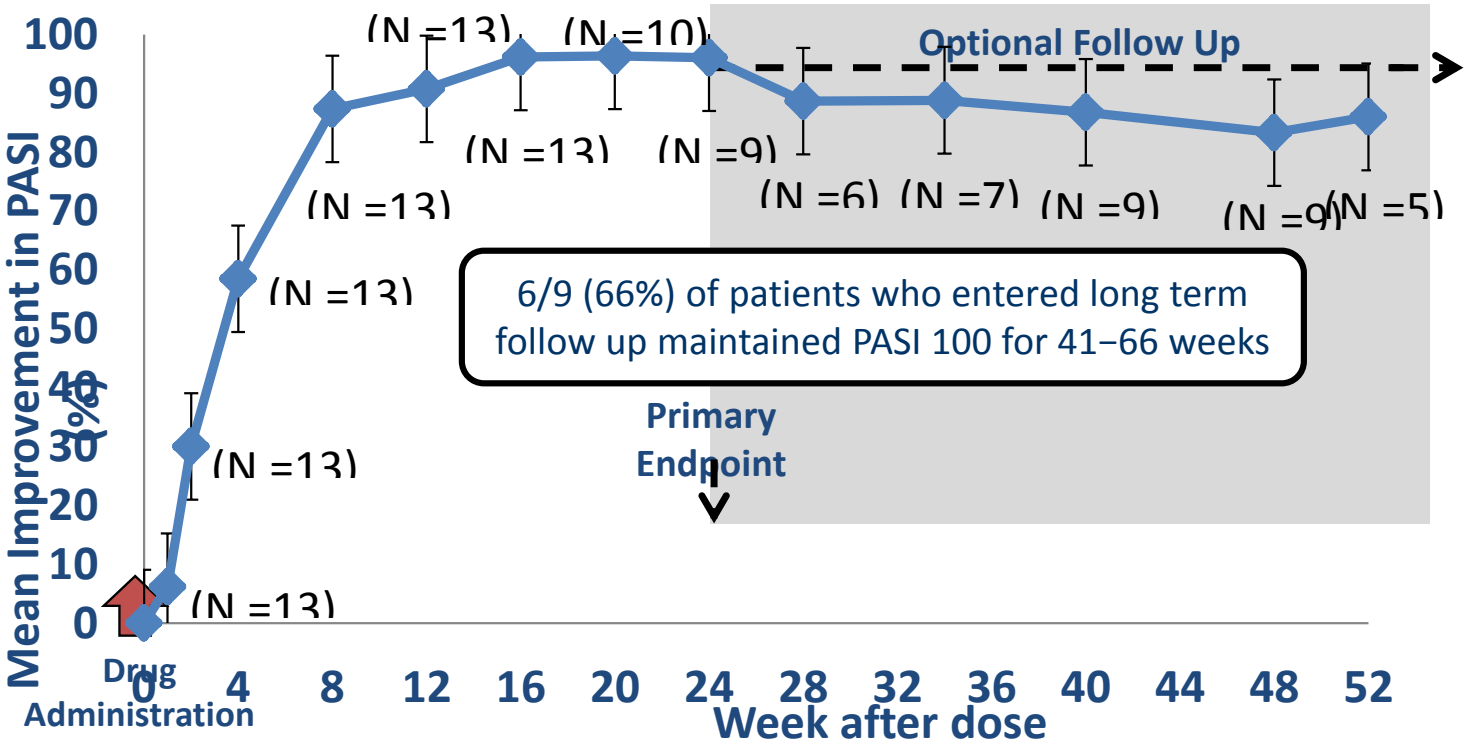
- How to choose?

Psoriasis whats new?



Hawkes JE, Chan TC, Krueger JG. JACI (2017).

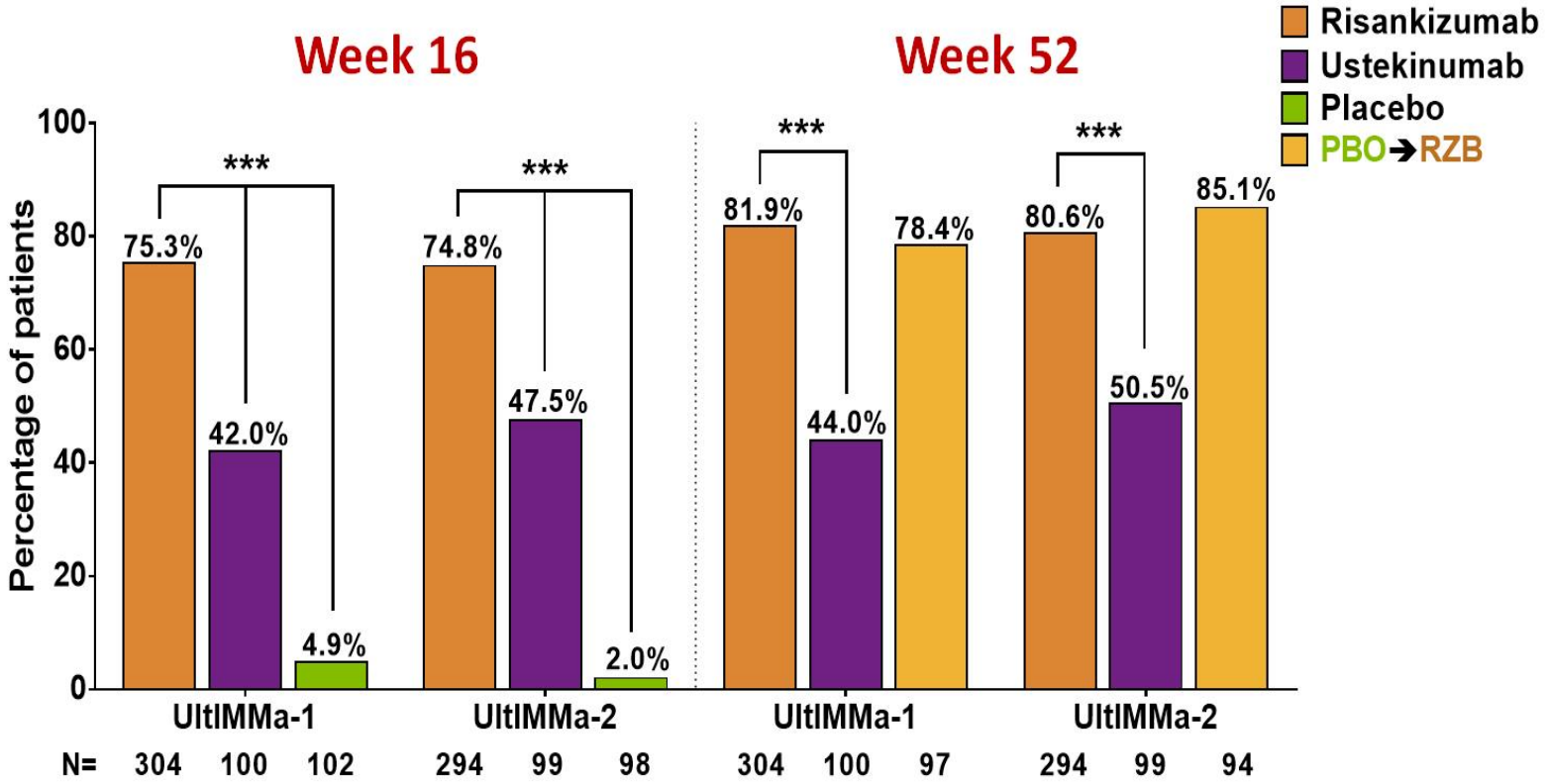
Mean PASI Improvement in Patients Treated with Subcutaneous RISANKIZUMAB (0.25 and 1.0 mg/kg)



Krueger et al. J. Allergy Clinical Immunology. Published on line 12 March 2015

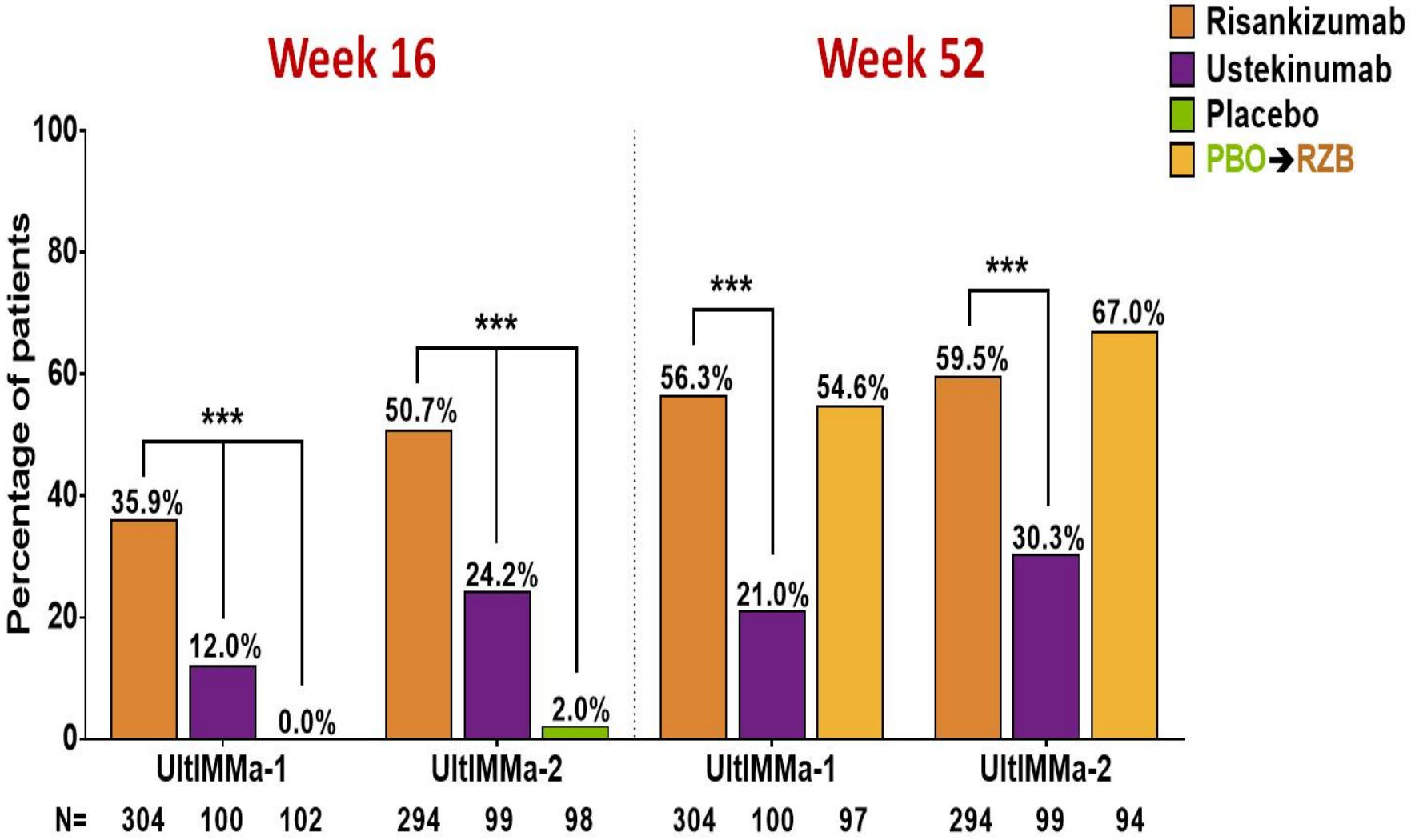
Efficacy and safety of risankizumab: results from two double blind, placebo and ustekinumab controlled, phase 3 trials in moderate to severe plaque Psoriasis, Ultimate 1&2

Results: PASI 90 Responses at Weeks 16 and 52 (NRI)



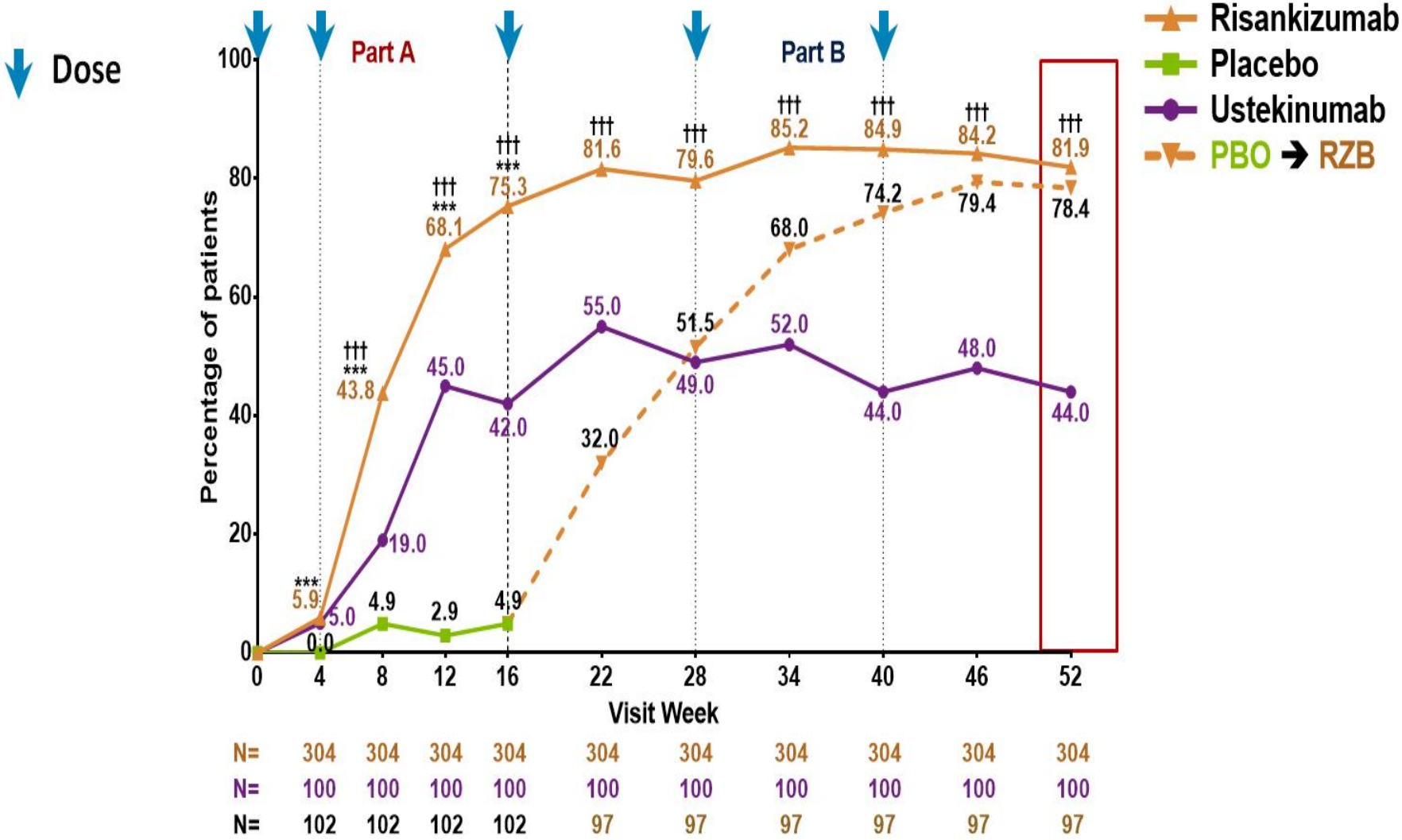
P-values for comparison vs placebo or ustekinumab: *, P <0.05; ***, P <0.001. NRI = Non-Responder Imputation; PASI = Psoriasis Area and Severity Index; PBO = Placebo; RZB = Risankizumab.

Results: PASI 100 Responses at Weeks 16 and 52 (NRI)



P-values for comparison vs placebo or ustekinumab: *, P <0.05; ***, P <0.001. NRI = Non-Responder Imputation; PASI = Psoriasis Area and Severity Index; PBO = Placebo; RZB = Risankizumab.

Results: Time Course of PASI 90 Responses (NRI) – UltIMMa-1



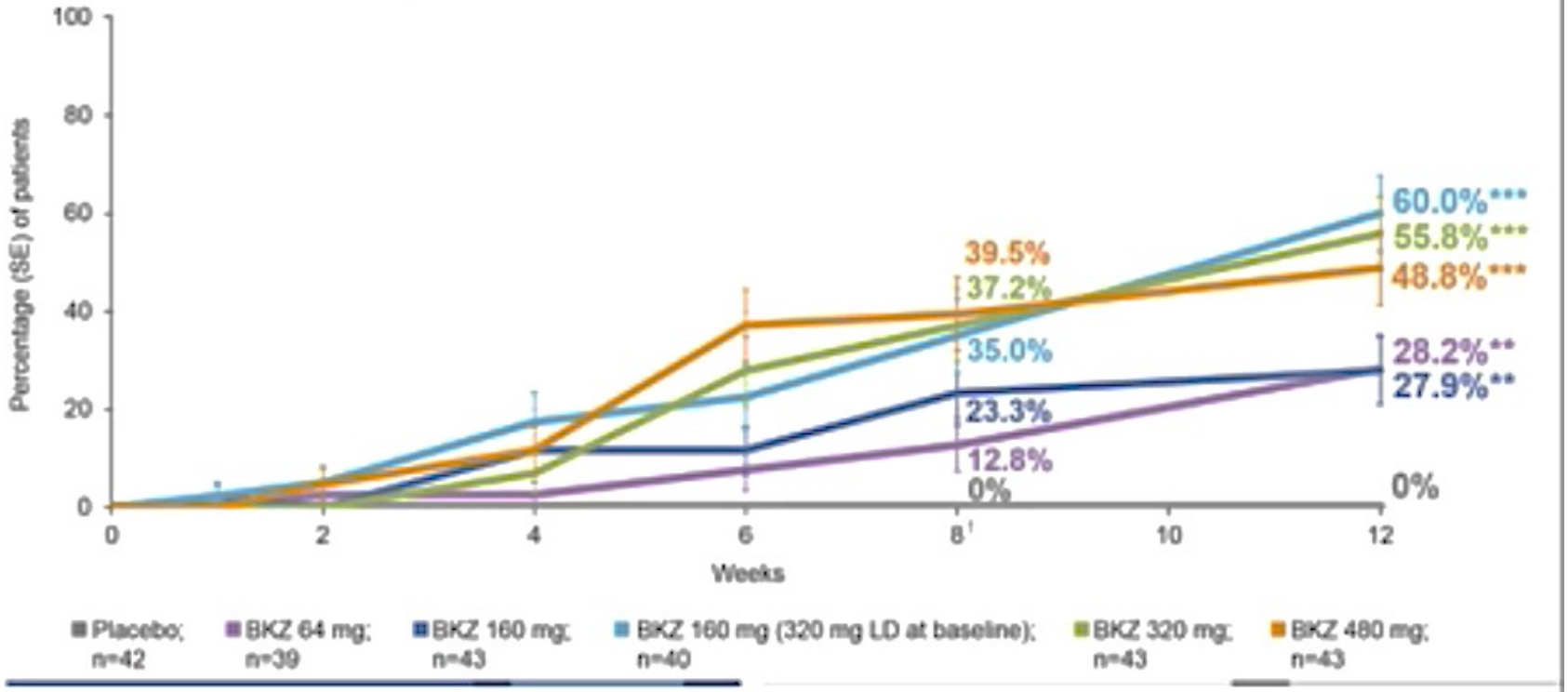
P-values for comparison vs placebo (*) or ustekinumab (†): *** or †††, P <0.001. NRI = Non-Responder Imputation; PASI = Psoriasis Area and Severity Index; PBO = Placebo; RZB = Risankizumab.

Dual Neutralization of Interleukin (IL)-17A and IL-17F with Bimekizumab in Moderate-to-severe Psoriasis: Results from a Phase 2b, Randomized, Double-blinded, Placebo-controlled, Dose-ranging Study

- **PASI 90** at **Week 12**- Bimekizumab: 46.2% **- 79.1%** patients placebo: 0% (P<0.0001)
- **PASI 100** at **Week 12**- Bimekizumab: 27%- **60.0%** versus 0%; (P≤0.0002)
- No unexpected or dose-related safety risks were observed

Bimekizumab BE ABLE 1 study

Complete skin clearance (PASI100) was achieved by significantly more bimekizumab-treated patients at Week 12



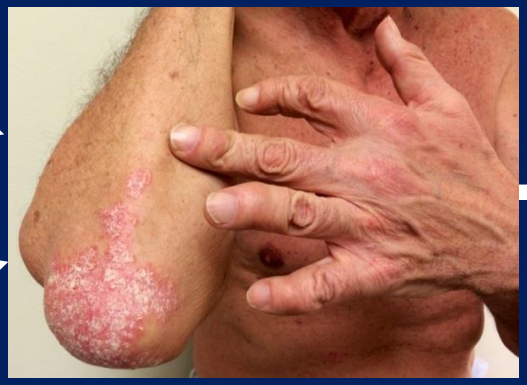
*p<0.05, **p<0.001; ***p<0.0001 versus placebo; Fisher's exact test. [1]p values were not calculated for PASI100 at Week 8 because this was not a predefined secondary endpoint
Note: placebo responses were zero at all time points for PASI100
Full analysis set, non-responder imputation

A Phase Iv, Randomized, Double-blind, Placebo-controlled Crossover Study of the Effects of Ustekinumab on Vascular Inflammation in Psoriasis (The Vip-U Trial)

Psoriasis and co-morbidities experimental model

Environmental risk factors
Smoking
Obesity

Genes and loci associated with psoriasis, diabetes and CV diseases
PSORS2/3/4
CDKAL1
ApoE4
TNFAIP3[2]



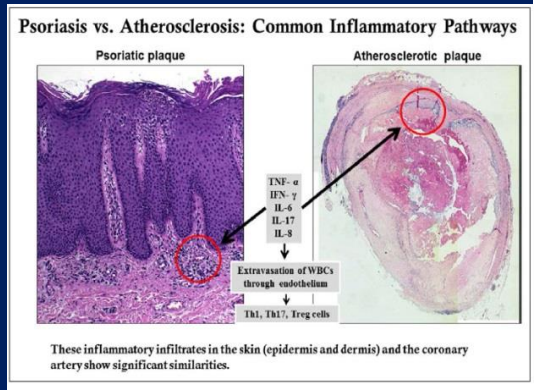


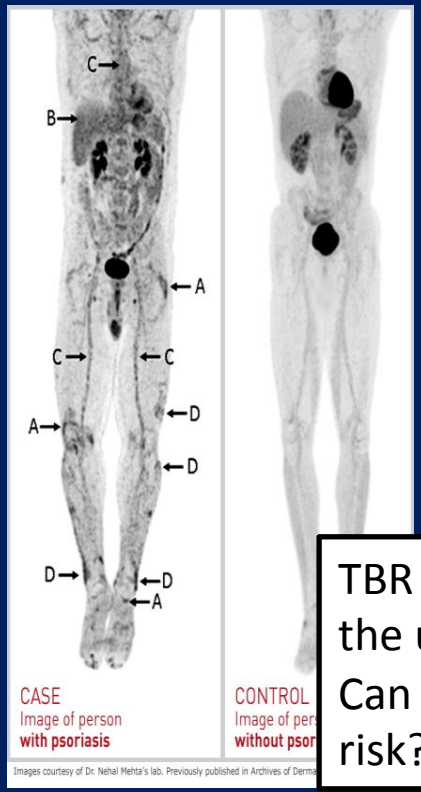
Figure from Kivelevitch et al Circ 2017;136:277-280

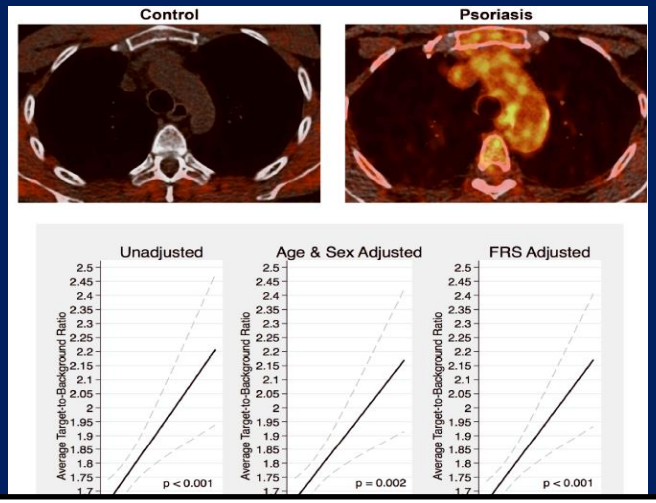
Mediating factors

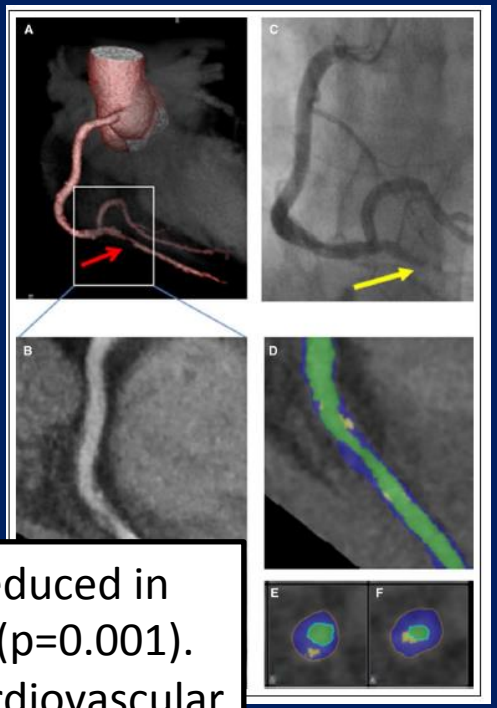
- Pathophysiology
  - Th1/17 inflammation (atherosclerosis, thrombosis, lipid metabolism)
  - Epidermal proliferation (↑uric acid, oxidative stress)
  - Angiogenesis (endothelial dysfunction)
- Treatment
  - Increase CV risk (e.g. cyclosporine, acitretin)?
  - Decrease CV risk (e.g. methotrexate, TNF inhibitors)?
- Psychosocial impact
  - Depression, alcohol and smoking, lower socioeconomic status

Azfar RS, Gelfand JM. *Curr Opin Rheum* 2008;20:416–422.

18-FDG PET CT demonstrates diffuse vascular inflammation, coronary CT reveals increased non calcified plaque and high risk plaque burden







TBR at baseline and at week 12 significantly reduced in the ustekinumab group compared to placebo (p=0.001). Can Inhibition of IL12/23 in psoriasis lower cardiovascular risk?

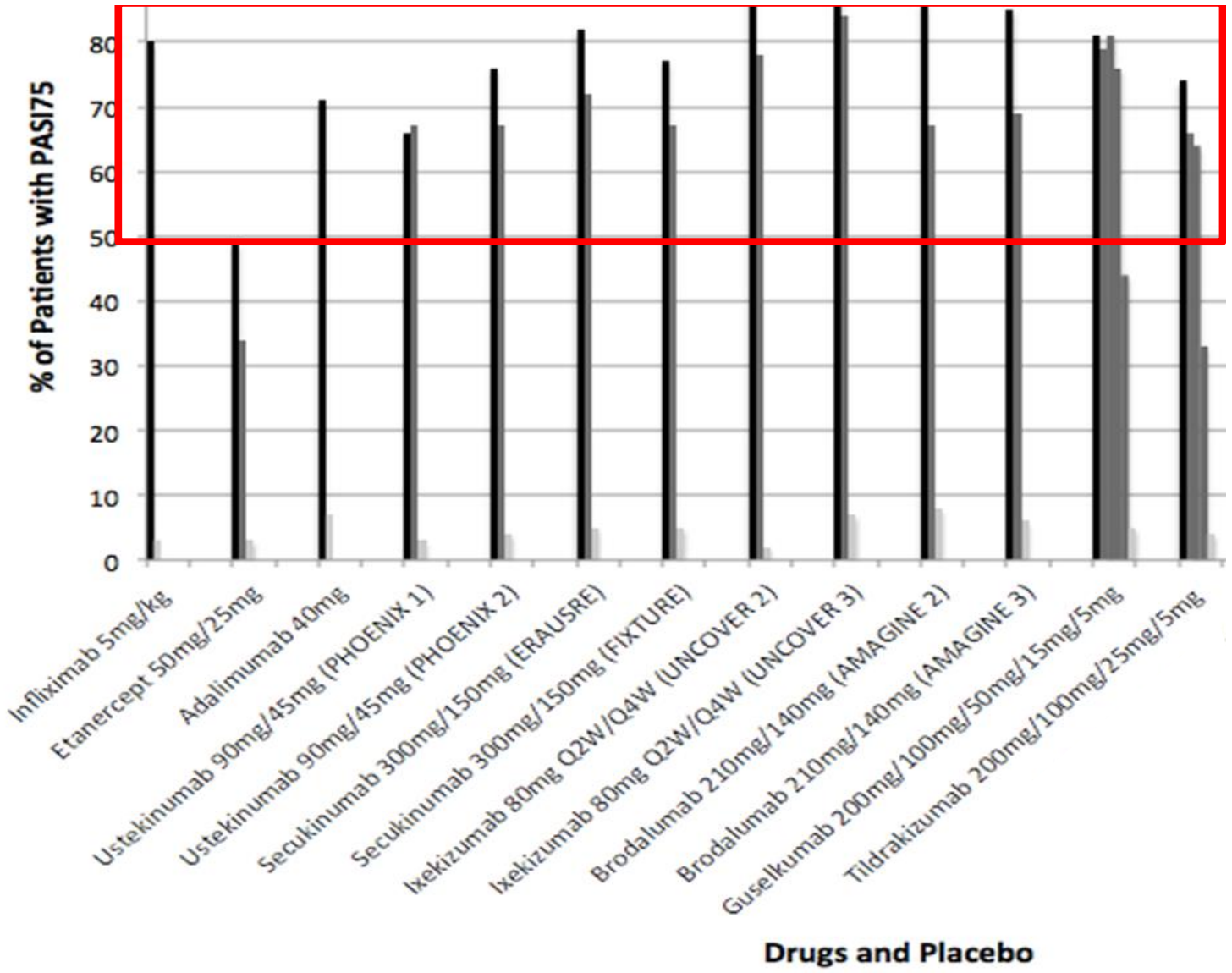
Dec;35(12):2667-76

Lerman et al Circ 2017;136:263-276

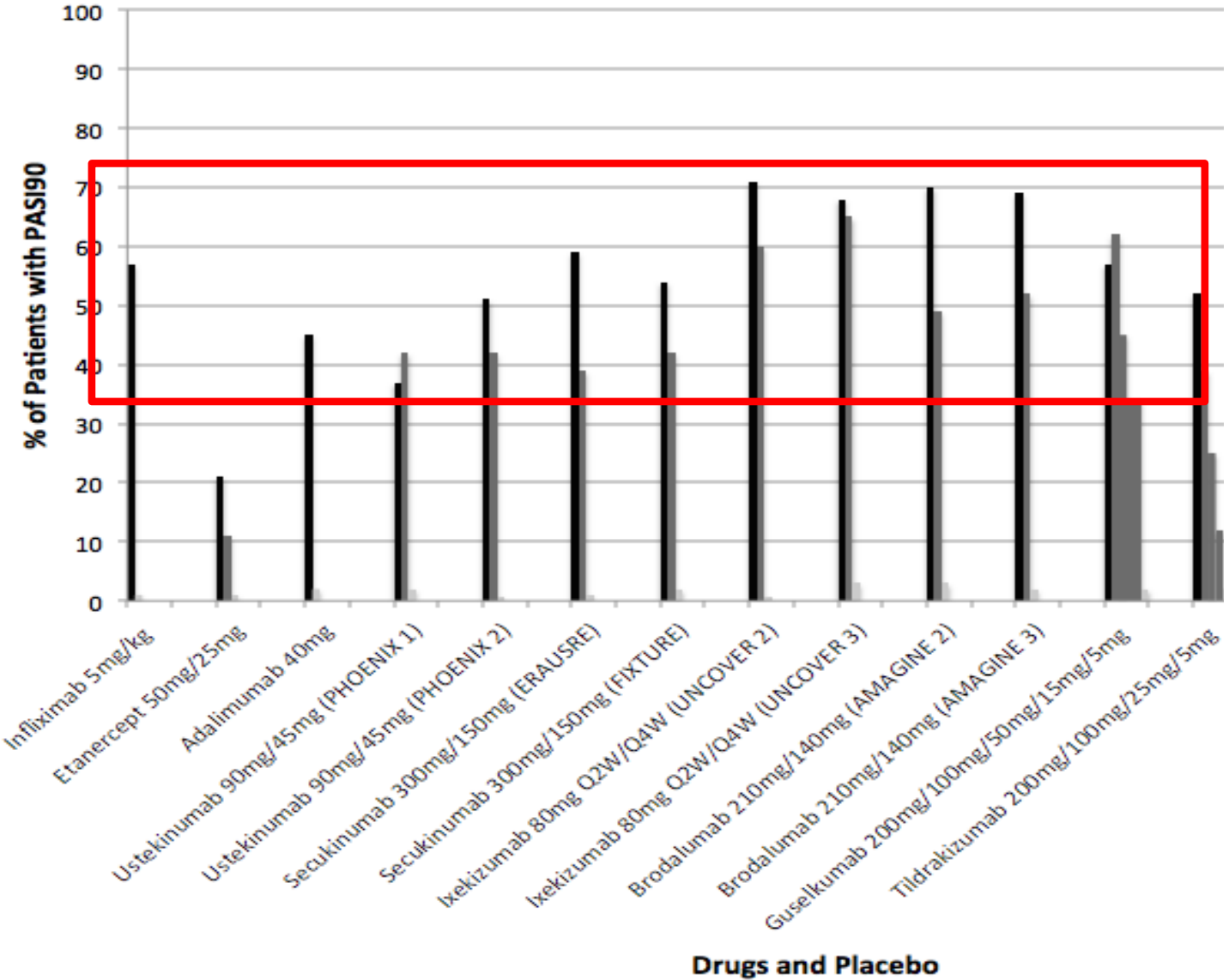
How to choose?

- 1. ? Efficacy
- 2. ? Sustainability
- 3. ? Speed of action
- 4. ? Comorbidities (PsA)
- 5. ? Safety

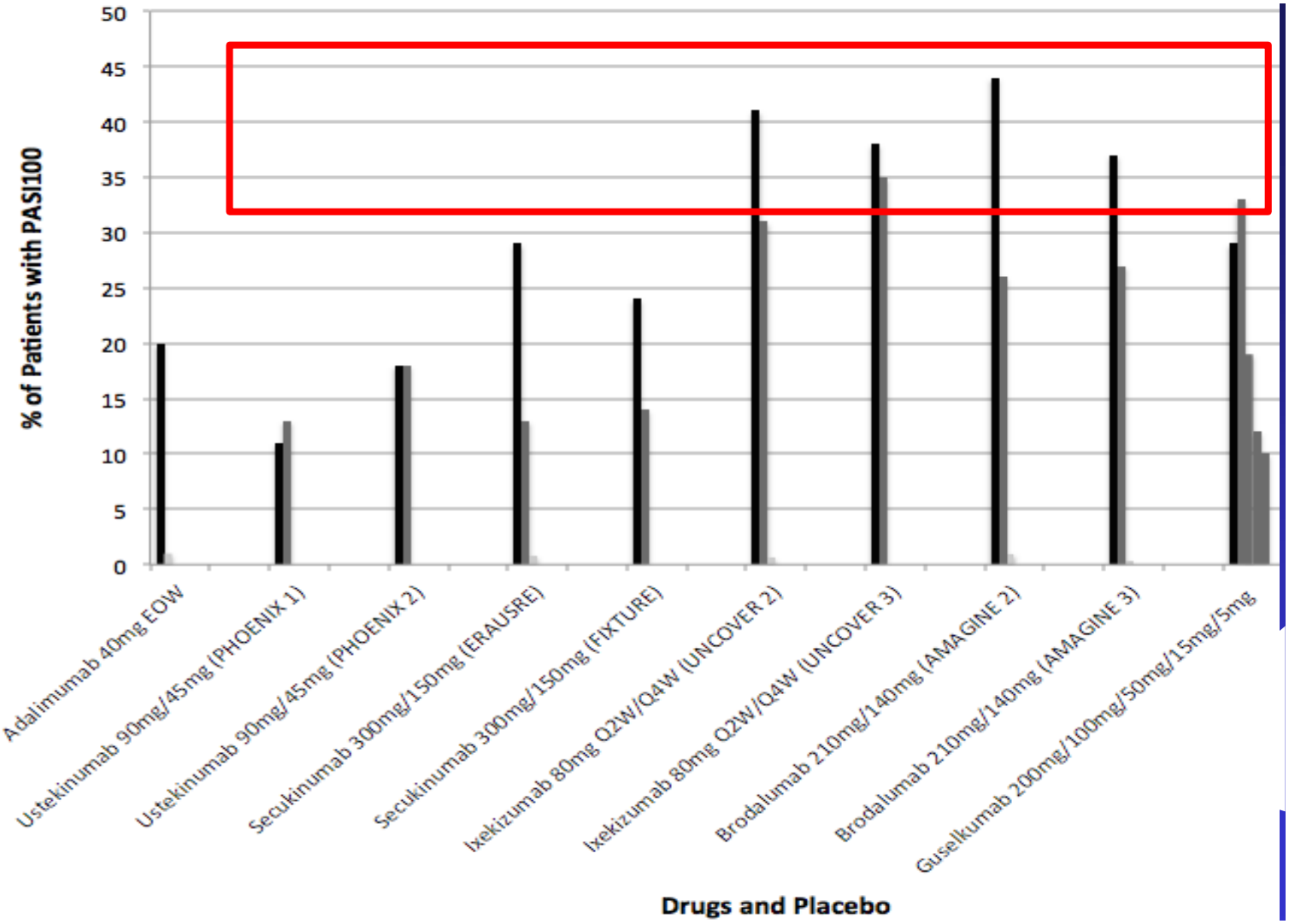
PASI 75


% of Patients with PASI75
80
70
60
50
40
30
20
10
0
Infliximab 5mg/kg
Etanercept 50mg/25mg
Adalimumab 40mg
Ustekinumab 90mg/45mg (PHOENIX 1)
Ustekinumab 90mg/45mg (PHOENIX 2)
Secukinumab 300mg/150mg (ERAUSRE)
Secukinumab 300mg/150mg (FIXTURE)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 2)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 3)
Brodalumab 210mg/140mg (AMAGINE 2)
Brodalumab 210mg/140mg (AMAGINE 3)
Guselkumab 200mg/100mg/50mg/15mg/5mg
Tildrakizumab 200mg/100mg/25mg/5mg
Drugs and Placebo

PASI 90


100
90
80
70
60
50
40
30
20
10
0
% of Patients with PASI90
Infliximab 5mg/kg
Etanercept 50mg/25mg
Adalimumab 40mg
Ustekinumab 90mg/45mg (PHOENIX 1)
Ustekinumab 90mg/45mg (PHOENIX 2)
Secukinumab 300mg/150mg (ERAUSRE)
Secukinumab 300mg/150mg (FIXTURE)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 2)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 3)
Brodalumab 210mg/140mg (AMAGINE 2)
Brodalumab 210mg/140mg (AMAGINE 3)
Guselkumab 200mg/100mg/50mg/15mg/5mg
Tildrakizumab 200mg/100mg/25mg/5mg
Drugs and Placebo

PASI 100


% of Patients with PASI100
50
45
40
35
30
25
20
15
10
5
0
Adalimumab 40mg EOW
Ustekinumab 90mg/45mg (PHOENIX 1)
Ustekinumab 90mg/45mg (PHOENIX 2)
Secukinumab 300mg/150mg (ERAUSRE)
Secukinumab 300mg/150mg (FIXTURE)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 2)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 3)
Brodalumab 210mg/140mg (AMAGINE 2)
Brodalumab 210mg/140mg (AMAGINE 3)
Guselkumab 200mg/100mg/50mg/15mg/5mg
Drugs and Placebo

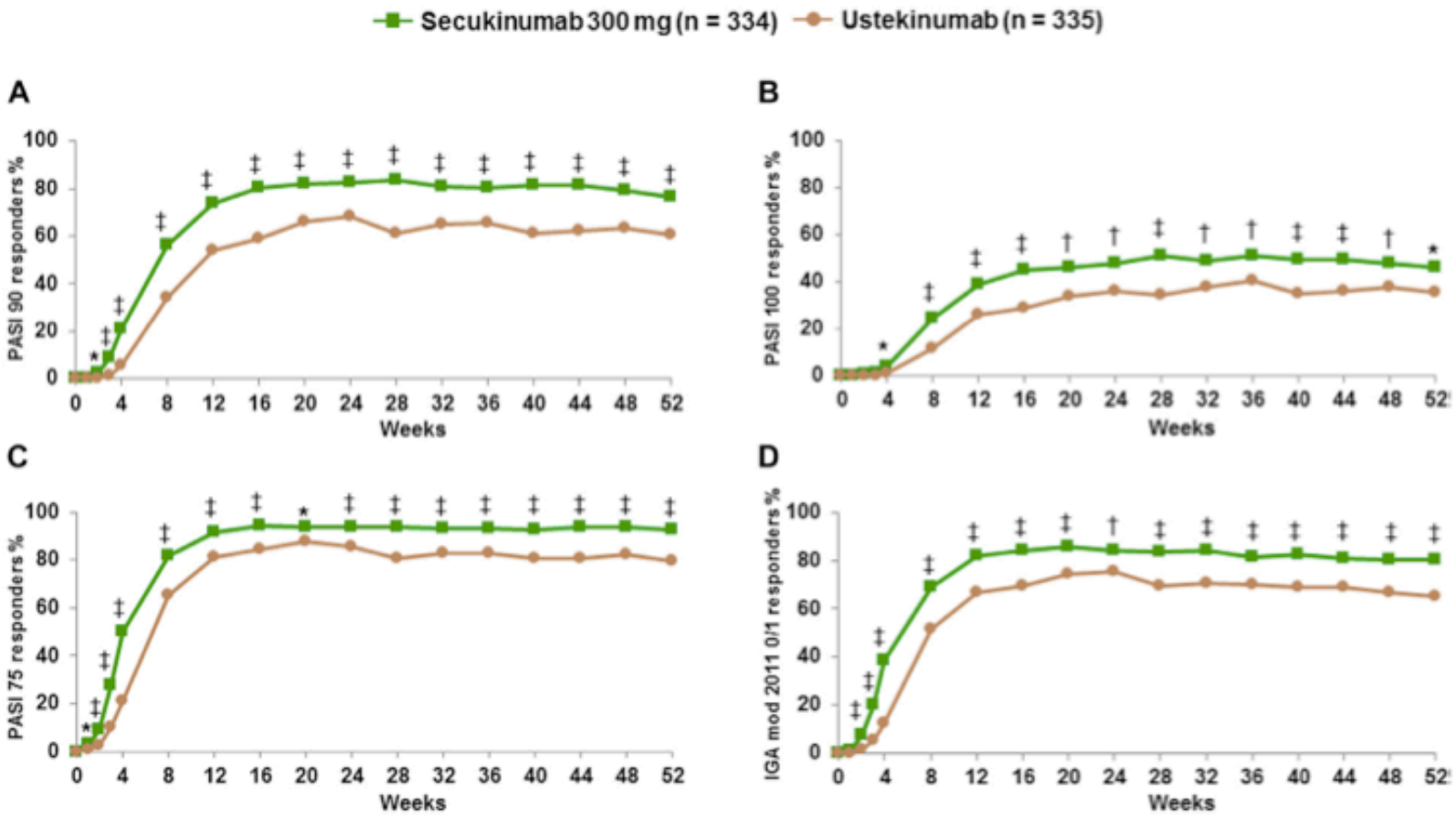
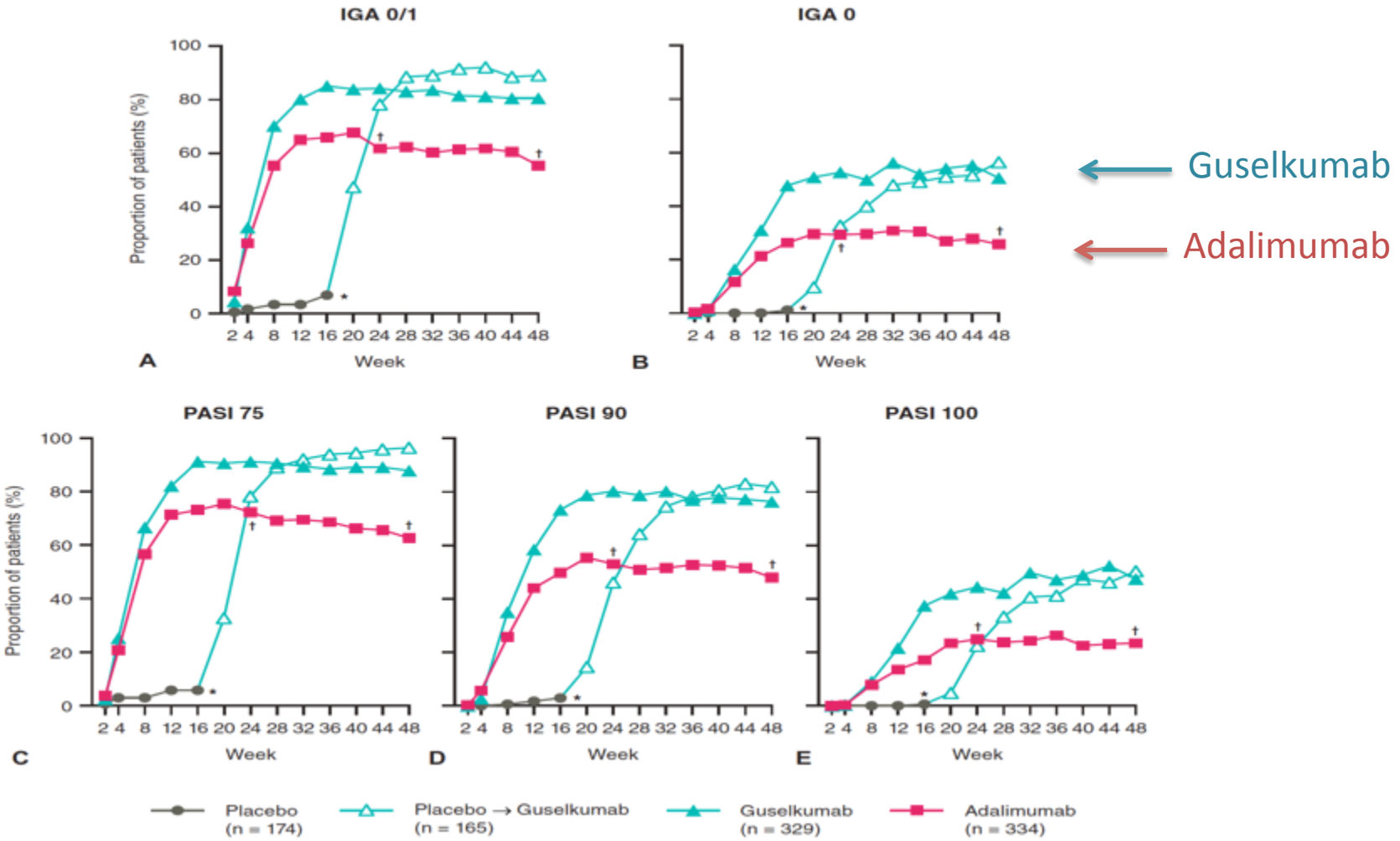


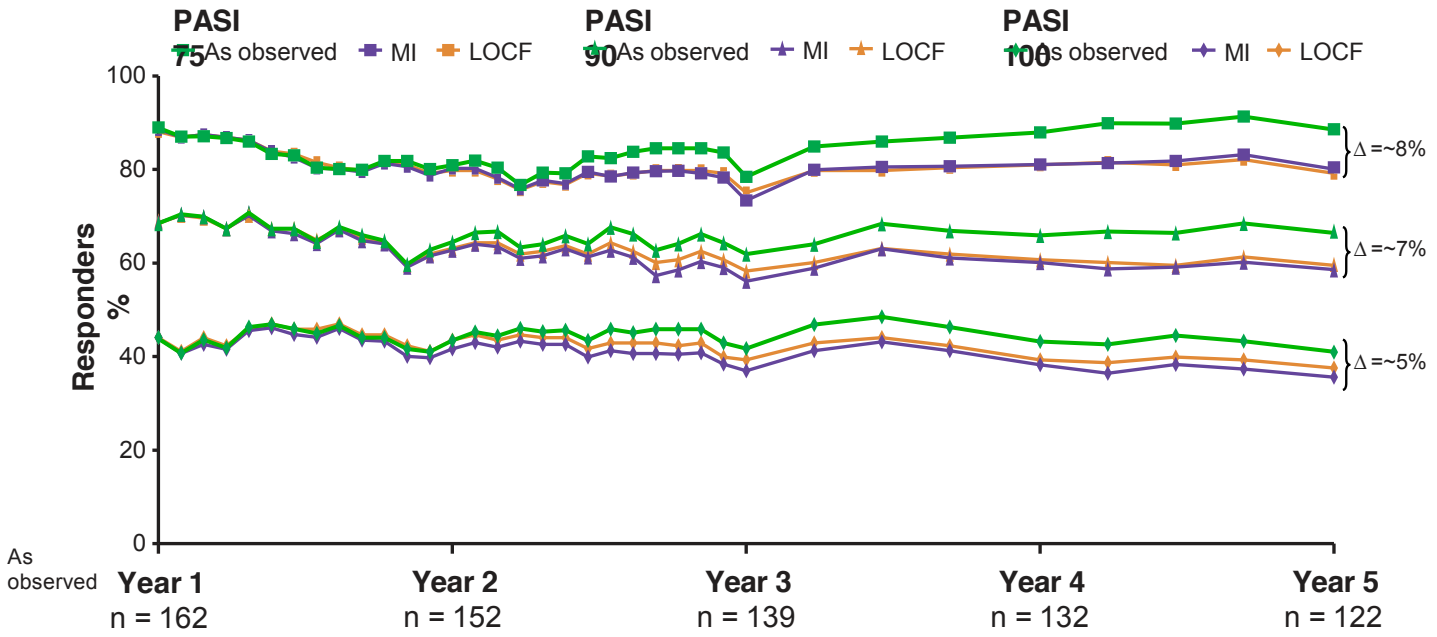
Fig 2. PASI 90 **(A)**, PASI 100 **(B)**, PASI 75 **(C)**, and IGA 0/1 **(D)** responses until week 52. Missing data were handled using multiple imputation. $^{*}P < .05$, $^{\dagger}P < .01$, and $^{\ddagger}P < .001$ vs ustekinumab by logistic regression. *IGA mod 2011 0/1*, Investigator's Global Assessment, 2011 modified version, score 0/1; *PASI 75/90/100*, ≥75%/≥90%/100% improvement from baseline Psoriasis Area and Severity Index score.



Blauvet et al. J. Am. Acad. Dermatol. 76: 405 (2017) Voyage 1 Study

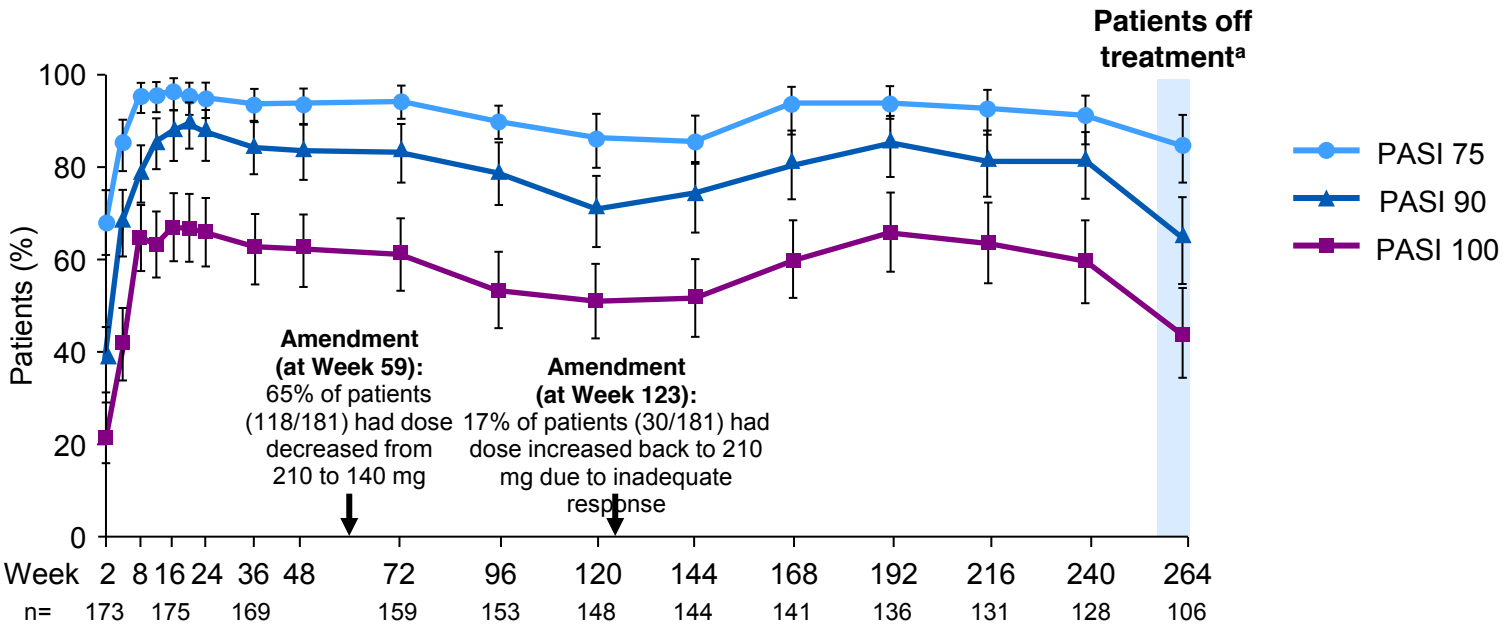
Sustainable efficacy?

Secukinumab Delivers High and Long-lasting Skin Improvement Through 5 Years



LOCF, last observation carried forward; MI, multiple imputation; n, number of evaluable patients in the as-observed analysis (the number of evaluable patients in the MI and LOCF analyses was 168 at each time point); PASI, Psoriasis Area and Severity Index

PASI responses with brodalumab over 5 years

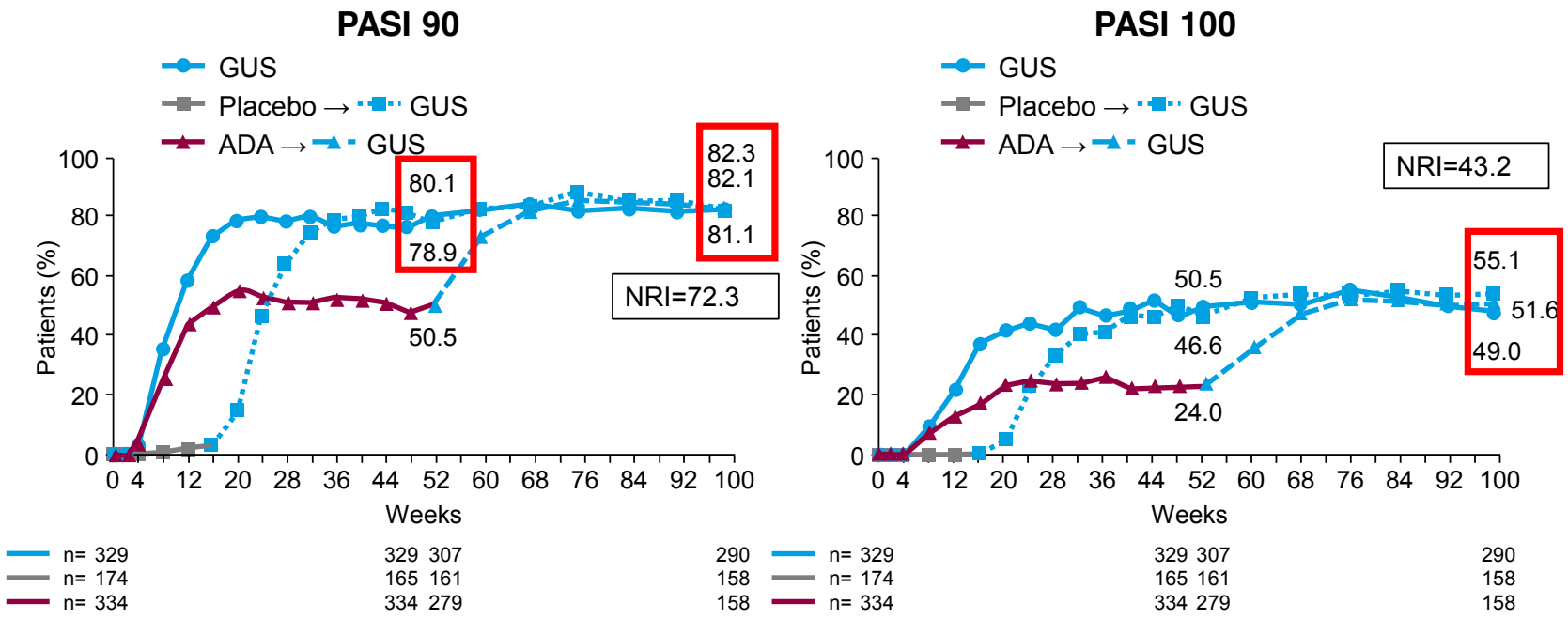


- "As observed" data
- Efficacy is maintained for up to 5 years

[a]At week 264, patients had been off treatment for ≥6 weeks. Error bars represent 95% CI

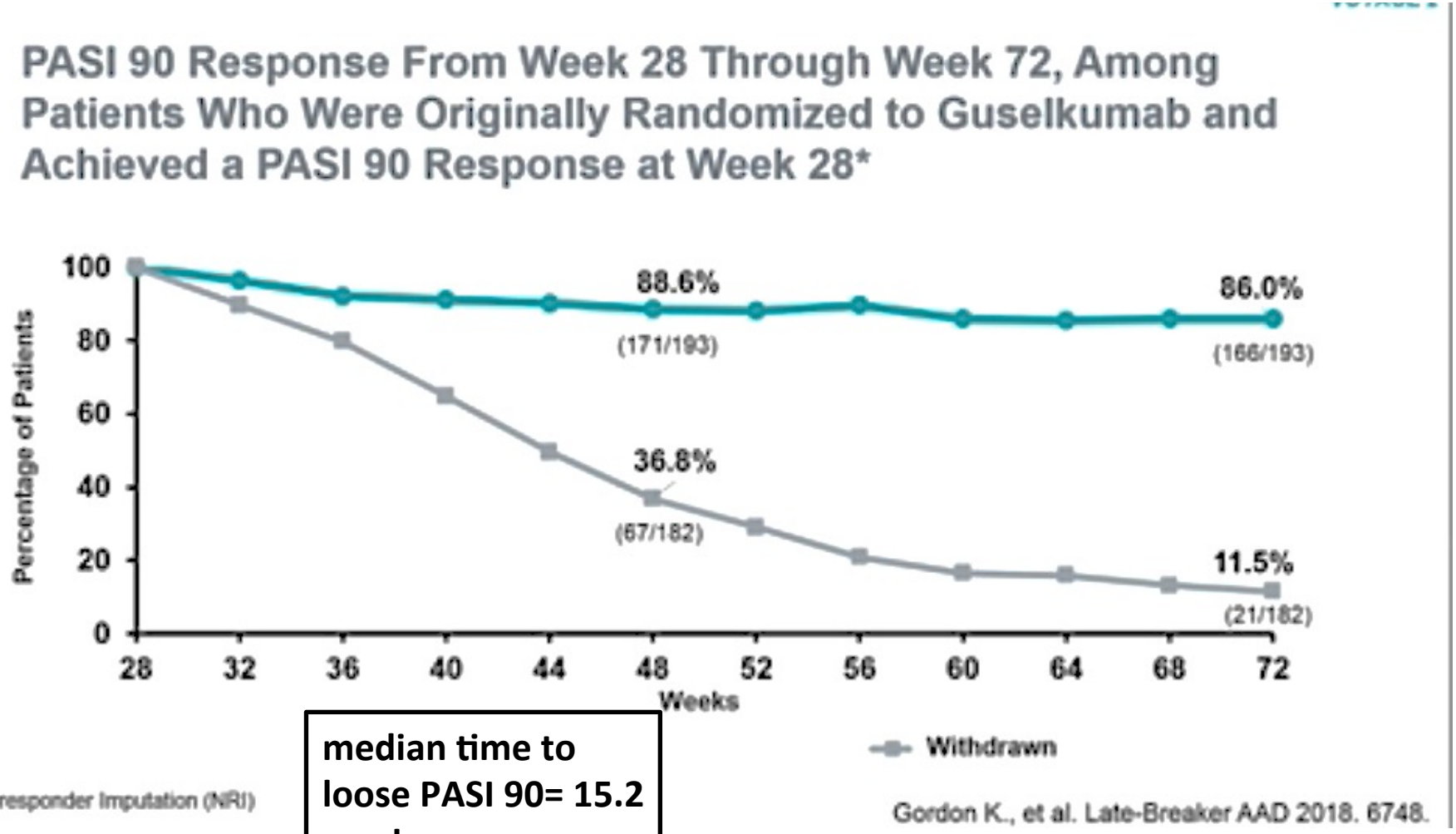
Papp K, et al. EADV 2017, P1798 Sponsored by LEO Pharma

VOYAGE1: PASI 90 & PASI 100 response with guselkumab through 2 years

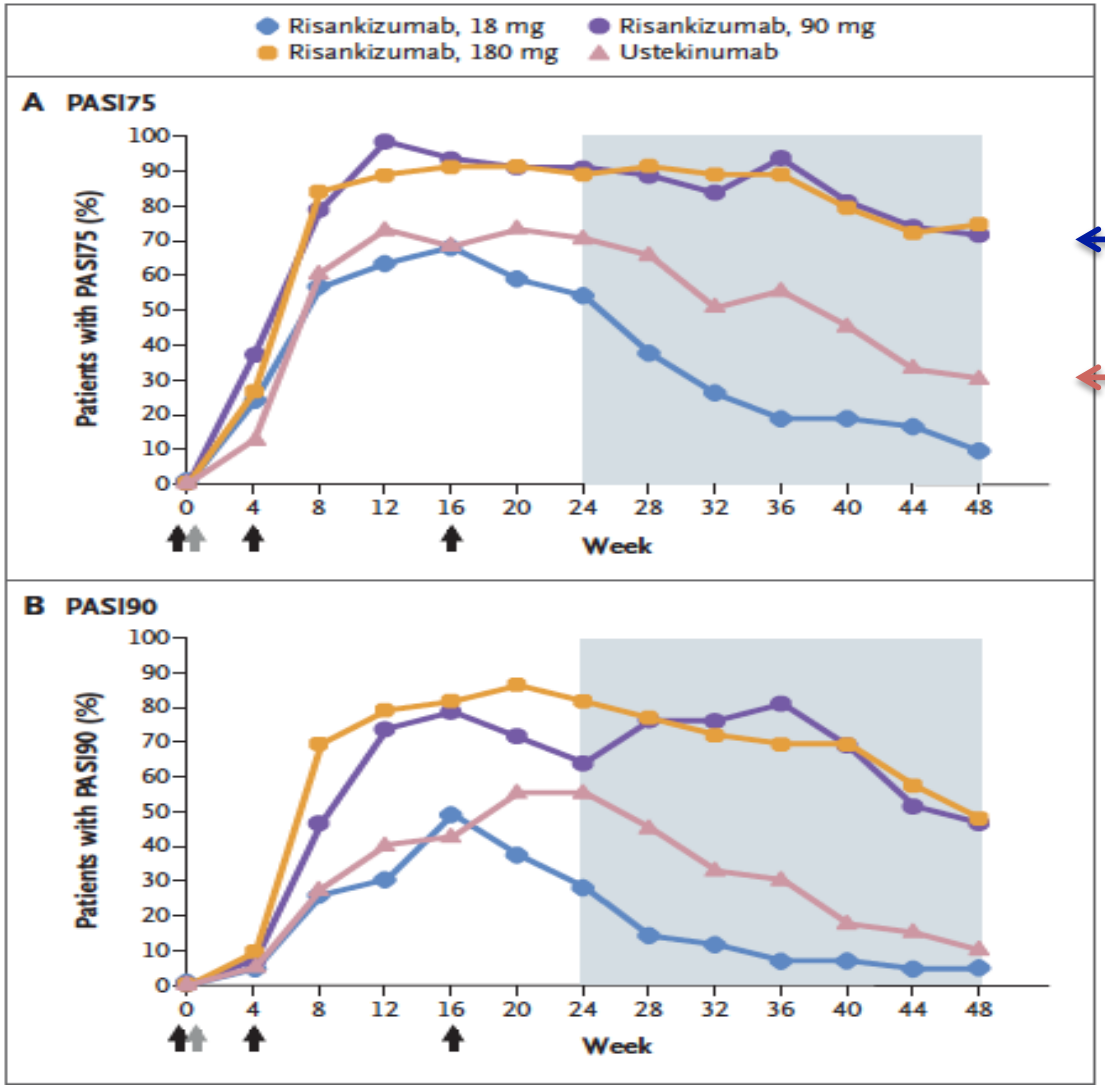


Griffiths CEM, et al. EADV 2017, D3T01.I Sponsored by Janssen Research and Development LLC

Long-term efficacy of Guselkumab treatment after drug withdrawal and retreatment in patients with moderate to severe psoriasis: results from VOYAGE2



median time to loose PASI 90= 15.2 weeks



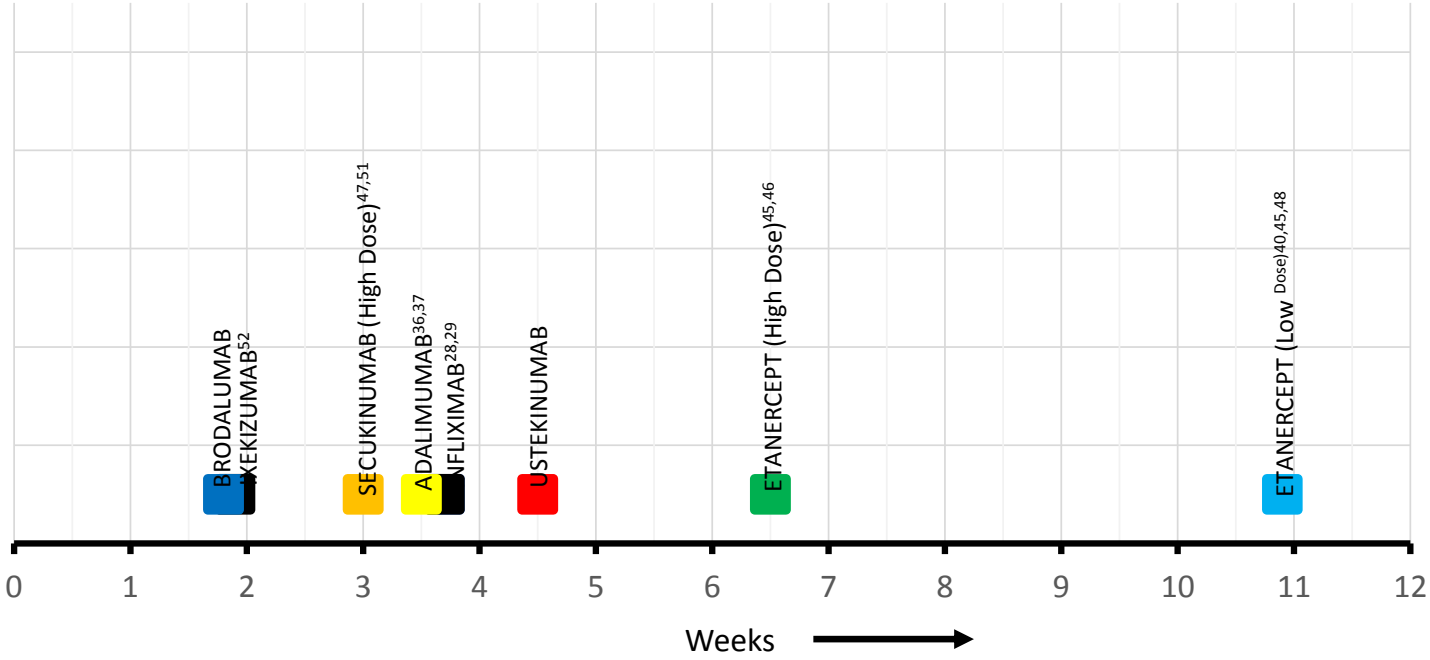
risankizumab

ustekinumab

Papp et al. NEJM 376:1551 (2017)

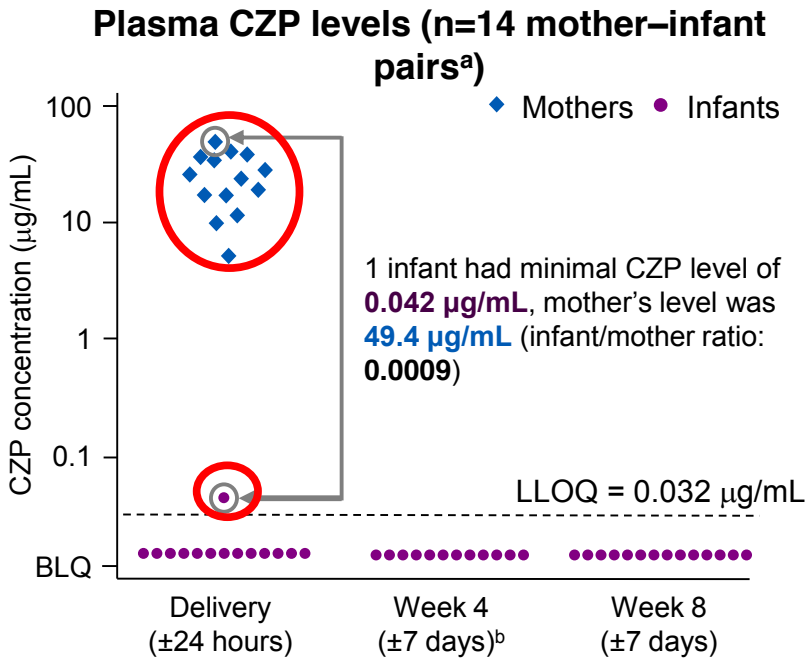
? Speed = IL-17s

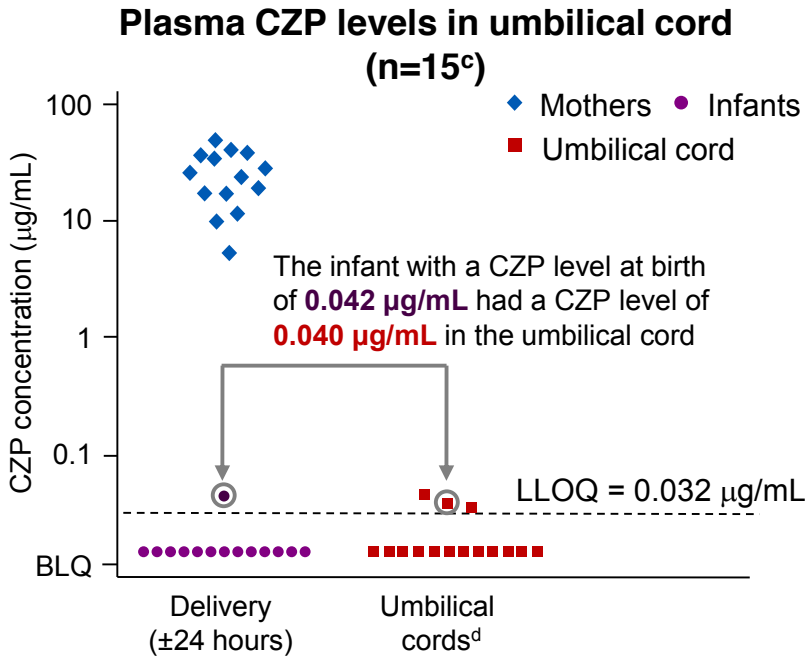
Time to achieve 50% improvement in baseline PASI scores (NRI) in induction phase (baseline to week 12). Time estimates based on linear progression. Comparative biologics shown as weighted means based on individual study published results.



? Pregnancy = CZP

CRIB: Maternal and infant plasma and umbilical cord levels of certolizumab pegol





[a]2/16 infant samples excluded from per protocol analysis set (1 missing data at birth, 1 due to implausible PK data [ie, data not consistent with pediatric CZP PK model, based on expected range of clearance, volume of distribution, and subsequent elimination $t_{½}$]); [b]2 samples not collected; [c]1 umbilical cord excluded due to missing data; [d]Umbilical cords were collected within 1 h of delivery. BLQ, below limits of quantitation of the assay; LLOQ, lower limit of quantitation

Kimball A, et al. EADV 2017, FC04.03 Sponsored by UCB Pharma

Psoriatic arthritis

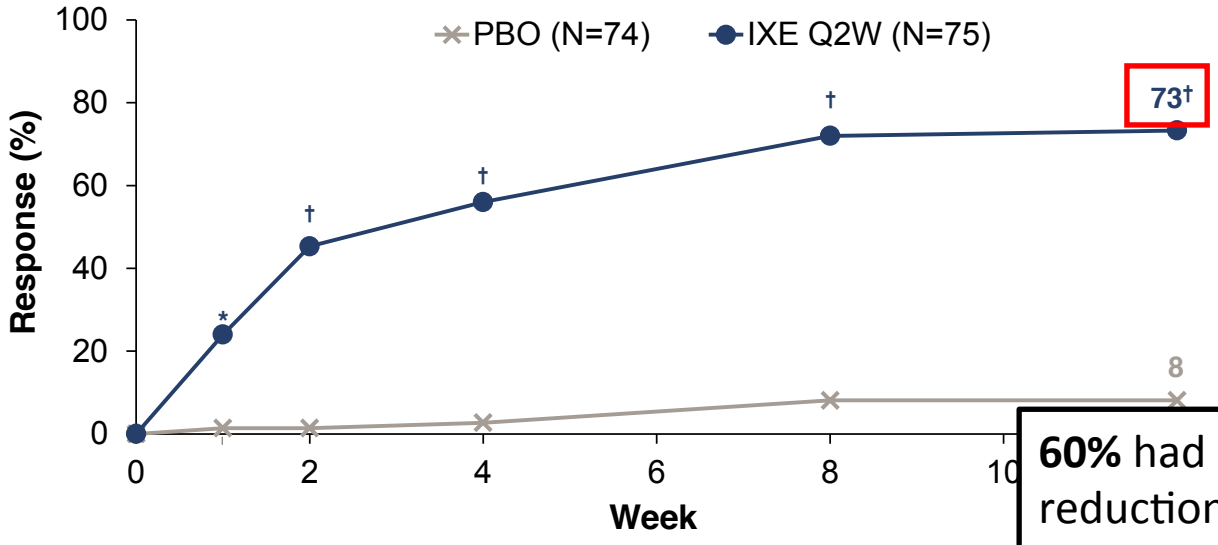
Class	Peripheral Arthritis: Signs/Symptoms	Inhibition of XRAY Progression	Enthesitis	Dactylitis	Skin	Nails
IL-17 Mabs	yes	yes	yes	yes	4+	Yes
IL-23 Mab	yes	?	yes	yes	4+	Probably yes
Tofacitinib	yes	?	?yes	?yes	1-2+	?yes
Abatacept	yes	?	?	?	no	?
TNF inhibitors	yes	yes	yes	yes	2-3.5+	yes

Genital PSO

sPGA of Genitalia (0,1)

NRI, Blinded Treatment Period, ITT Population

- 7 out of 10 ixekizumab-treated patients achieved clear or almost clear genital skin at Week 12
- Percentage of patients achieving clear or almost clear genital skin was significantly greater for ixekizumab as early as Week 1



60% had a >3 point reduction in **NRS Itch at 12 weeks**

* p<.01 vs. PBO; † p<.001 vs. PBO

ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; sPGA=static Physician's Global A

Palmoplanter psoriasis

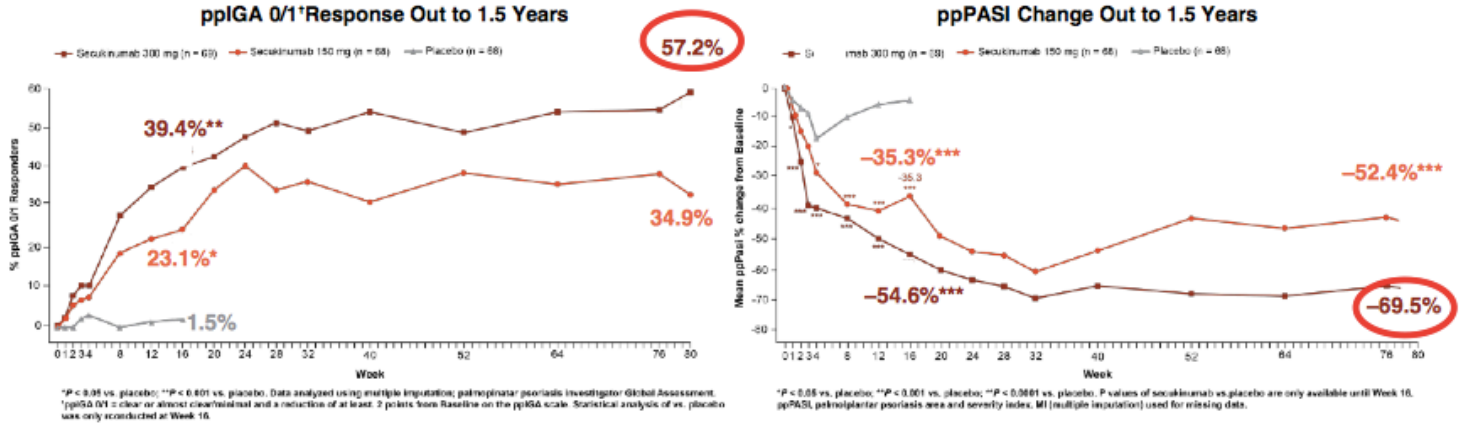
ORIGINAL ARTICLE

Increased expression of IL-17A and limited involvement of IL-23 in patients with palmo-plantar (PP) pustular psoriasis or PP pustulosis; results from a randomised controlled trial

R. Bissonnette,[1]* S. Nigen,[1] R.G. Langley,[2] C.W. Lynde,[3] J. Tan,[4] J. Fuentes-Duculan,[5] J.G. Krueger[5]

[1]Innovaderm Research Inc., Montreal, QC, Canada
[2]Division of Dermatology, Dalhousie University, Halifax, NS, Canada
[3]Lynderm Research Inc., Markham, ON, Canada
[4]Windsor Clinical Research, Windsor, ON, Canada
[5]The Rockefeller University, New York, NY, USA
*Correspondence: R. Bissonnette. E-mail: rbissonnette@innovaderm.ca

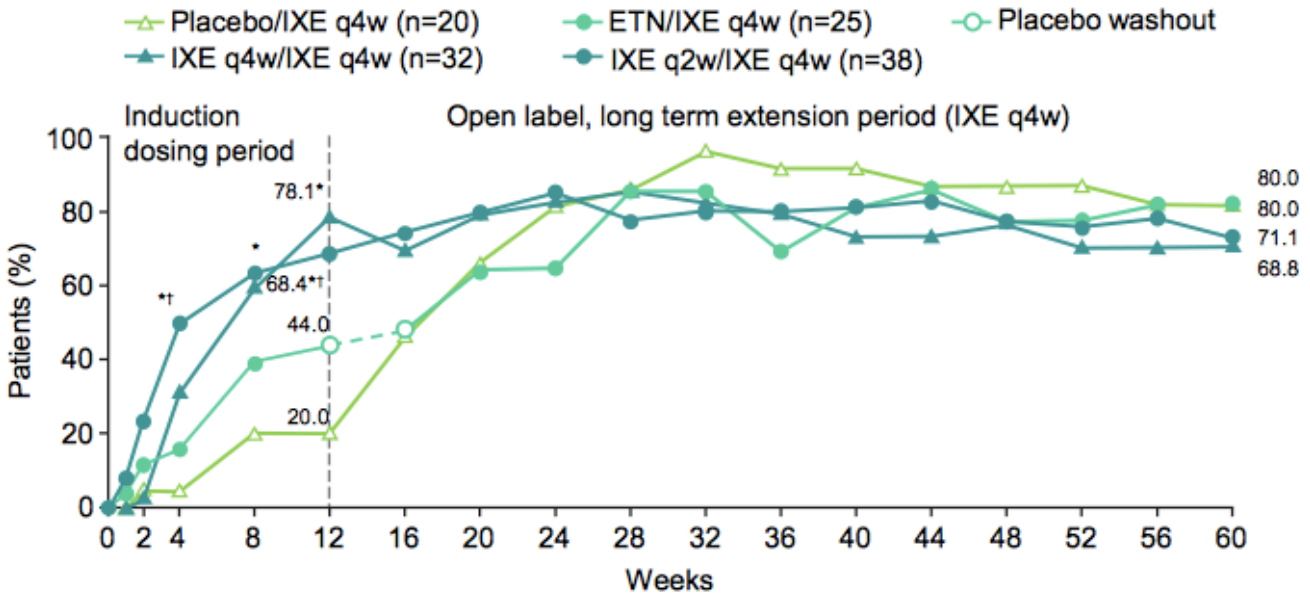
More than Half of All Subjects on Secukinumab 300 mg Achieved Clear/Almost Clear Palms and Soles at 1.5 Years



Palmoplantar disease improved by approximately 70% at 1.5 years in subjects receiving secukinumab 300 mg

Gottlieb A. Secukinumab shows significant efficacy in palmoplantar psoriasis: Results from GESTURE, a randomized controlled trial. J Am Acad Dermatol. 2017

UNCOVER-3: Ixekizumab in patients with palmoplantar involvement: ppPASI 75 response rates



- These patients have plaque psoriasis of the hands and feet, this does not address efficacy in pustular disease nor patients with predominantly palmoplantar disease

Menter A, et. al. EADV 2016, FC03.08; Sponsored by Eli Lilly and Company

Selection is multifactorial

Scenario	TNF	IL-12/23	IL-23	IL-17
Long term data	★	Emerging	No long term data	emerging
PsA	★	FDA approved	? Phase 2	FDA approved
Crohns disease	★	FDA approved	TBD	Warning
Associated MI/ CVA	Yes	TBD	TBD	TBD
CHF	Warning	No warning	No warning	No warning
MS	Warning			
Ease of Administration		★	★	★
Obesity	Infliximab preferred	Weight based dosing		Flexible dosing
Rapid onset				★
Long term persistence		★	Yes +	Yes +