Secukinumab Retreatment Shows Rapid Recapture of Treatment Response: an Analysis of a Phase 3 Extension Trial in Psoriasis

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Disclosures of the Lead Author

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Disclosures

- Abbvie
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- Janssen Ortho Biotech
- Merck
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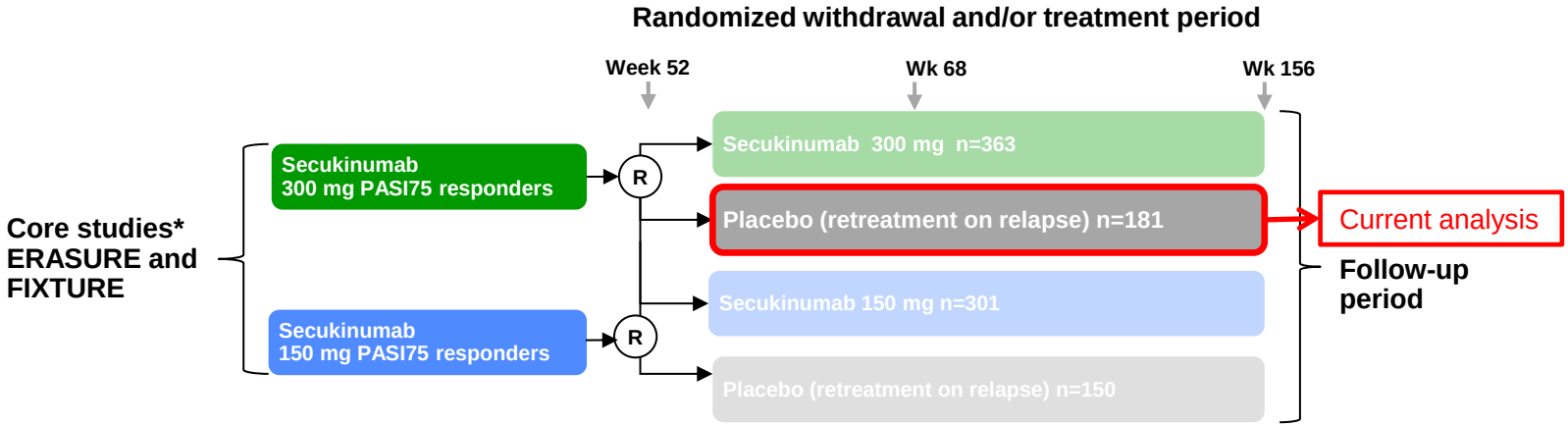
Background

- Plaque psoriasis is a chronic disease, therefore sustaining treatment benefit is important. Treatment interruption is common in psoriasis[1] and may lead to reduced efficacy upon retreatment[2]
- Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate to severe psoriasis, starting at early time points, with a sustained effect and a favorable safety profile[3-7]
- Secukinumab 300 mg has been shown to sustain high levels of skin clearance up to 4 years.[8]
- Retreatment with secukinumab following treatment withdrawal and relapse was evaluated in the extension phase of the Phase 3 ERASURE and FIXTURE studies
- Here we present efficacy and safety data for subjects retreated with the 300 mg dose following relapse for up to 2 years

1. Brezinski EA, Armstrong AW. *PLoS One.* 2012;7(4):e33486. 2. Moore A, Gordon KB, Kang S, et al. *J Am Acad Dermatol.* 2007;56:598-603.3. Hueber W et al. Sci Transl Med 2010;2:52ra72; 4. Langley RG et al. N Engl J Med. 2014;371:326–338; 5. Thaci D et al. JAAD. 2015;73:400; 6. Blauvelt et al. JAAD. 2016;[Epub ahead of print]; 7. Mease et al. N Engl J Med. 2015;373:1329-39; 8. Bissonnette R et al. Oral presentation at: *European Academy of Dermatology and Venereology* 24th Annual Meeting. 7 October 2015. IL, interleukin.

Treatment Withdrawal and Retreatment in the ERASURE and FIXTURE Extension Study

- Subjects who had PASI75 responses at Week 52 were randomized in the extension study 2:1 to continue on the same dose of secukinumab or to receive placebo every 4 weeks. Subjects who relapsed in the two placebo arms (300 mg-placebo and 150 mg-placebo) were retreated with secukinumab at Week 0 (week of relapse), Weeks 1, 2, 3, and 4 and then every 4 weeks
  - Relapse was defined as a loss of >50% of the maximum PASI gain compared with Baseline in the core studies
  - Multiple imputation was used for missing values
- **This poster is an analysis of the 300 mg – placebo treatment withdrawal arm of the extension study, representing the label dose of secukinumab**



*In the core studies, subjects were randomized 1:1:1 to secukinumab 300 mg, 150 mg or matching placebo, or etanercept 50 mg (FIXTURE only).[1] Treatments were administered at Baseline, Wk 1, 2, 3 and then every 4 wks from Wk 4 until end of study (Wk 208) or discontinuation. At Wk 12, placebo group subjects who did not achieve a PASI 75 response were re-randomized to receive secukinumab 300 mg or 150 mg. 1. Langley RG et al. *N Engl J Med*. 2014;371:326–38. PASI, Psoriasis Area Severity Index.

Characteristics of Secukinumab 300 mg Treatment Withdrawal Group

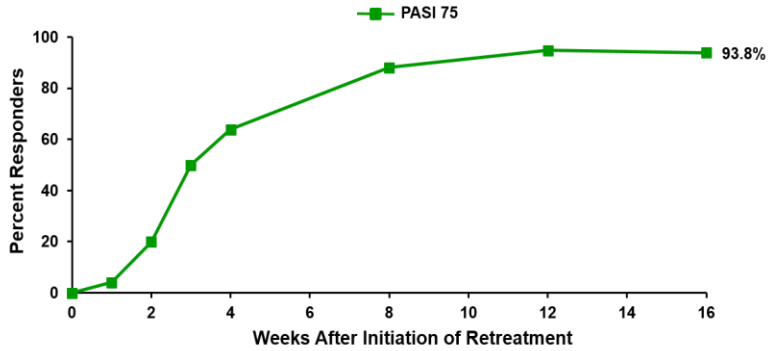
Demographics and Characteristics: Extension study (Week 52)	
Characteristic	**Placebo / Secukinumab 300 mg (n = 181)**
Age, years (Mean ± SD)	45.4 ± 13.1
Gender (males) n (%)	119 (65.7)
Race (white) n (%)	136 (75.1)
Weight, kg (Mean ± SD)	85.4 ± 20.0
BMI, kg/m^2 (Mean ± SD)	28.9 ± 6.1
Absolute mean PASI score ± SD	0.9 ± 1.5
PASI90 responders, n (%)	157 (86.7)
Previous systemic treatment, n (%)	
Any	81 (54.0)
Conventional agent	72 (48.0)
Biologic agent	23 (15.3)
Previous failure to biologic treatment	6 (4.0)

BMI, body mass index; SD, standard deviation.

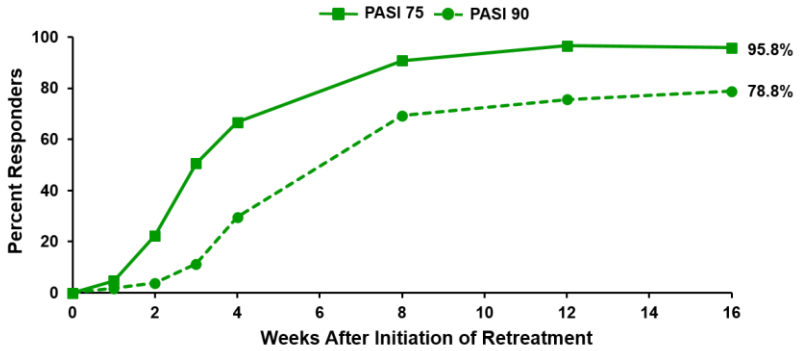
Secukinumab Response is Rapidly Recaptured on Retreatment

Similar Response Regained by Majority after Relapse

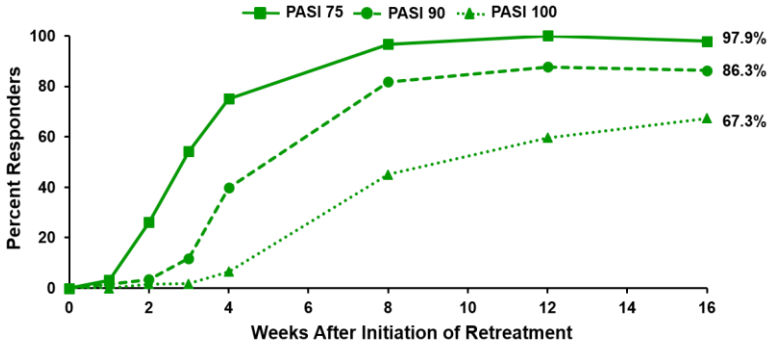
A. Prior PASI 75 Responders (n=136)



B. Prior PASI 90 Responders (n=117)



C. Prior PASI 100 Responders (n=67)



- 136 subjects (75.1%) met the relapse criterion
- Median time to relapse following withdrawal from secukinumab 300 mg was 28.0 weeks (95% CI: 24.14, 32.00)

PASI, Psoriasis Area Severity Index; CI, confidence interval. Missing data were handled using multiple imputation. Cut-off for analysis was Week 104. Subjects who relapsed late and had not reached Week 16 post relapse are not included in Week 16 analysis. Prior PASI 90 and 100 responders are included within PASI75 response groups, and PASI90 responders within PASI100 response groups.

No Evidence of New or Cumulative Adverse Events or Anti-drug Antibodies with Secukinumab Retreatment

Frequencies of Treatment-emergent Adverse Events	Secukinumab 300 mg - Placebo (n = 181)
Subjects with any AE(s), n (%)	107 (59.1)
Deaths	0
SAEs, n (%)	11 (6.1)
Infections and infestations, n (%)	4 (2.2)
Most common AEs by preferred term, IR per 100 subject-years	
Nasopharyngitis	20.7
Arthralgia	12.6
Upper respiratory tract infections	12.4
Presence of anti-drug antibodies	
Positive, n (%)	0 (0)

- Total secukinumab exposure in the 300 mg treatment withdrawal arm during one year of follow-up was 100.2 subject-years, with a mean exposure per subject of 202.2 days. Secukinumab showed a favorable safety profile. Adverse events were consistent with previous studies and presented no unexpected safety findings[1-4]
- AEs of special interest:
  - There were 4 serious infections (IR 4.1), no cases of candidiasis, no cases of neutropenia CTCAE Grade 2 or higher (i.e., absolute neutrophil levels < 1.5 - 1.0 x 109/L), no major adverse cardiovascular events, no malignant or unspecified tumors, and no cases of Crohn's disease or ulcerative colitis

There were no subjects in the 300 mg treatment withdrawal arm who tested positive for anti-secukinumab antibodies

1. Langley RG et al. *N Engl J Med*. 2014;371:326–38; 2. Papp KA et al. *Br J Dermatol*. 2013;168:412–21; 3. Rich P et al. *Br J Dermatol*. 2013; 168:402–11; 4. Thaci D et al. *J Am Acad Dermatol*. Jun 16. pii: S0190-9622(15)01683. AE, adverse event; SAE, serious adverse event; IR, incidence rate.

Conclusions: Secukinumab retreatment rapidly restored efficacy in subjects relapsing after being withdrawn from therapy

- PASI75 response was regained within 16 weeks by 94% of PASI75 responders retreated with the label dose of secukinumab 300 mg after relapse and by 96% of PASI90 and PASI100 responders on retreatment
- The majority of subjects who exhibit the highest levels of response to secukinumab (PASI90, PASI100) can expect to regain a high response level (PASI75 or higher) 12-16 weeks after treatment interruption and resumption of therapy
- The safety profile for secukinumab was favorable and was consistent with previous reports. No anti-drug antibodies were observed during retreatment

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PASI, psoriasis area severity index

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Safety and Efficacy of Apremilast Through 104 Weeks in Patients With Moderate to Severe Psoriasis Who Continued on Apremilast or Switched From Etanercept Treatment in the LIBERATE Study

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Acknowledgments, Correspondence, and Disclosures

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Disclosures

KR: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Covagen, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, Merck Sharp & Dohme, Novartis, Ocean Pharma, Pfizer (Wyeth), Regeneron, Takeda, UCB Pharma, and XenoPort – consultant, advisory board member, speaker, and investigator. **MG:** has no conflicts of interest to disclose. **LG:** AbbVie, Amgen, Celgene Corporation, LEO Pharma, Novartis, Pfizer, and Valeant – investigator and/or speaker and/or consultant. **KN, RC, & EL:** Celgene Corporation – employment. **RGBL:** AbbVie, Amgen, Celgene Corporation, Eli Lilly, LEO Pharma, Merck, Novartis, and Pfizer – advisory board member and/or paid speaker and/or participated in clinical trials.

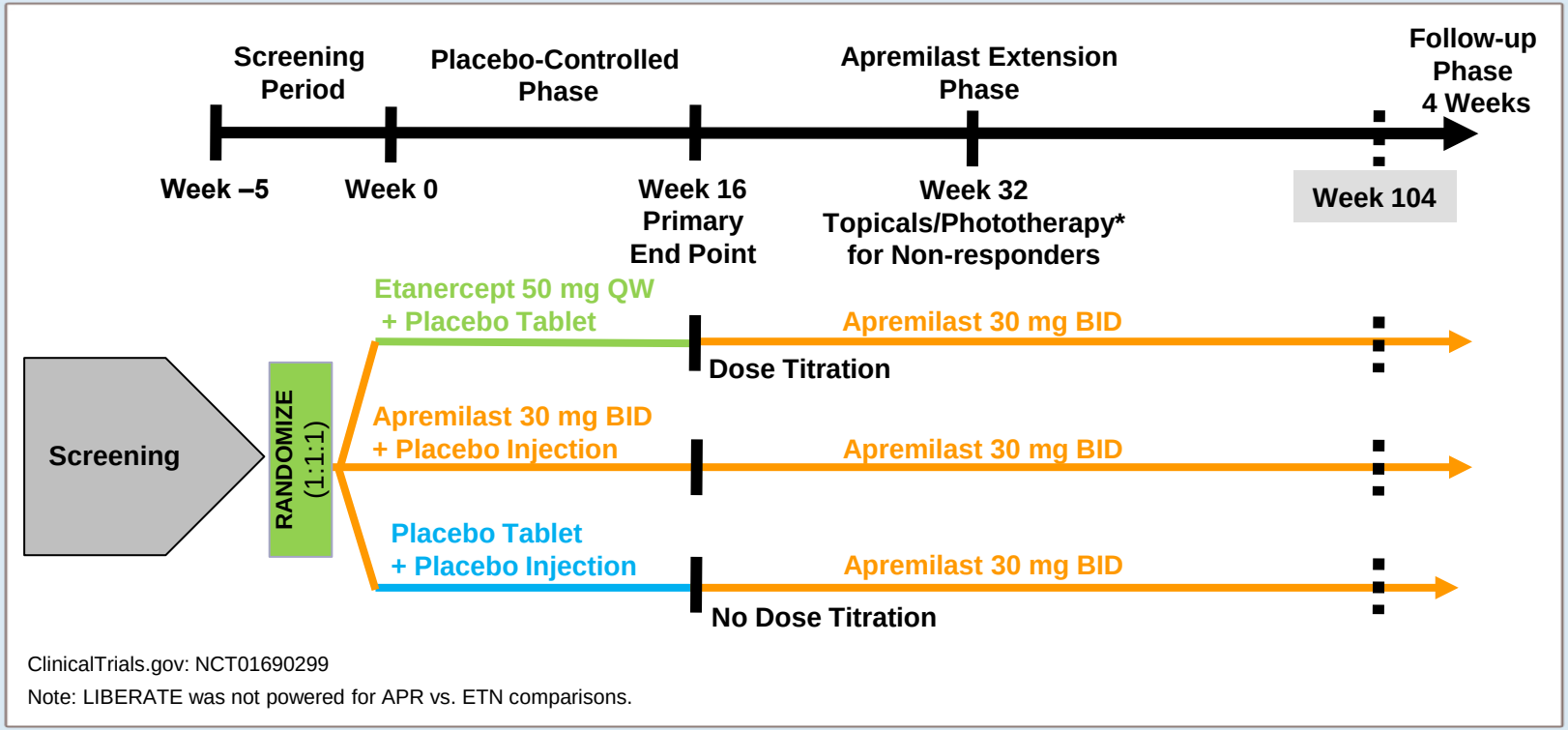
Introduction

- Psoriasis is a chronic, systemic inflammatory disease affecting 1% to 3% of the world's population.[1-3]
- Currently available therapies are often compromised by adverse events (AEs), safety and tolerability issues, and route of administration (injection/infusion vs. oral).[4]
- Apremilast, an oral, small-molecule phosphodiesterase 4 inhibitor, works intracellularly within immune cells to regulate the production of inflammatory mediators.[5]
- Apremilast was approved by the US Food and Drug Administration and by the European Commission for treatment of psoriasis and psoriatic arthritis.
- LIBERATE (NCT01690299) is a global phase 3b study of apremilast 30 mg twice daily (APR) or etanercept 50 mg once weekly (ETN), compared with placebo (PBO) for the treatment of biologic-naive patients with moderate to severe plaque psoriasis.
- The objective of the current analysis was to explore the efficacy of APR and ETN in patients for 16 weeks and through 104 weeks of the LIBERATE study.

LIBERATE=Evaluation in a Placebo-Controlled Study of Oral Apremilast and Etanercept in Plaque Psoriasis.

1. Helmick CG, et al. *Am J Prev Med*. 2014;47:37-45. 2. Rachakonda TD, et al. *J Am Acad Dermatol*. 2014;70:512-516. 3. Parisi R, et al. *J Invest Dermatol.* 2013;133:377-385. 4. Schmitt J, et al. *Br J Dermatol*. 2008;159:513-526. 5. Schafer PH, et al. *Cell Signal*. 2014;26:2016-2029.

LIBERATE: Study Design



ClinicalTrials.gov: NCT01690299

Note: LIBERATE was not powered for APR vs. ETN comparisons.

*Starting at Week 32, all non-responders (<PASI-50) had the option of adding topical therapies and/or ultraviolet B phototherapy (excluding oral psoralen combined with ultraviolet A) to their treatment regimen. Two patients in each group received topical therapy and/or phototherapy. BID=twice daily; QW=once weekly; PASI-50=≥50% reduction from baseline in Psoriasis Area and Severity Index score.

LIBERATE: Study Population

- Biologic-naive patients with a diagnosis of chronic, moderate to severe plaque psoriasis at screening and baseline
  - Psoriasis Area and Severity Index (PASI) score ≥12
  - Body surface area (BSA) ≥10%
  - Static Physician's Global Assessment (sPGA) score ≥3
- Patients must have had an inadequate response, intolerance, or contraindication to at least 1 conventional systemic agent for the treatment of psoriasis.
- Pre-planned efficacy analyses included patients with psoriasis in difficult-to-treat areas*:
  - Scalp psoriasis, moderate to very severe: Scalp Physician Global Assessment (ScPGA) score ≥3
  - Nail psoriasis: Nail Psoriasis Severity Index (NAPSI) score ≥1[§]
- Missing values were imputed using the last-observation-carried-forward (LOCF) methodology.

*At baseline. [§]NAPSI score for target nail representing worst nail psoriasis at baseline.

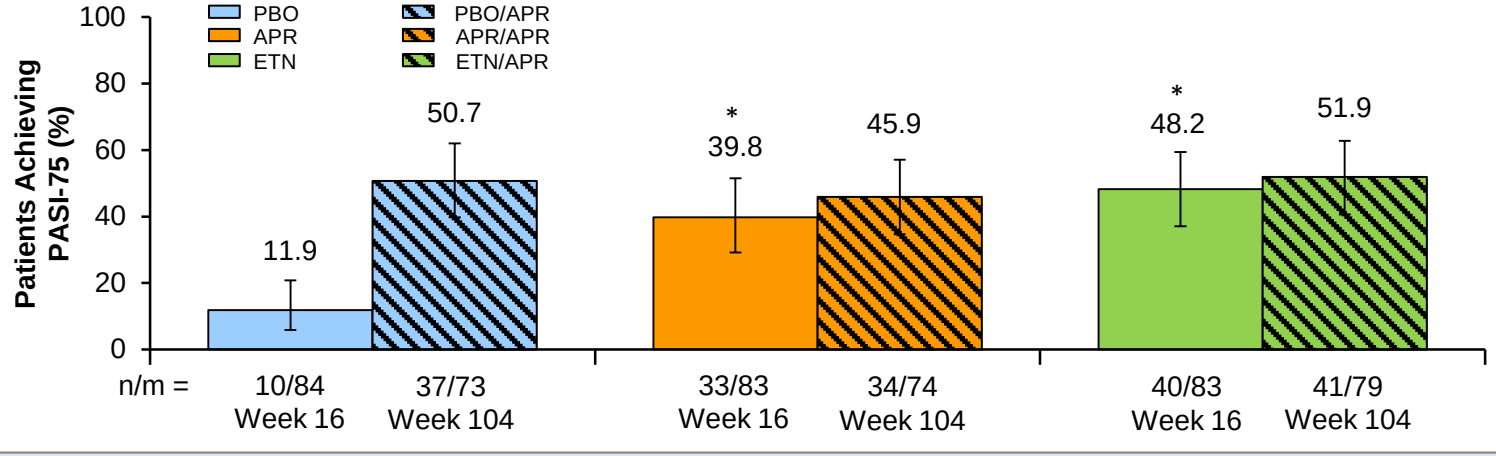
Baseline Patient Demographics and Disease Characteristics

	PBO n=84	APR n=83	ETN n=83
Age, mean, years	43.4	46.0	47.0
Male, n (%)	59 (70.2)	49 (59.0)	49 (59.0)
BMI, mean, kg/m^2	29.54	29.15	29.86
Weight, mean, kg	89.51	88.52	88.08
Duration of psoriasis, mean, years	16.6	19.7	18.1
PASI score (0-72), mean	19.4	19.3	20.3
PASI score >20, n (%)	32 (38.1)	28 (33.7)	34 (41.0)
BSA, mean, %	27.3	27.1	28.4
BSA >20%, n (%)	42 (50.0)	45 (54.2)	47 (56.6)
NAPSI score ≥1, n (%)	46 (54.8)	52 (62.7)	50 (60.2)
NAPSI score*, mean (SD)	4.1 (1.9)	4.2 (2.0)	4.3 (2.2)
ScPGA ≥3, n (%)	58 (69.0)	54 (65.1)	54 (65.1)
Prior use of conventional systemic medications, n (%) §	70 (83.3)	66 (79.5)	58 (69.9)

*In patients with NAPSI ≥1 for target nail, representing worst nail psoriasis at baseline. §No prior exposure to biologic therapy for treatment of psoriatic arthritis or psoriasis. BMI=body mass index.

PASI-75 Response

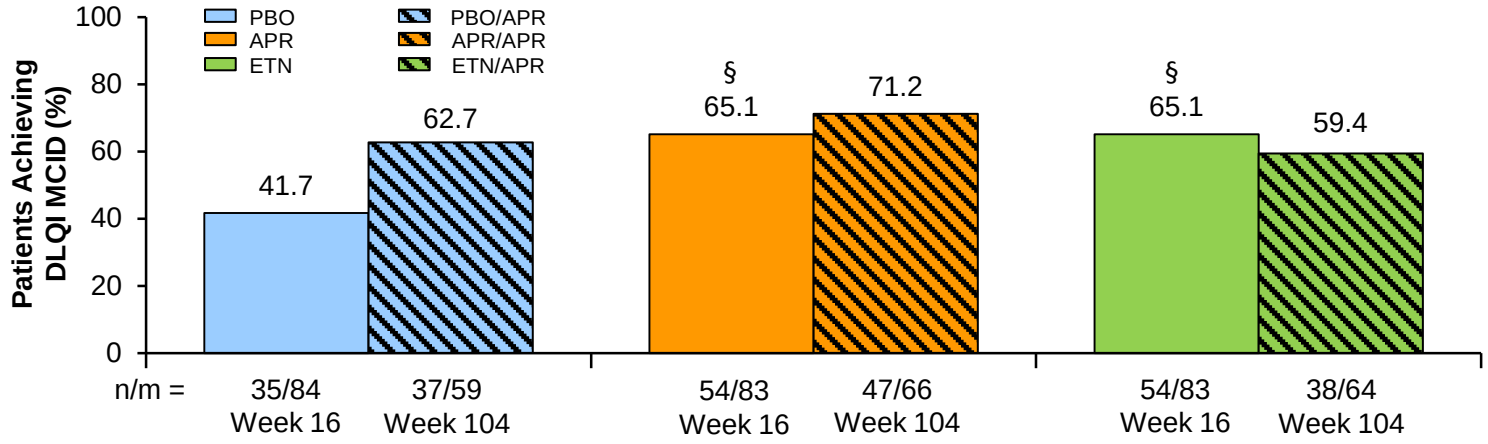
- The ≥75% reduction from baseline in PASI score (PASI-75) response achieved at Week 16 was sustained through Week 104 in patients continuing APR or switching from ETN to APR at Week 16.



*P<0.0001 vs. PBO.
Response at Week 16 and Week 104 was determined using the LOCF methodology. The analysis for Week 16 includes all patients in the modified intent-to-treat (mITT) group, while the Week 104 analysis includes patients who entered the apremilast extension phase and were treated in the phase. The vertical lines indicate 2-sided 95% confidence intervals.

DLQI MCID Response

- At Week 16, significantly more patients achieved a minimal clinically important difference (MCID)* in the Dermatology Life Quality Index (DLQI) with APR or ETN vs. PBO.
- DLQI MCID rates were generally maintained at Week 104 in APR/APR patients and ETN/APR patients. Responses at Week 104 among PBO/APR patients were generally similar to those in APR/APR patients.



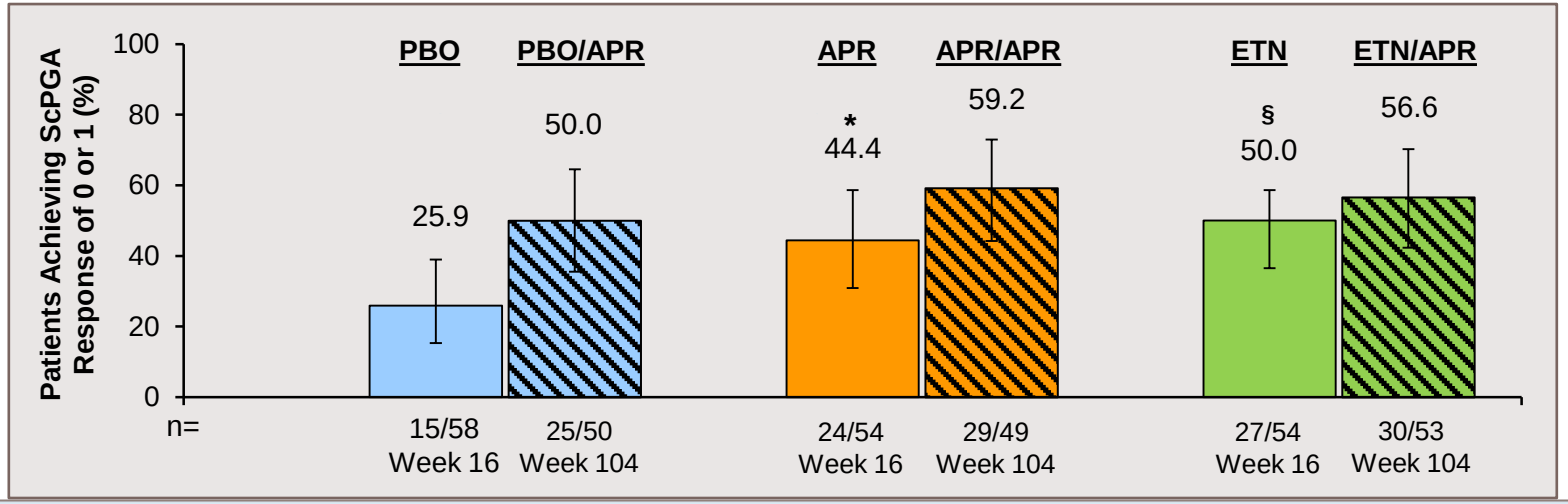
*Response defined as a decrease of ≥5 points in DLQI total score in patients with baseline DLQI total score >5. §Response at Week 16 and Week 104 was determined using the LOCF methodology. The analysis for Week 16 includes all patients in the mITT group, while the Week 104 analysis includes patients who entered apremilast extension phase and were treated in the phase.

§*P*=0.0032 vs. PBO.

Scalp Response

- Among patients with baseline ScPGA ≥3 (moderate or greater), ScPGA response of 0 (clear) or 1 (almost clear) was achieved by significantly more patients receiving APR compared with patients receiving PBO at Week 16.
- The ScPGA response achieved at Week 16 was sustained through Week 104 in APR/APR patients and ETN/APR patients. Responses at Week 104 among PBO/APR patients were generally similar to those in APR/APR patients.

ScPGA Response (mITT, LOCF)‡

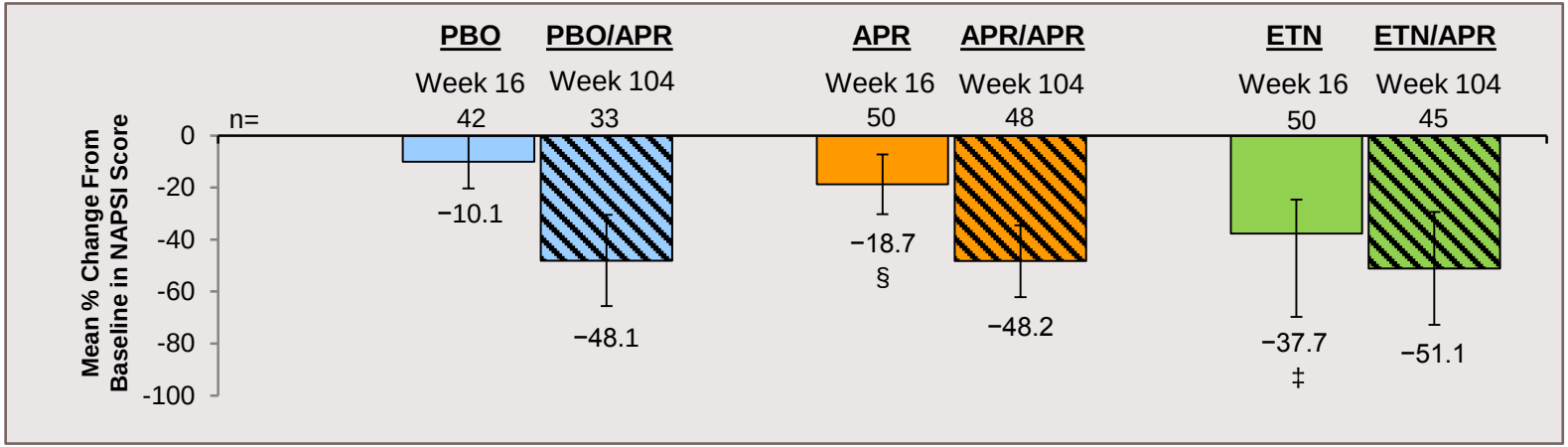


*P=0.0458 vs. PBO. §P=0.0083 vs. PBO. ‡Response at Week 16 and Week 104 was determined using the LOCF methodology. Week 104 analysis includes patients who entered the apremilast extension phase and were treated in the phase. The vertical lines indicate 2-sided 95% confidence intervals.

Nail Response

- The proportions of patients with nail psoriasis at baseline (NAPSI ≥1) who achieved NAPSI-50 at Week 16 were higher with APR (25.0%) or ETN (48.0%) than PBO (10.9%; *P*=0.0701 vs. APR and *P*<0.0001 vs. ETN).
- At Week 104, NAPSI-50 response was 60.4% (APR/APR), 65.2% (ETN/APR), and 48.6% (PBO/APR).
- The mean percentage change from baseline in NAPSI score continued to improve in APR/APR patients and was sustained in ETN/APR patients through Week 104.

Mean Percentage Change in NAPSI Score*



*In patients with NAPSI score ≥1 at baseline. Includes all patients with a baseline value and a post-baseline value at the study week. Missing scores were imputed using the LOCF methodology. The mean NAPSI score at baseline was 4.14 (PBO), 4.18 (APR), and 4.30 (ETN). §*P*=0.4959 vs. PBO. ‡*P*<0.0024 vs. PBO.

Overview of Adverse Events

Patients, n (%)*	APR Extension Phase (Weeks 16 to 104)					
	PBO/APR§ n=73		APR/APR n=74		ETN/APR‡ n=79	
	n=73; Pt-Yrs=95.6		n=74; Pt-Yrs=89.4		n=79; Pt-Yrs=102.3	
	n (%)	EAIR/ 100 Pt-Yrs	n (%)	EAIR/ 100 Pt-Yrs	n (%)	EAIR/ 100 Pt-Yrs
≥1 AE	45 (61.6)	100.88	49 (66.2)	112.74	54 (68.4)	104.58
≥1 severe AE	4 (5.5)	4.37	4 (5.4)	4.55	7 (8.9)	7.15
≥1 SAE	5 (6.8)	5.49	3 (4.1)	3.45	4 (5.1)	4.01
AE leading to drug withdrawal	3 (4.1)	3.14	4 (5.4)	4.49	2 (2.5)	1.96
AE leading to death	0 (0.0)	0.00	0 (0.0)	0.00	0 (0.0)	0.00

- Incidence of SAEs was low during the PBO-controlled period and was similar across groups during the APR extension phase.
- Discontinuation rates due to AEs were generally low across groups during the 0 to 16 week PBO-controlled period and the APR extension phase.
- No deaths occurred in either study period.
- Changes in laboratory parameters were infrequent and transient; incidence remained low across groups through 104 weeks.

*Safety population. §No dose titration for APR. ‡Dose titration for APR. SAE=serious adverse event.

Adverse Events in ≥5% of Patients in Any Treatment Group

Patients, n (%)*,§	APR Extension Phase (Weeks 16 to 104)					
	PBO/APR‡ n=73; Pt-Yrs=95.6		APR/APR n=74; Pt-Yrs=89.4		ETN/APR‖ n=79; Pt-Yrs=102.3	
	n (%)	EAIR/ 100 Pt-Yrs	n (%)	EAIR/ 100 Pt-Yrs	n (%)	EAIR/ 100 Pt-Yrs
Diarrhea	13 (17.8)	15.99	4 (5.4)	4.76	6 (7.6)	6.26
Nausea	5 (6.8)	5.46	3 (4.1)	3.46	5 (6.3)	5.15
URTI	5 (6.8)	5.50	5 (6.8)	5.91	1 (1.3)	0.99
Bronchitis	1 (1.4)	1.05	4 (5.4)	4.55	1 (1.3)	0.98
Nasopharyngitis	4 (5.5)	4.33	2 (2.7)	2.29	5 (6.3)	5.09
Headache	5 (6.8)	5.56	2 (2.7)	2.29	3 (3.8)	3.02
Sinusitis	0 (0.0)	0.00	1 (1.4)	1.14	5 (6.3)	5.02
Pain in extremity	1 (1.4)	1.06	3 (4.1)	3.48	4 (5.1)	4.11
Arthralgia	4 (5.5)	4.32	4 (5.4)	4.64	3 (3.8)	2.98
Rebound psoriasis	1 (1.4)	1.05	2 (2.7)	2.24	7 (8.9)	6.82
Psoriasis	2 (2.7)	2.09	4 (5.4)	4.55	0 (0.0)	0.00

- No increase in incidence of AEs occurring in ≥5% of patients in the PBO-controlled period was observed among patients in the APR/APR group with long-term exposure to APR.
- All cases of diarrhea and nausea occurring in the APR extension phase were mild to moderate in severity and generally resolved within 1 month.

*Each patient is counted once for each applicable category. §Safety population. ‡No dose titration for APR. ‖Dose titration for APR. URTI=upper respiratory tract infection.

Conclusions

- APR demonstrated significant efficacy vs. PBO at Week 16 that was sustained through Week 104 in biologic-naive patients with moderate to severe plaque psoriasis.
- APR and ETN each demonstrated statistically significant improvements in scalp psoriasis compared with PBO at Week 16 that were sustained through Week 104.
- Improvements in QOL achieved with APR and ETN at Week 16 (compared with PBO) were sustained through Week 104.
- Improvements in nail psoriasis were achieved with APR at Week 16, and continued APR treatment over 104 weeks resulted in further improvements in nail psoriasis.
- Efficacy was maintained in ETN patients who switched to APR.
- AEs did not increase with prolonged APR exposure, and no new safety or tolerability issues were observed through Week 104 in patients with moderate to severe plaque psoriasis.

P4768 - Efficacy of Guselkumab Within Specific Body Regions in Patients With Moderate-to-Severe Plaque Psoriasis: Results From the Phase 3 VOYAGE 1 Study

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guselkumab

Introduction

- Psoriasis involving the scalp, nails, hands and/or feet is common, troubling to patients, and particularly difficult to treat

Objective

- To compare the efficacy of guselkumab with placebo and adalimumab in patients with moderate-to-severe plaque psoriasis with involvement of the scalp, nails, hands and/or feet

Blauvelt A, et al. AAD 2017. P4768.

Methods

- VOYAGE 1 is a phase 3, multicenter, randomized, double-blinded, placebo- and active comparator-controlled study of guselkumab in adult patients with moderate-to-severe plaque psoriasis (Investigator's Global Assessment [IGA] ≥3, Psoriasis Area and Severity Index [PASI] ≥12, and body surface area [BSA] ≥10) for ≥6 months

- Patients were randomized to one of 3 treatment arms:
  - Placebo at Weeks 0, 4, and 12, followed by crossover to guselkumab 100 mg subcutaneously (SC) at Weeks 16 and 20, then every (q)8 weeks through Week 44 (n=174)
  - Guselkumab 100 mg SC at Weeks 0, 4, and 12, then q8 weeks through Week 44 (n=329)
  - Adalimumab 80 mg SC at Week 0, 40 mg at Week 1, then 40 mg q2 weeks through Week 47 (n=334)

- Efficacy assessments included scalp specific IGA (ss-IGA), fingernail Physician's Global Assessment (f-PGA), Nail Psoriasis Severity Index (NAPSI), and PGA of hands and/or feet (hf-PGA), between guselkumab and placebo at Week 16, and between guselkumab and adalimumab at Weeks 24 and 48

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Voyage 1 Study Design

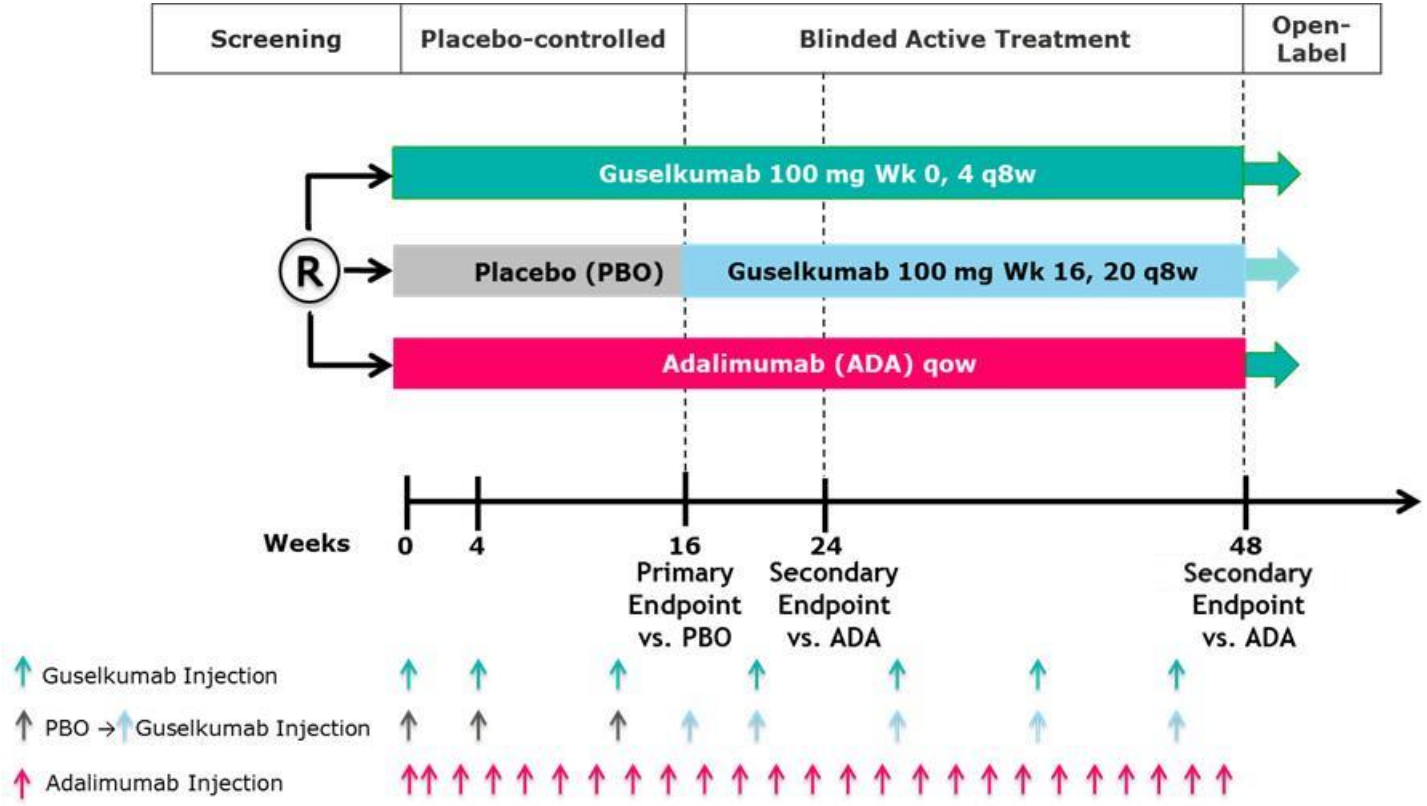

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Table 1. Summary of Demographics, Disease Characteristics, and Psoriasis Treatments at Baseline

	RANDOMIZED PATIENTS			
	PLACEBO	GUSELKUMAB	ADALIMUMAB	TOTAL
Randomized patients, n	174	329	334	837
Age [years], mean (SD)	44.9 (12.9)	43.9 (12.7)	42.9 (12.6)	43.7 (12.7)
Male, n (%)	119 (68.4%)	240 (72.9%)	249 (74.6%)	608 (72.6%)
Caucasian, n (%)	145 (83.3%)	262 (79.6%)	277 (82.9%)	684 (81.7%)
BMI (kg/m^2), mean (SD)	28.9 (6.9)	29.7 (6.2)	29.8 (6.5)	29.6 (6.5)
Duration of psoriasis [years], mean (SD)	17.6 (12.4)	17.9 (12.3)	17.0 (11.3)	17.5 (11.9)
Prior psoriasis treatments, n (%)				
Topical agents	154 (88.5%)	299 (90.9%)	309 (92.8%)	762 (91.1%)
Phototherapy (PUVA or UVB)	86 (49.4%)	188 (57.3%)	180 (53.9%)	454 (54.3%)
Non-biologic systemic (PUVA, methotrexate, cyclosporine, acitretin, apremilast, or tofacitinib)	92 (52.9%)	210 (63.8%)	215 (64.4%)	517 (61.8%)
Biologics (etanercept, infliximab, alefacept, efalizumab, ustekinumab, briakinumab, secukinumab, ixekizumab, or brodalumab)	34 (19.5%)	71 (21.6%)	70 (21.0%)	175 (20.9%)
Psoriatic arthritis, n (%)	30 (17.2%)	64 (19.5%)	62 (18.6%)	156 (18.6%)

BMI=Body mass index; PUVA=Psoralen and Ultraviolet A; UVB=Ultraviolet B

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Table 1. Summary of Demographics, Disease Characteristics, and Psoriasis Treatments at Baseline (continued)

- Among randomized patients, 84.6%, 52.0%, and 27.2% had baseline scores of ≥2 (i.e., ≥mild disease) for ss-IGA, f-PGA, and hf-PGA, respectively, and were included in analyses of regional psoriasis

	RANDOMIZED PATIENTS			
	PLACEBO	GUSELKUMAB	ADALIMUMAB	TOTAL
Randomized patients, n	174	329	334	837
Patients with scalp psoriasis, n (%)	150 (86.2%)	291 (88.4%)	295 (88.3%)	736 (87.9%)
Patients with nail psoriasis, n (%)	99 (56.9%)	198 (60.2%)	194 (58.1%)	491 (58.7%)
Patients with hand and/or foot psoriasis, n (%)	44 (25.3%)	100 (30.4%)	101 (30.2%)	245 (29.3%)
ss-IGA score, N	150	291	295	736
Mild (2), n (%)	31 (20.7%)	49 (16.8%)	54 (18.3%)	134 (18.2%)
Moderate (3), n (%)	89 (59.3%)	171 (58.8%)	175 (59.3%)	435 (59.1%)
Severe (4), n (%)	25 (16.7%)	57 (19.6%)	57 (19.3%)	139 (18.9%)
f-PGA score, N	99	198	194	491
Mild (2), n (%)	33 (33.3%)	62 (31.3%)	66 (34.0%)	161 (32.8%)
Moderate (3), n (%)	42 (42.4%)	83 (41.9%)	90 (46.4%)	215 (43.8%)
Severe (4), n (%)	13 (13.1%)	29 (14.6%)	17 (8.8%)	59 (12.0%)
NAPSI score (0-8), N	99	194	191	484
Mean (SD)	4.7 (1.9)	4.9 (2.0)	4.6 (2.0)	4.7 (2.0)
Median	4.0	5.0	4.0	4.0
hf-PGA score, N	44	100	101	245
Mild (2), n (%)	15 (34.1%)	34 (34.0%)	37 (36.6%)	86 (35.1%)
Moderate (3), n (%)	21 (47.7%)	42 (42.0%)	45 (44.6%)	108 (44.1%)
Severe (4), n (%)	7 (15.9%)	14 (14.0%)	13 (12.9%)	34 (13.9%)

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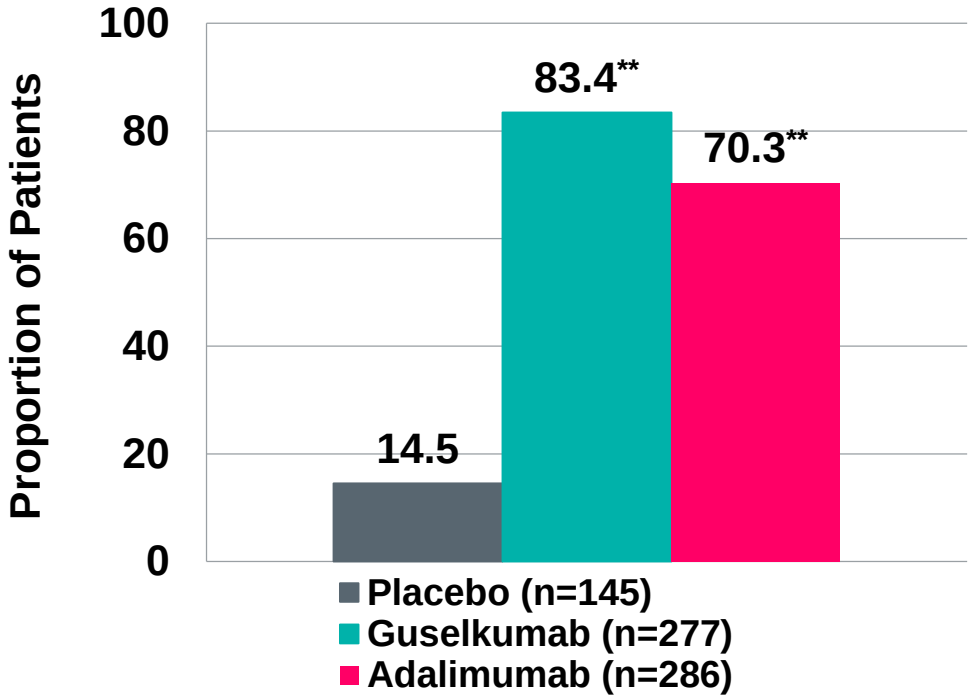
Figure 1. Proportions of Patients Achieving Scalp Specific (ss)-IGA Score of Absence of Disease (0) or Very Mild Disease (1) and ≥2-Grade Improvement From Baseline at Week 16*



**P<0.001 vs. placebo

*Among patients with ss-IGA score ≥2 at baseline

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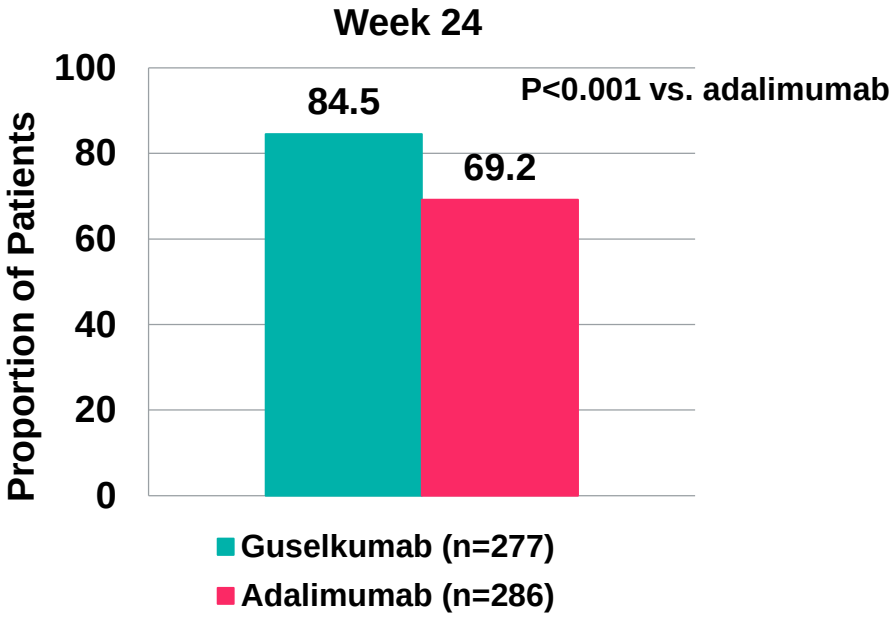
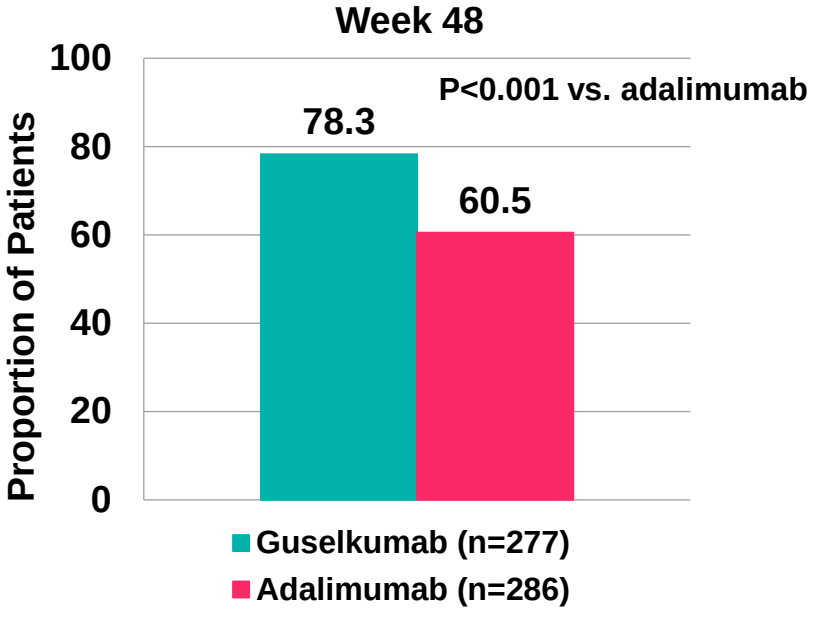
guselkumab

Figure 2. Proportions of Patients Achieving Scalp Specific (ss)-IGA Score of Absence of Disease (0) or Very Mild Disease (1) and ≥2-Grade Improvement From Baseline at Weeks 24 and 48*





*Among patients with ss-IGA score ≥2 at baseline

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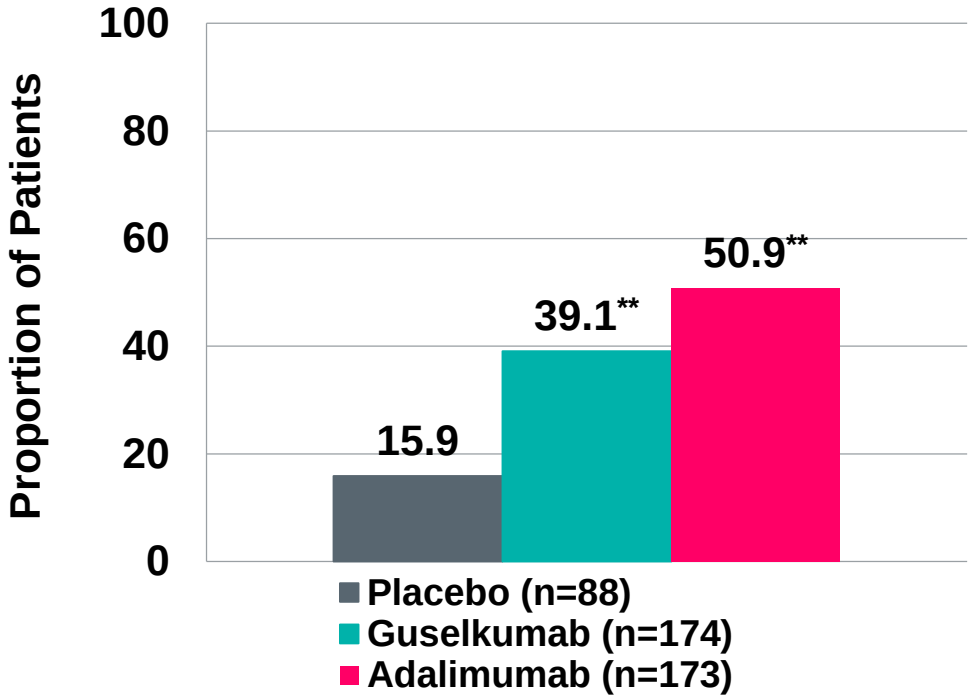
Figure 3. Proportions of Patients Achieving Fingernail (f)-PGA Score of Clear (0) or Minimal (1) at Week 16*



**P<0.001 vs. placebo

*Among patients with f-PGA score ≥2 at baseline

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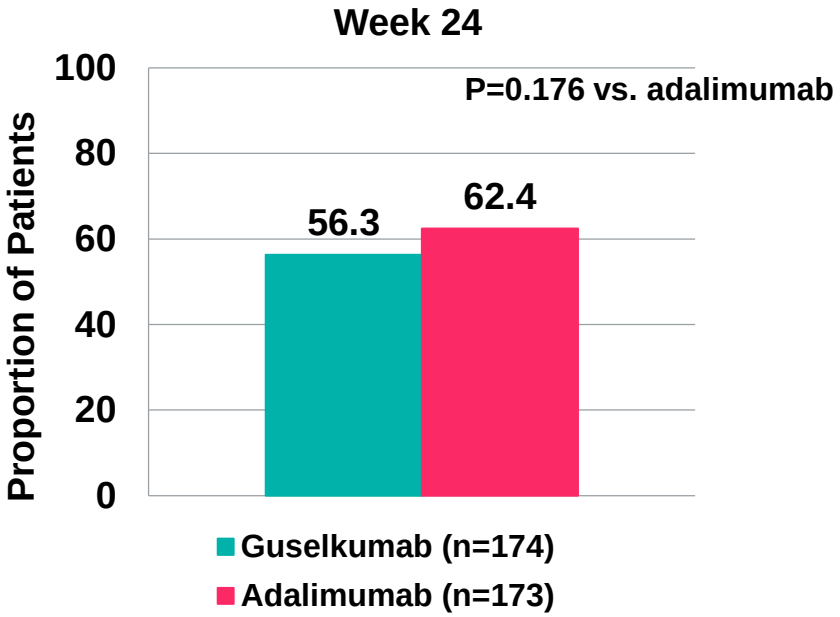
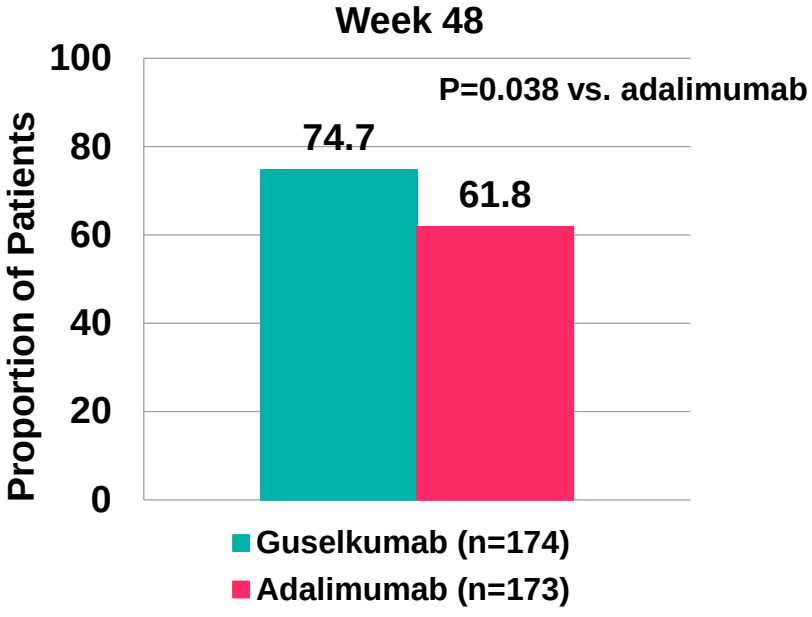
Figure 4. Proportions of Patients Achieving Fingernail (f)-PGA Score of Clear (0) or Minimal (1) at Weeks 24 and 48*





*Among patients with f-PGA score ≥2 at baseline

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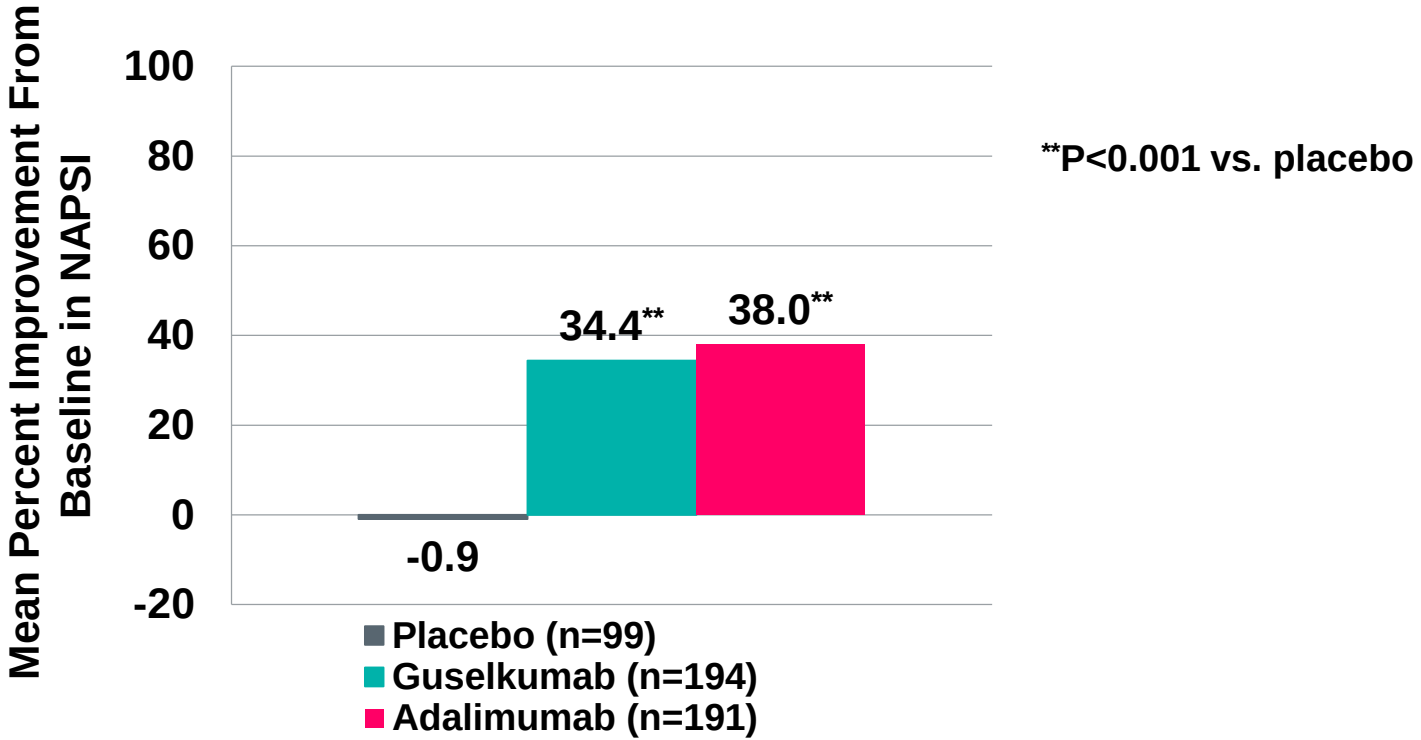
Figure 5. Mean Percent Improvement From Baseline in Nail Psoriasis Severity Index (NAPSI) at Week 16*



*Among patients with NAPSI score >0 at baseline

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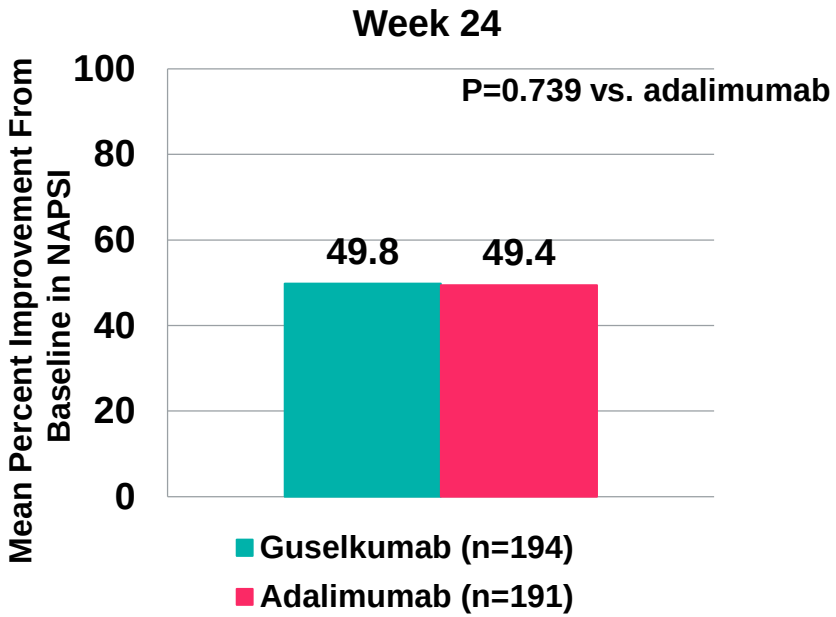
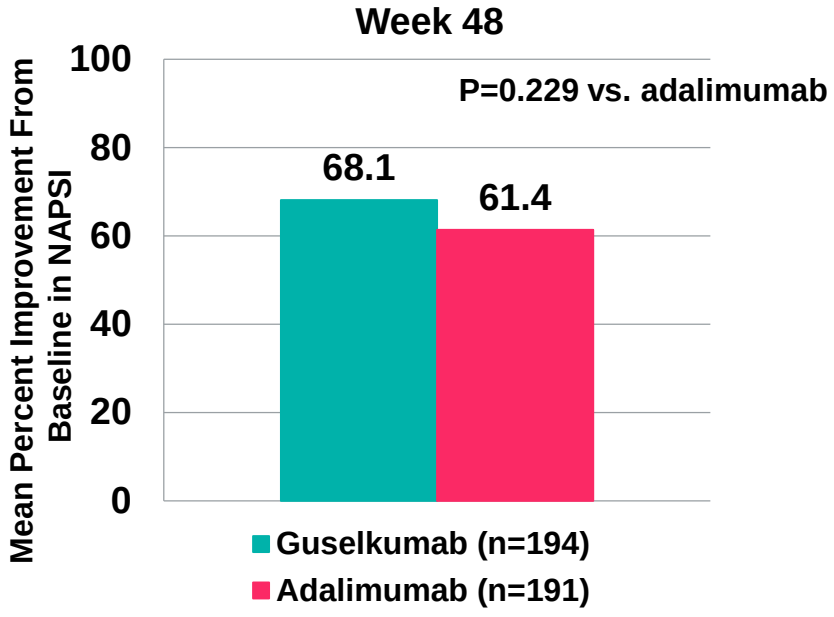
Figure 6. Mean Percent Improvement From Baseline in Nail Psoriasis Severity Index (NAPSI) at Weeks 24 and 48*





*Among patients with NAPSI score >0 at baseline

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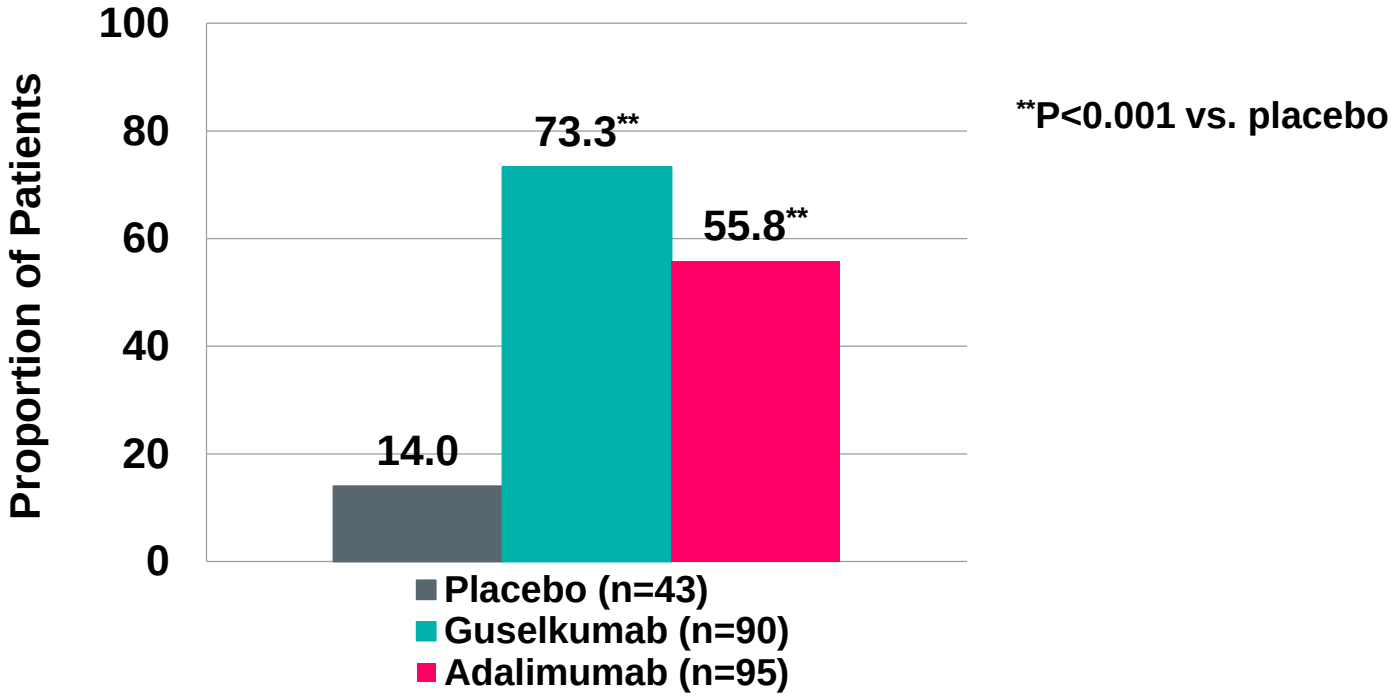
Figure 7. Proportions of Patients Achieving Hands and/or Feet (hf)-PGA Score of Clear (0) or Almost Clear (1) and ≥2-Grade Improvement From Baseline at Week 16*



*Among patients with hf-PGA score ≥2 at baseline

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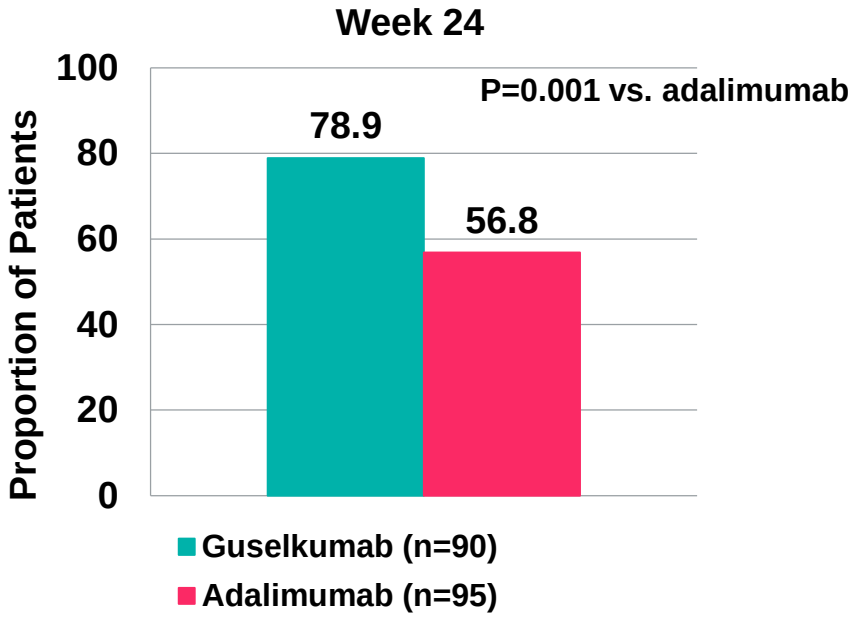
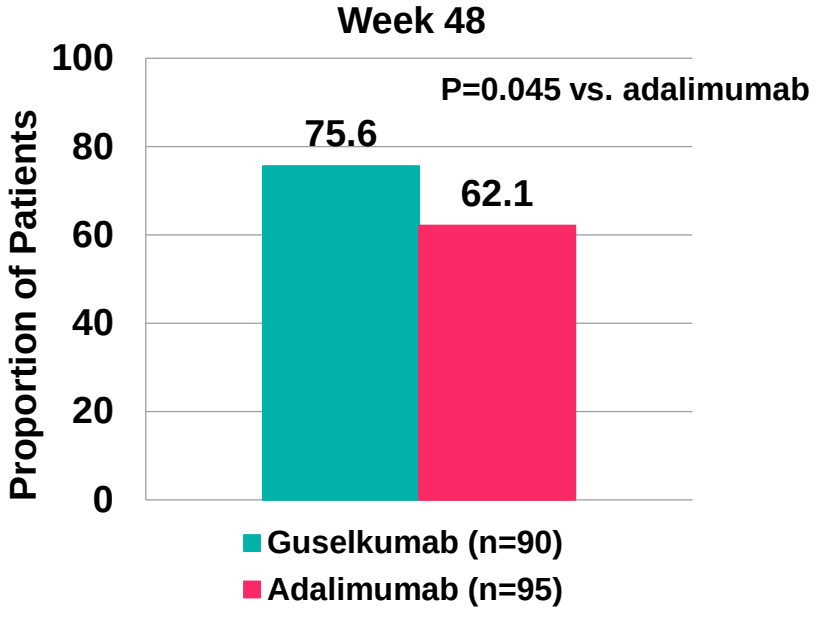
Figure 8. Proportions of Patients Achieving Hands and/or Feet (hf)-PGA Score of Clear (0) or Almost Clear (1) and ≥2-Grade Improvement From Baseline at Weeks 24 and 48*





*Among patients with hf-PGA score ≥2 at baseline

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Table 2. Adverse Events (AEs) Through Week 48

	WEEKS 0-16 (PLACEBO-CONTROLLED)			WEEKS 0-48 (ACTIVE COMPARATOR-CONTROLLED)	
	PLACEBO	GUSELKUMAB	ADALIMUMAB	GUSELKUMAB	ADALIMUMAB
Treated patients, n	174	329	333	329	333
Avg. duration of follow-up, weeks	15.9	16.3	16.1	46.5	45.6
≥1 AE, n (%)	86 (49.4%)	170 (51.7%)	170 (51.1%)	243 (73.9%)	248 (74.5%)
Common AEs, n (%)*					
Nasopharyngitis	17 (9.8%)	30 (9.1%)	35 (10.5%)	83 (25.2%)	74 (22.2%)
Upper respiratory tract infection	9 (5.2%)	25 (7.6%)	16 (4.8%)	47 (14.3%)	42 (12.6%)
Injection site erythema	1 (0.6%)	6 (1.8%)	15 (4.5%)	8 (2.4%)	22 (6.6%)
Headache	7 (4.0%)	12 (3.6%)	13 (3.9%)	18 (5.5%)	25 (7.5%)
Arthralgia	3 (1.7%)	11 (3.3%)	9 (2.7%)	18 (5.5%)	16 (4.8%)
Pruritus	10 (5.7%)	5 (1.5%)	7 (2.1%)	8 (2.4%)	12 (3.6%)
Back pain	2 (1.1%)	6 (1.8%)	4 (1.2%)	12 (3.6%)	17 (5.1%)
Discontinued due to ≥1 AE, n (%)	2 (1.1%)	4 (1.2%)	3 (0.9%)	9 (2.7%)	12 (3.6%)
≥1 SAE, n (%)	3 (1.7%)	8 (2.4%)	6 (1.8%)	16 (4.9%)	15 (4.5%)
Infections, n (%)	44 (25.3%)	85 (25.8%)	85 (25.5%)	172 (52.3%)	167 (50.2%)
Requiring antibiotics	13 (7.5%)	20 (6.1%)	24 (7.2%)	54 (16.4%)	60 (18.0%)
Serious infections	0	0	2 (0.6%)	2 (0.6%)	3 (0.9%)
Malignancies other than NMSC, n (%)**	0	0	0	2 (0.6%)	0
NMSC, n (%)†	0	1 (0.3%)	0	2 (0.6%)	1 (0.3%)
MACE, n (%)‡	0	1 (0.3%)	1 (0.3%)	1 (0.3%)	1 (0.3%)

NMSC=Nonmelonoma skin cancer; MACE=Major adverse cardiovascular event

*Occurred in ≥5% of patients in any treatment group; **Included prostate and breast cancer; †Included basal cell carcinoma; ‡Includes cardiovascular death, myocardial infarction, and stroke

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Conclusions

- Treatment with guselkumab for one year was efficacious in treating regional disease of the scalp, nails, hands and/or feet in patients with moderate-to-severe psoriasis
- Guselkumab was well-tolerated

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P4449

Secukinumab Provides Faster and More Sustained 52-Week Complete Relief From Psoriasis-Related Pain, Itching, and Scaling Than Ustekinumab in Subjects With Moderate to Severe Plaque Psoriasis

Bruce Strober,[1] Sasha Jazayeri,[2] Diamant Thaçi,[3] Matthias Augustin,[4] Yang Zhao,[5] Isabelle Gilloteau,[6] Lori McLeod,[7] Bintu Sherif,[7] Vivian Herrera,[5] Judit Nyirady,[5] Adriana Guana,[6] Mark Lebwohl[8]

(Please see authors' affiliations on the last panel)

Background

- Secukinumab, a fully human monoclonal antibody that selectively neutralizes IL-17A, has been shown to have significant efficacy in the treatment of moderate to severe psoriasis and psoriatic arthritis, demonstrating a rapid onset of action and sustained responses with a favorable safety profile[1-4]
- In a head-to-head, double-blind study, secukinumab demonstrated sustained superior efficacy versus ustekinumab in clearing skin through Week 52, greater improvement in quality of life, and a favorable and comparable safety profile[5]

Objective

- To compare the effect of secukinumab versus ustekinumab over 52 weeks on patient-reported assessments of psoriasis-related pain, itching, and scaling

The study was sponsored by Novartis Pharmaceuticals, East Hanover, NJ.

Methods

Subjects' Assessment of Psoriasis-Related Pain, Itching, and Scaling (Assessed at Baseline and Weeks 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 48, and 52 via numeric rating scale—see table below)

- Complete relief of symptom was defined as absence of symptom (item score of 0)

Subject's Assessment Item	Intensity score
Overall, how severe was your psoriasis-related pain over the past 24 hours?	0 = No pain 10 = Pain as bad as it could be
Overall, how severe was your psoriasis-related itch over the past 24 hours?	0 = No itching 10 = Itching as bad as it could be
Overall, how severe was your psoriasis-related scaling over the past 24 hours?	0 = No scaling 10 = Scaling as bad as it could be

Analyses

- Analysis of covariance was used to assess change from baseline to Week 52, with body weight stratum and baseline score as covariates; Fisher's exact test was used for the responder analysis
- Missing values were imputed using last observation carried forward (LOCF)

Results

Baseline scores were similar across the secukinumab (n = 336)/ustekinumab (n = 339) treatment groups:

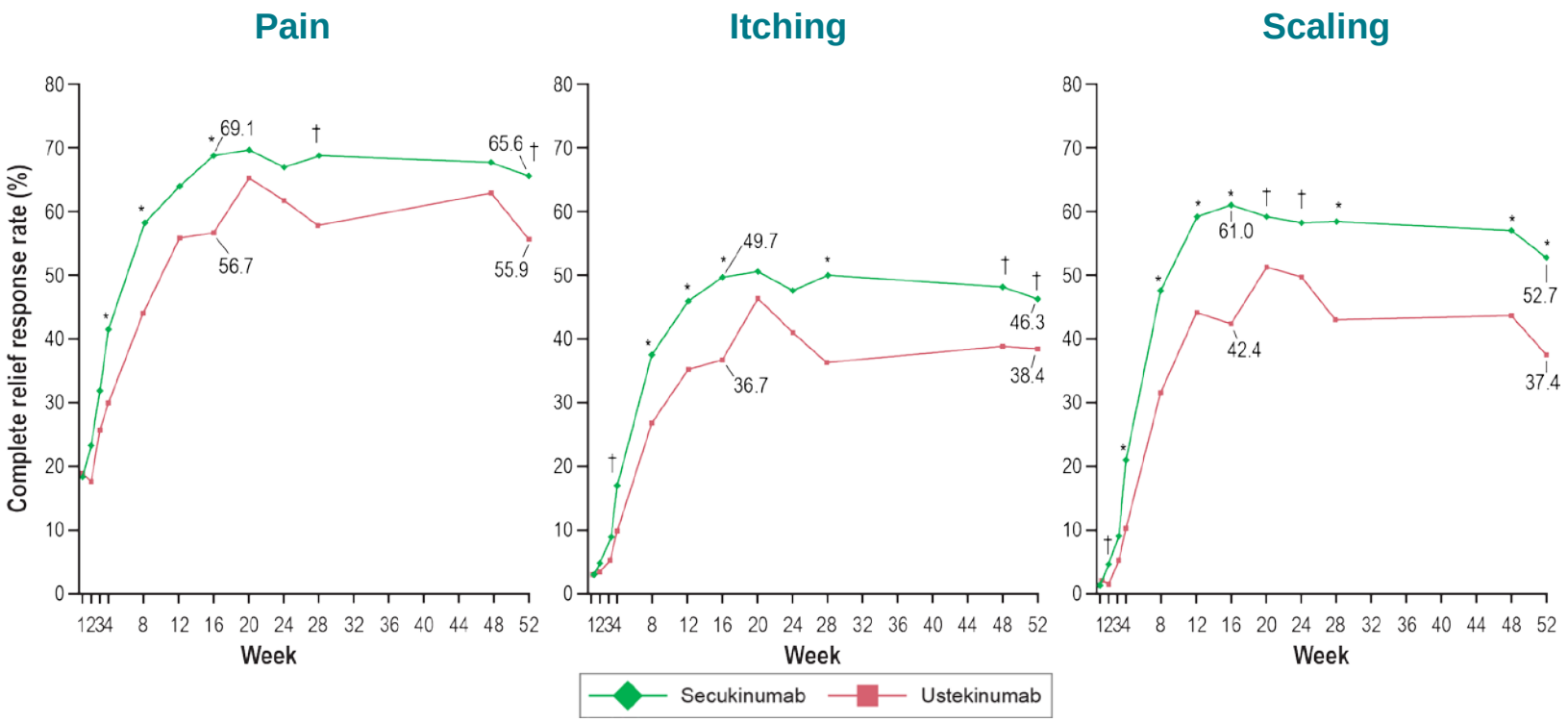
- Pain mean (standard deviation): 4.0 (3.18)/3.8 (3.09)
- Itching mean (standard deviation): 6.3 (2.74)/6.3 (2.66)
- Scaling mean (standard deviation): 6.5 (2.66)/6.5 (2.52)

Subjects treated with secukinumab achieved significantly greater mean improvement (reductions) in psoriasis-related pain, itching, and scaling as early as Week 2 (P < 0.05)

- At Weeks 16 and 52, the mean change (reduction) from baseline was significantly greater for secukinumab than ustekinumab in subjects' assessment of:
  - **Pain**: Week 16: –3.07 versus – 2.81; Week 52: – 3.02 versus – 2.56; all P < 0.05
  - **Itching**: Week 16: –4.97 versus –4.57; Week 52: –4.88 versus –4.27; all P < 0.05
  - **Scaling**: Week 16: –5.62 versus –5.14; Week 52: –5.41 versus –4.68; all P < 0.05

At Weeks 16 and 52, Significantly More Subjects With Secukinumab Reported Complete Relief of Psoriasis-Related Pain, Itching, and Scaling Than Those Treated With Ustekinumab

- A significantly greater proportion of secukinumab-treated subjects achieved complete relief of pain, itching, and scaling than ustekinumab-treated subjects ($P < 0.05$); differences were observed as early as Week 4.



* $P < 0.01$; † $P < 0.05$; Data presented using LOCF
Note: Complete relief of symptoms response defined as score of 0 (for those with symptom score > 0 at baseline)

LOCF = last observation carried forward.

Conclusion

Secukinumab achieved and sustained significantly greater proportions of subjects reporting complete relief of pain, itching, and scaling than ustekinumab over 52 weeks, consistent with superior and sustained clinical efficacy results in CLEAR

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Efficacy and Safety of Ixekizumab for the Treatment of Moderate-to-Severe Plaque Psoriasis: Results Through 108 Weeks of a Randomized, Phase III Clinical Trial (UNCOVER-3)

Andrew Blauvelt,[1] Melinda Gooderham,[2] Lars Iversen,[3] Susan Ball,[4] Lu Zhang,[4] Noah Agada,[4] Kristian Reich[5]

[1]Oregon Medical Research Center, Portland, USA; [2]SKiN Centre for Dermatology, Peterborough, Canada; [3]Aarhus University Hospital, Aarhus, Denmark; [4]Eli Lilly and Company, Indianapolis, USA; [5]Dermatologikum Hamburg and SCIderm Research Institute, Hamburg, Germany

This study was sponsored by Eli Lilly and Company.

Disclosures

- A. Blauvelt has served as a scientific adviser/clinical study investigator for: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Genentech, GlaxoSmithKline, Janssen, Eli Lilly and Company, Merck, Novartis, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, UCB, and Valeant and as a paid speaker for: Eli Lilly and Company; M. Gooderham has served as an investigator/speaker/advisory board member for: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly and Company, Galderma, Janssen, Leo Pharma, Novartis, and Pfizer and as an investigator for: Dermira, UCB, and Coherus; L. Iversen has been an investigator/paid speaker/consultant/advisory board member for: MSD, Pfizer, AbbVie, Janssen-Cilag, Eli Lilly and Company, Leo Pharma, and Novartis, has been a paid speaker/consultant/advisory board member for: Almirall, has been an investigator for: Amgen, and has received research and educational grants from: Pfizer, AbbVie, Novartis, MSD, and Leo Pharma; K. Reich has been an advisory board member, and/or speaker, and/or consultant, and/or has participated in clinical studies for: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Leo Pharma, Eli Lilly and Company, Medac, MSD, Novartis, Pfizer, Regeneron, Takeda, UCB Pharma, and Xenoport; S. Ball; N. O. Agada; and L. Zhang are shareholders of Eli Lilly and Company and are employees of Eli Lilly and Company
- The studies were sponsored by Eli Lilly and Company. Medical writing services were provided by David Sunter PhD, of ProScribe – part of the Envision Pharma Group, and were funded by Eli Lilly and Company

Background and Objective

Background

- In moderate-to-severe plaque psoriasis, long-term treatment is usually required to maintain adequate control of disease activity[1-4]
- Ixekizumab is a high affinity monoclonal antibody that selectively targets interleukin-17A[5]
  - Has shown significant efficacy in the treatment of moderate-to-severe plaque psoriasis for up to 60 weeks treatment duration[6-9]

Objective

- To assess the long-term efficacy and safety of ixekizumab through 108 weeks of treatment in the UNCOVER-3 study – a randomized, double-blind, multicenter, Phase 3 clinical trial of ixekizumab for the treatment of moderate-to-severe plaque psoriasis

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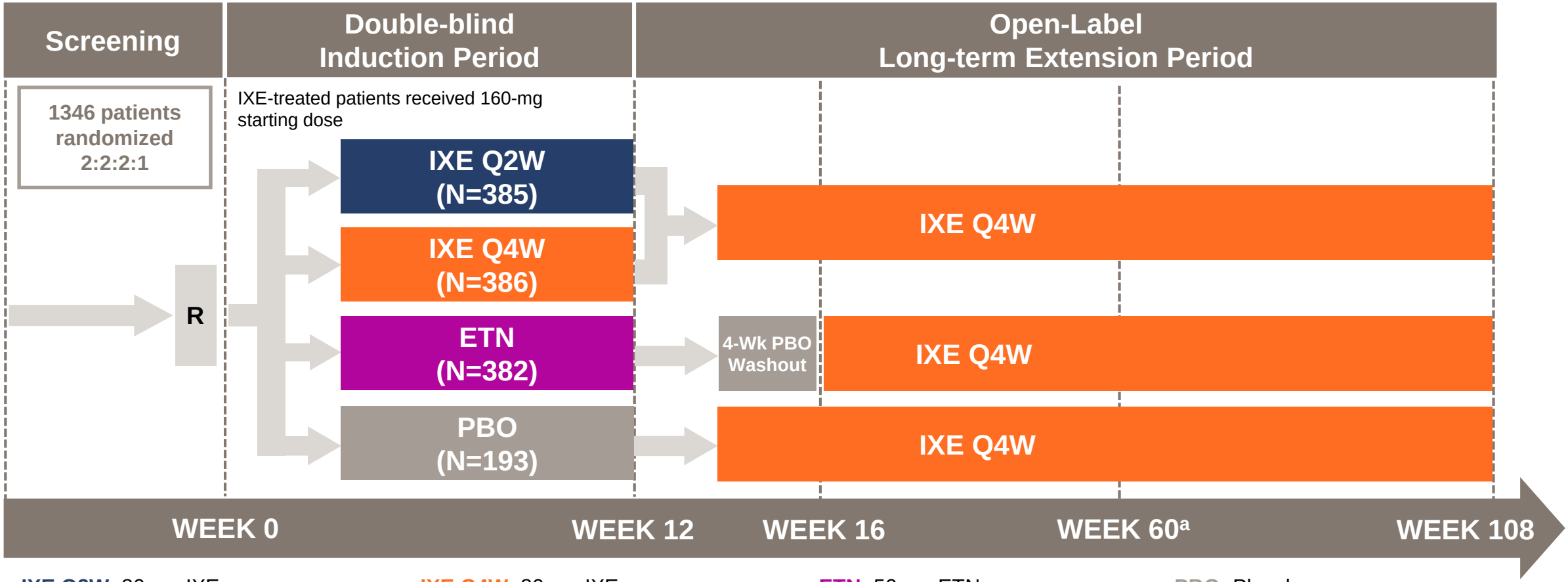
Study Design
UNCOVER-3



IXE Q2W: 80 mg IXE every 2 weeks

IXE Q4W: 80 mg IXE every 4 weeks

ETN: 50 mg ETN twice weekly

PBO: Placebo

[a] At Week 60, patients could increase dosage to IXE Q2W until the end-of-study at the investigator's discretion

ETN=etanercept; IXE=ixekizumab; R=randomization

Methods

- Efficacy was measured by the percentage of patients achieving a 75%, 90%, or 100% improvement from baseline in the Psoriasis Area and Severity Index (PASI) and a static Physician's Global Assessment (sPGA) score of 0,1 or 0
- Efficacy data were summarized based on observed case, last observation carried forward, and multiple imputation (the partial imputation of non-monotone missing data using Markov chain Monte Carlo method with the simple imputation model, followed by a sequential regression imputation with the baseline score)
- At Week 60, patients could increase dosage to IXE Q2W until the end-of-study at the investigator's discretion

Baseline Demographics and Disease Characteristics

ITT Population

	Total Randomized (N=1346)	Total IXE Randomized Population (N=771)
Age, years	45.8 (13.1)	45.6 (12.9)
Male, n (%)	918 (68.2)	512 (66.4)
Previous biologic therapy, n (%)	209 (15.5)	116 (15.0)
Psoriasis duration, years	18.1 (12.2)	18.1 (12.3)
Percentage of BSA involved	28.3 (17.1)	28.2 (16.9)
PASI	20.9 (8.2)	20.9 (8.2)
sPGA	3.5 (0.6)	3.5 (0.6)

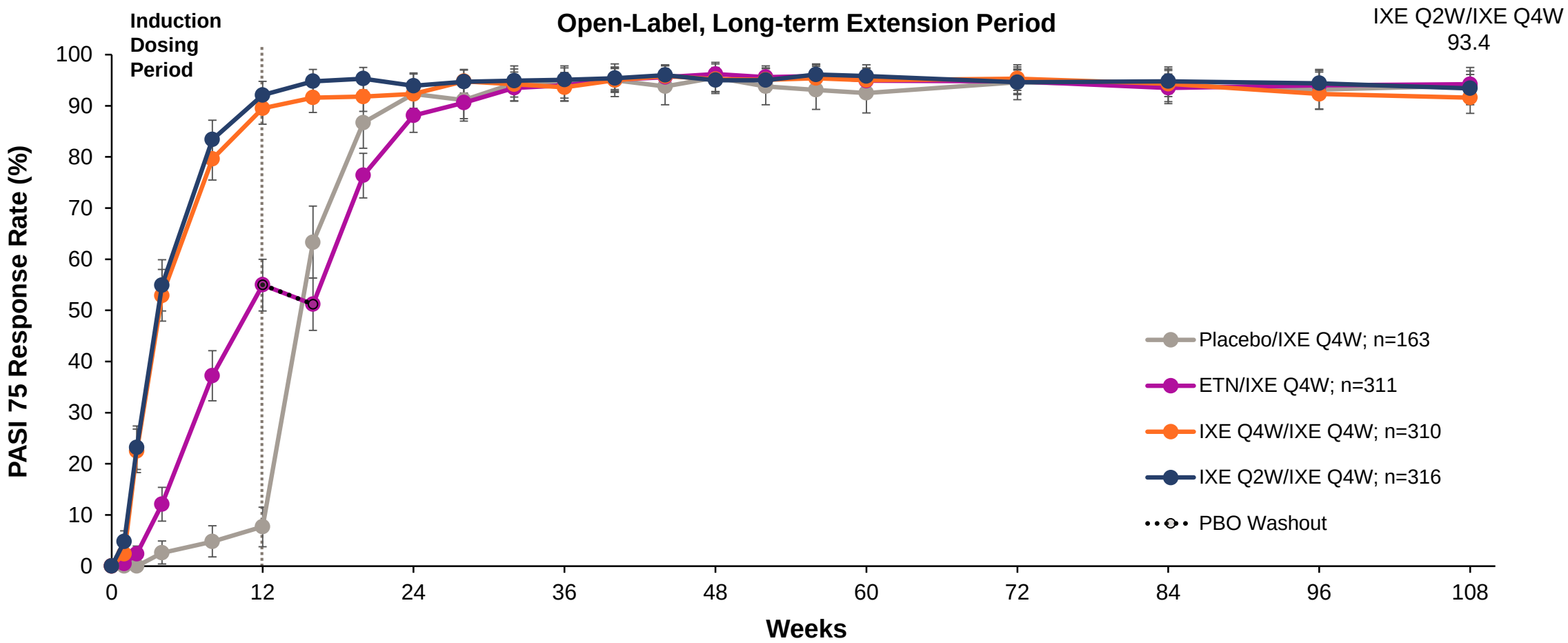
Values are mean (standard deviation) unless otherwise stated

For inclusion criteria see Gordon KB, et al. *N Eng J Med*. 2016;375:345-356

BSA=Body Surface Area; ITT=intent to treat; IXE=ixekizumab; PASI=Psoriasis Area and Severity Index; sPGA=static Physician's Global Assessment

PASI 75 Response Rate Over 2 Years

Maintenance of Response, All Treatments: As-Observed; ITT Population

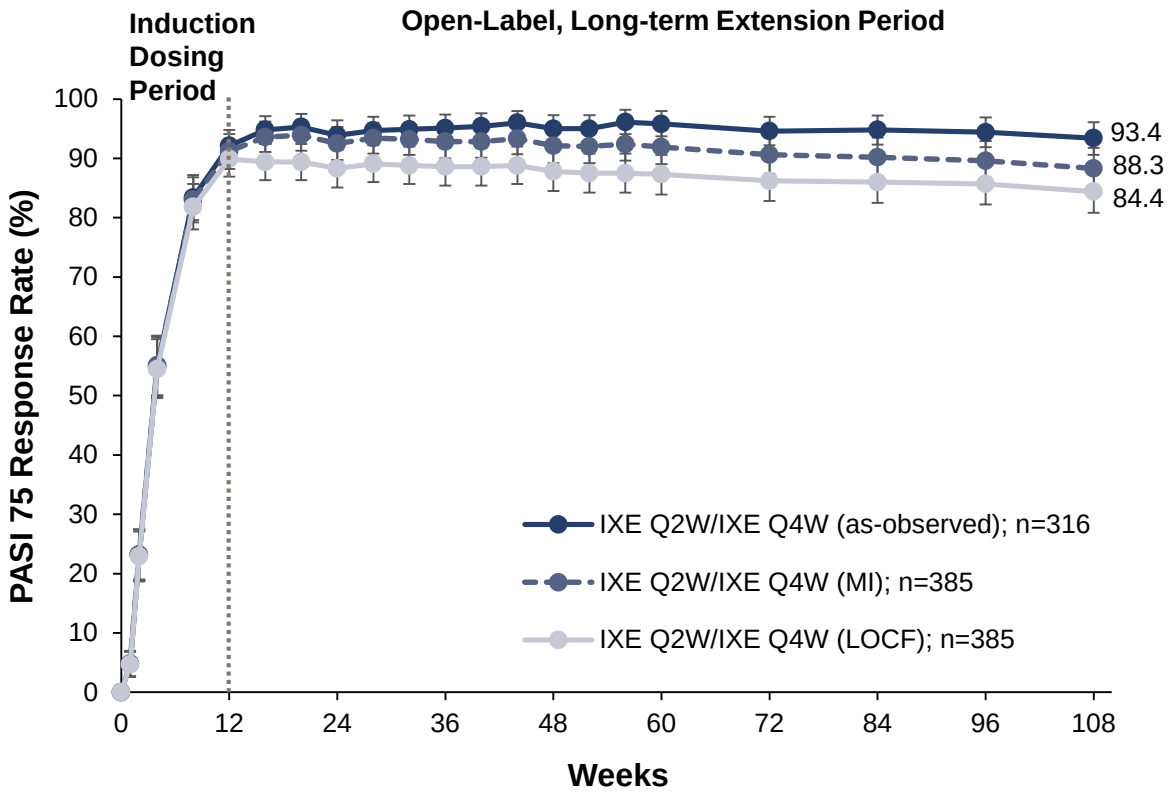


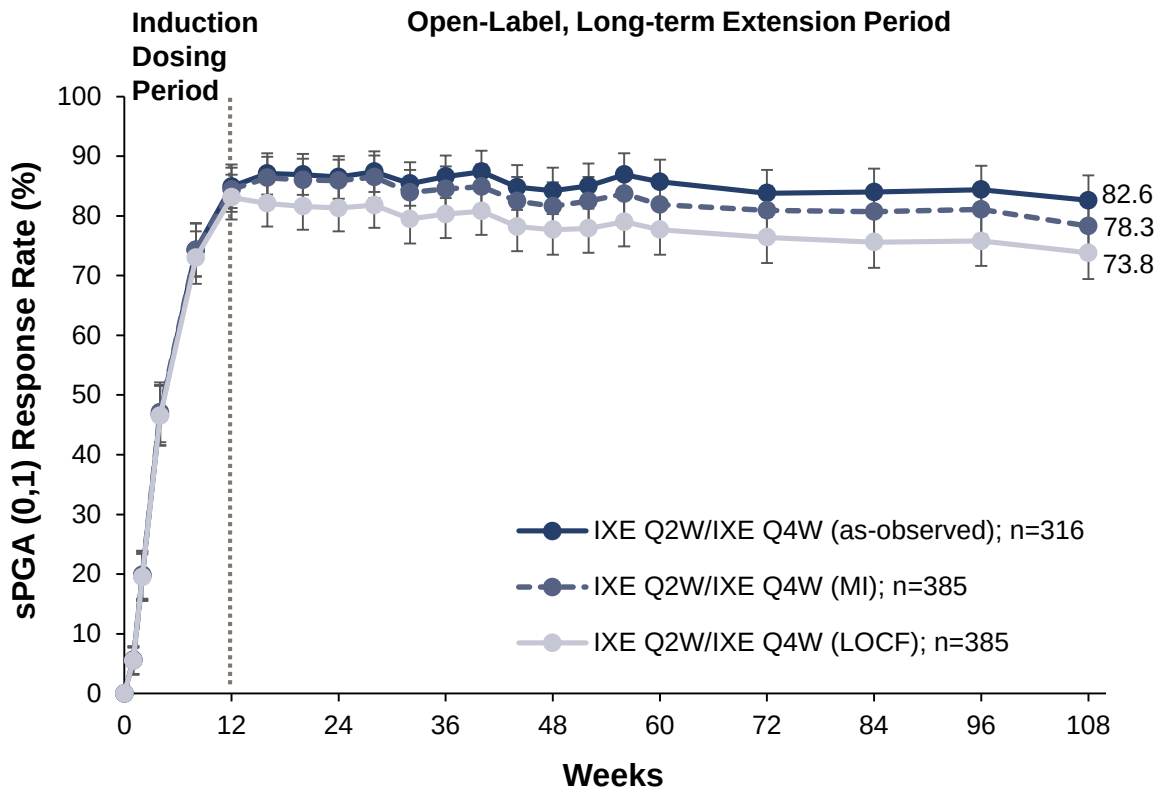
PASI 75 response rate at each post-baseline visit. The sample sizes are provided for the Week 108 visit. Error bars represent 95% CI

CI=confidence interval; ETN=50 mg etanercept twice weekly; ITT=intent to treat; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; IXE Q2W/IXE Q4W=IXE Q2W during induction then IXE QW4 during LTE; PASI=Psoriasis Area and Severity Index; PASI 75=Psoriasis Area and Severity Index 75% Response; PBO=placebo

PASI 75 and sPGA (0,1) Response Rates Over 2 Years

IXE Q2W/IXE Q4W: As-Observed, LOCF and MI; ITT Population



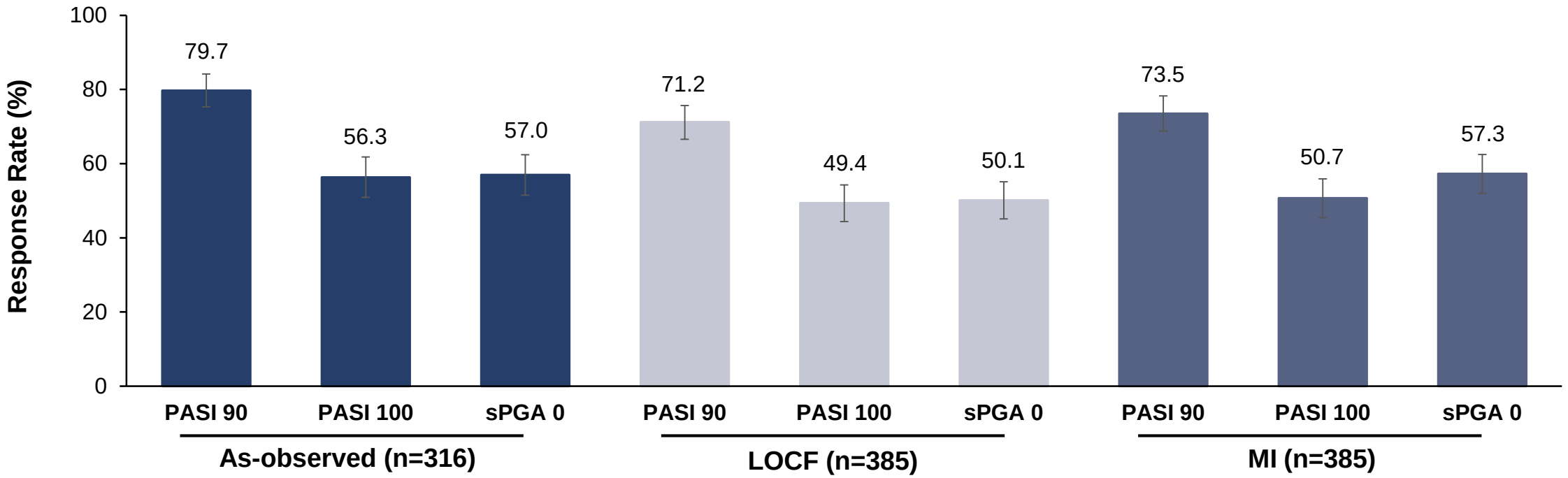


PASI 75 and sPGA (0,1) response rates for the IXE Q2W/IXE Q4W dosing regimen. The as-observed population sample size is provided for the Week 108 visit. Error bars represent 95% CI

CI=confidence interval; ITT=intent to treat; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; IXE Q2W/IXE Q4W=IXE Q2W during induction then IXE QW4 during LTE; LOCF=last observation carried forward; MI=multiple imputation; PASI=Psoriasis Area and Severity Index; PASI 75=Psoriasis Area and Severity Index 75% Response; sPGA=static Physician's Global Assessment

PASI and sPGA Response Rates at Week 108

IXE Q2W/IXE Q4W: As-Observed, LOCF, and MI; ITT Population



PASI and sPGA and response rates at Week 108 for the IXE Q2W/IXE Q4W dosing regimen. Error bars represent 95% CI

CI=confidence interval; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; IXE Q2W/IXE Q4W=IXE Q2W during induction then IXE QW4 during LTE; LOCF=last observation carried forward; MI=multiple imputation; PASI=Psoriasis Area and Severity Index; PASI 90=Psoriasis Area and Severity Index 90% Response; PASI 100=Psoriasis Area and Severity Index 100% Response; PBO=placebo; sPGA=static Physician's Global Assessment

Psoriasis Measures for Patients Who Increased Dose to IXE Q2W

Visit Prior to Titration – LTE Period Population

Results at Visit Prior to IXE Q2W Titration

	IXE Q2W/IXE Q4W (N=11)	Total IXE Population That Increased Dose (N=48)
sPGA score, n (%)		
0	2 (18.2)	9 (18.8)
1	2 (18.2)	11 (22.9)
2	5 (45.5)	15 (31.3)
3	2 (18.2)	13 (27.1)
PASI % improvement from baseline, n (%)		
≥75	9 (81.8)	38 (79.2)
≥90	6 (54.5)	20 (41.7)
100	1 (9.1)	8 (16.7)

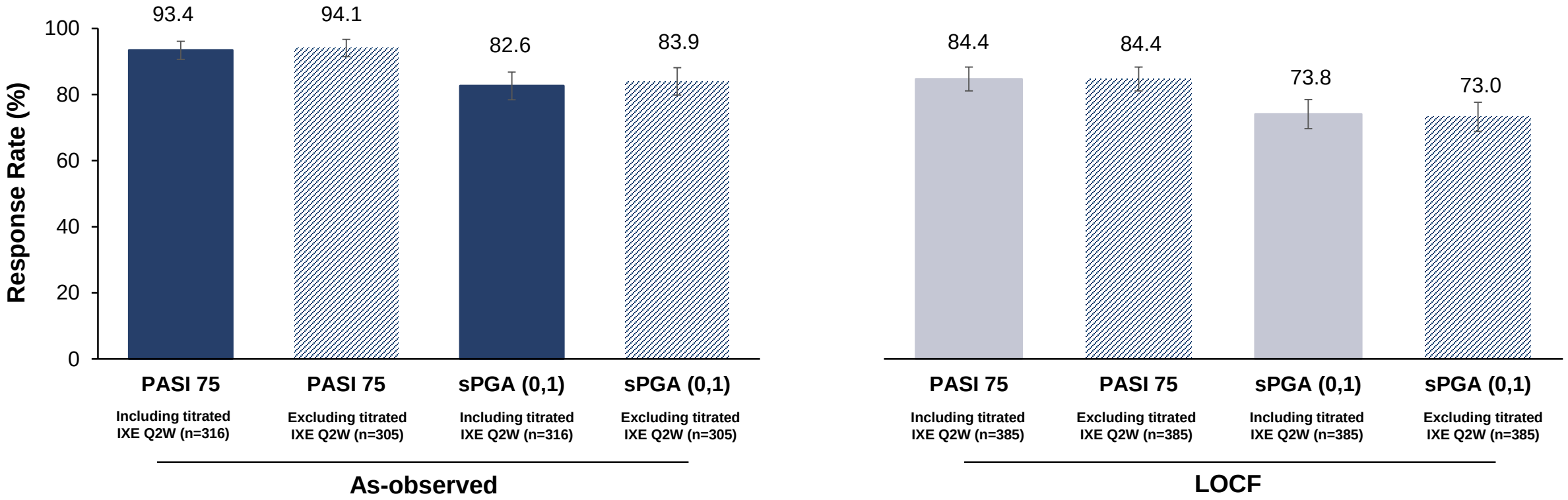
Data shown is from the LTE period population

- Following Week 60, 48 of 1274 (3.8% of all patients) increased ixekizumab dosage to 80 mg every 2 weeks (IXE Q2W) at the investigator's decision

IXE=ixekizumab; IXE Q2W=80 mg ixekizumab every 2 weeks; PASI= Psoriasis Area and Severity Index; PASI 75=Psoriasis Area and Severity Index 75% Response PASI 90=Psoriasis Area and Severity Index 90% Response; PASI 100=Psoriasis Area and Severity Index 100% Response; PBO=placebo; sPGA=static Physician's Global Assessment

Week 108 Response Rates +/- Data From Visits Where Dose was Increased to IXE Q2W

IXE Q2W/IXE Q4W; ITT Population



Data presented are for the IXE Q2W/Q4W dosing group. All values are presented as n (%). Error bars represent 95% CI

- By Week 108, the average duration of titrated IXE Q2W treatment was 98.4 days for the IXE Q2W/Q4W dosing group
- Increasing dose had little effect on overall efficacy profiles when excluded from the analysis

IXE=ixekizumab; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; IXE Q2W/IXE Q4W=IXE Q2W during induction then IXE QW4 during LTE; LOCF=last observation carried forward; PASI=Psoriasis Area and Severity Index PBO=placebo; sPGA=static Physician's Global Assessment

Summary of Adverse Events

LTE Period Population

	PBO/IXE Q4W (N=183)	ETN/IXE Q4W (N=369)	IXE Q4W/IXE Q4W (N=360)	IXE Q2W/IXE Q4W (N=362)
Patients with ≥1 treatment-emergent AE	153 (83.6)	313 (84.8)	305 (84.7)	306 (84.5)
Mild	46 (25.1)	108 (29.3)	96 (26.7)	100 (27.6)
Moderate	80 (43.7)	153 (41.5)	157 (43.6)	170 (47.0)
Severe	27 (14.8)	52 (14.1)	52 (14.4)	36 (9.9)
Serious AEs	28 (15.3)	47 (12.7)	43 (11.9)	30 (8.3)
Discontinuation due to AEs	12 (6.6)	26 (7.0)	25 (6.9)	19 (5.2)
Death	1 (0.5)	2 (0.5)	1 (0.3)	1 (0.3)
Most common AEs				
Nasopharyngitis	42 (23.0)	87 (23.6)	82 (22.8)	89 (24.6)
Upper respiratory tract infection	12 (6.6)	25 (6.8)	32 (8.9)	27 (7.5)
Injection site reaction	17 (9.3)	24 (6.5)	32 (8.9)	23 (6.4)
Candida infection	8 (4.4)	11 (3.0)	18 (5.0)	12 (3.3)
Crohn's disease	1 (0.5)	1 (0.3)	1 (0.3)	0
Ulcerative colitis	0	1 (0.3)	0	1 (0.3)
Neutropenia, Grade 3 or worse[a]	1 (0.5)	3 (0.8)	4 (1.1)	0

All values are presented as n (%). Given the small number of patients that increased dose frequency, and the short exposure time to the increased dose frequency at week 108, the number of adverse events in this population are insufficient to compare at this time

- Most TEAEs were mild or moderate in severity. Cumulative rates of the most frequent (≥7.5%) TEAEs were nasopharyngitis (23.5%), upper respiratory infection (7.5%), and injection site reactions (7.5%). Five deaths were reported and were evaluated to be unrelated to ixekizumab exposure

[a] Percentages for neutropenia were calculated based on the number of patients with a baseline and at least one post-baseline neutrophil count (PBO/IXE Q4W=182, ETN/IXE Q4W=368, IXE Q4W/IXE Q4W=357, IXE Q2W/Q4W=362)

AE=adverse event; ETN=50 mg etanercept twice weekly; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; IXE Q2W/IXE Q4W=IXE Q2W during induction then IXE QW4 during LTE LTE=long-term extension; PBO=placebo

Conclusions

- Over 2 years, ixekizumab showed maintenance of efficacy across all endpoints with high skin clearance rates
- When allowed, only 3.8% of all patients increased ixekizumab dose to every 2 weeks (following week 60) and the majority had PASI scores above 75 at the time of titration
- The safety profile of ixekizumab over 108 weeks was comparable to shorter treatment periods[9]

9. Gordon KB, et al. *N Eng J Med*. 2016;375:345-356.

PSYCHIATRIC ADVERSE EVENTS IN BRODALUMAB PSORIASIS STUDIES

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This study was sponsored by Valeant Pharmaceuticals North America LLC. Medical writing support was provided by MedThink SciCom and funded by Valeant Pharmaceuticals North America LLC.

Introduction and Objective

INTRODUCTION

- Psoriasis has profound psychosocial implications that can affect the ability of patients to socialize with family members, interact with coworkers, and make friends[1]
- Psychiatric comorbidities, such as depression and anxiety, are common in patients with psoriasis[2,3]
- Suicidal ideation has been reported in as many as 17.3% of patients with psoriasis compared with 8.3% of healthy controls[4]
- Brodalumab is a monoclonal antibody that targets interkeukin-17 (IL-17) receptor A and is under investigation for use in the treatment of psoriasis[5]
- Brodalumab has demonstrated efficacy in the treatment of plaque psoriasis[5,6]
- Reports of suicide in patients with psoriasis enrolled in clinical trials for brodalumab led to concerns that brodalumab may be linked to psychiatric adverse events (AEs)[6,7]

OBJECTIVE

- To assess psychiatric AEs and improvements in depression and anxiety in patients with psoriasis treated with brodalumab in clinical trials

1. Krueger et al. *Arch Dermatol.* 2001;137:280-284. **2.** Dowlatshahi et al. *J Invest Dermatol.* 2014;134:1542-1551. **3.** Kurd et al. *Arch Dermatol.* 2010;146:891-895. **4.** Dalgard et al. *J Invest Dermatol*. 2015;135:984-991. **5.** Lebwohl et al. *N Engl J Med.* 2015;373:1318-1328. **6.** Papp et al. *Br J Dermatol*. 2016;175:273-286. **7.** Danesh and Kimball. *J Am Acad Dermatol.* 2016;74:190-192.

Methods

Clinical Studies

- Efficacy and safety of brodalumab (140 or 210 mg every 2 weeks [Q2W]) were investigated in one phase 2 trial and in three phase 3, multicenter, randomized trials of patients with moderate-to-severe plaque psoriasis (AMAGINE-1/-2/-3)[1,2]
- In the phase 3 studies, more than 80% of patients were being treated with brodalumab 210 mg Q2W by the end of the week 52 controlled period
- There were no specific exclusion criteria for psychiatric disorders or substance abuse

Endpoints

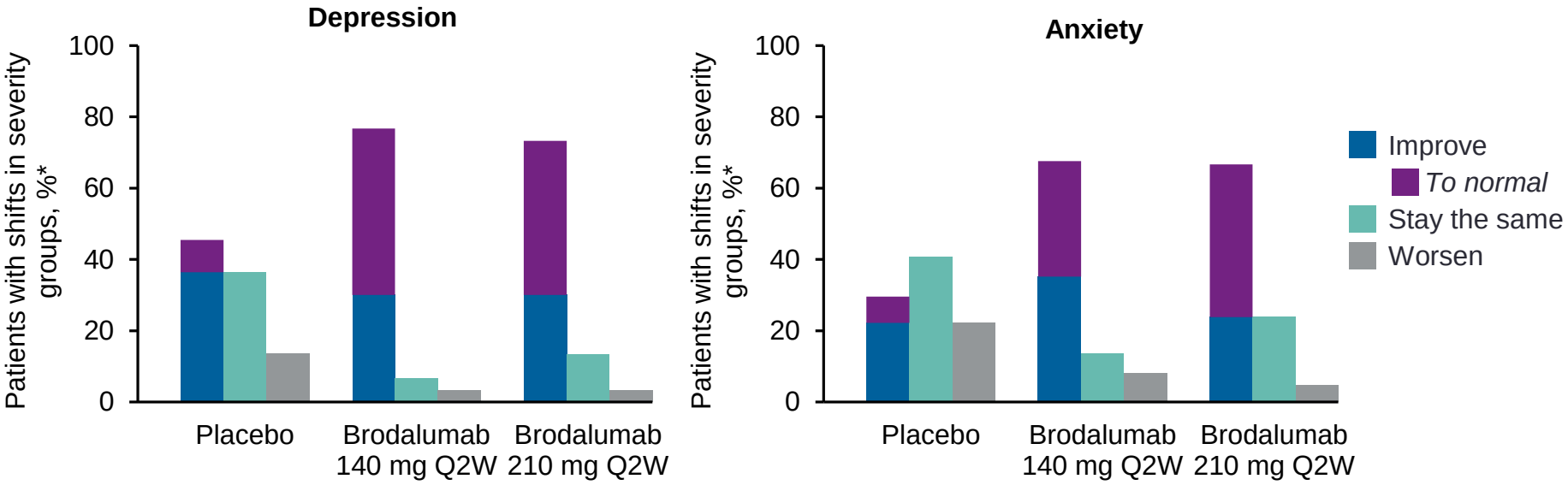
- The hospital anxiety and depression scale (HADS), which determines anxiety and depression on a 21-point scale each, was measured in AMAGINE-1
- The dermatology life quality index (DLQI) assesses the socio-psychological impact of the skin disease[3] on patients' lives and was measured in AMAGINE-1/-2/-3
- Data on psychiatric AEs were pooled for all trials and were summarized as follow-up time–adjusted event rates
  - The follow-up time–adjusted event rate is the total number of events reported during the follow-up observation time divided by total patient-years of observation; this includes gaps and interruptions in exposure and time beyond the exposure period

1. Lebwohl et al. *N Engl J Med.* 2015;373:1318-1328. **2.** Papp et al. *Br J Dermatol*. 2016;175:273-286. **3.** Lewis and Finlay. *J Investig Dermatol Symp Proc.* 2004;9:169-180.

Changes in HADS Severity at Week 12

RESULTS

Figure 1. Shifts in HADS severity at week 12 in patients who scored “moderate” or “severe” at baseline in the AMAGINE-1 trial.

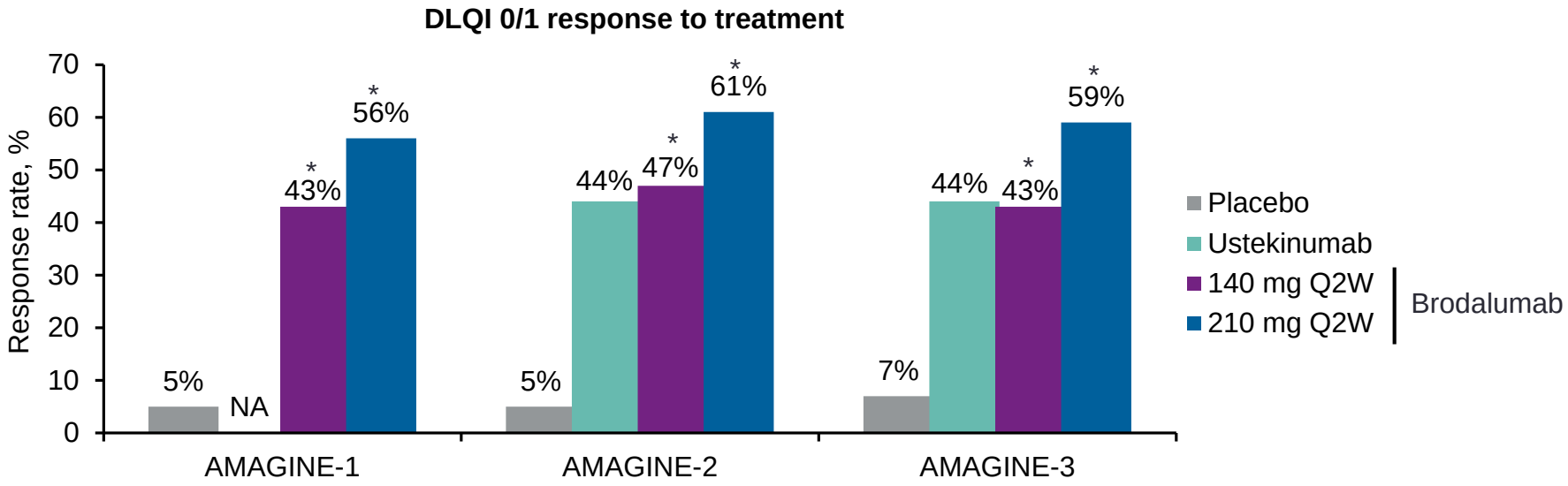


HADS, hospital anxiety and depression scale; Q2W, every 2 weeks.
Shifts in HADS severity at week 12 in patients who scored “moderate” or “severe” at baseline.
*Data are shown as observed; percentages do not add to 100%.

Improvements in Patient Satisfaction in Those Treated With Brodalumab

RESULTS (cont)

Figure 2. DLQI 0/1 response rate at week 12 in patients from the AMAGINE-1, -2, and -3 trials.



DLQI, dermatology life quality index.
DLQI response = score 0/1.
*P<0.001 vs placebo.

Psychiatric Adverse Events

RESULTS (cont)

Table 1. Incidence of Psychiatric Adverse Events Occurring in ≥0.1% of Patients Treated With Brodalumab During the Initial Placebo-Controlled Study Period[a]

Preferred term, n (%)	Placebo (N=879)	Ustekinumab (N=613)	Brodalumab[b] (N=3066)
Psychiatric disorders SOC	16 (1.8)	12 (2.0)	61 (2.0)
Insomnia	6 (0.7)	4 (0.7)	17 (0.6)
Depression	5 (0.6)	3 (0.5)	14 (0.5)
Anxiety	2 (0.2)	2 (0.3)	13 (0.4)
Libido decreased	0 (0.0)	0 (0.0)	5 (0.2)
Depressed mood	1 (0.1)	2 (0.3)	3 (0.1)
Mood swings	0 (0.0)	0 (0.0)	3 (0.1)
Stress	1 (0.1)	0 (0.0)	3 (0.1)

SOC, system organ class.
[a]Includes data from the placebo-controlled phase 2 study, AMAGINE-1, AMAGINE-2, and AMAGINE-3. [b]All brodalumab dose groups combined.

Suicidal Ideation and Behavior Rates in Psoriasis Studies

RESULTS (cont)

Table 2. Integrated Analysis of Follow-up Time–Adjusted Patient Incidence Rates of SIB Events Through Week 52 and in Long-term Follow-up

	52-week pool[a]		Long-term pool[b]
	Ustekinumab (N=613; pt-yr = 503.6) n (r) [95% CI]	**Brodalumab (N=4019; pt-yr = 3545.7) n (r) [95% CI]**	**Brodalumab (N=4464; pt-yr = 9161.8) n (r) [95% CI]**
Suicidal ideation adverse event	1 (0.20) [0.01, 1.11]	3 (0.08) [0.02, 0.25]	22 (0.24) [0.15, 0.36]
Suicidal behavior adverse event	1 (0.20) [0.01, 1.11]	4 (0.11) [0.03, 0.29]	15 (0.16) [0.09, 0.27]
Completed suicide[c]	0 (0.00) [0.00, 0.73]	2 (0.06) [0.01, 0.20]	4 (0.04) [0.01, 0.11]
Intentional self-injury	0 (0.00) [0.00, 0.73]	1 (0.03) [<0.01, 0.16]	1 (0.01) [0.00, 0.06]
Suicide attempt	1 (0.20) [0.01, 1.11]	1 (0.03) [<0.01, 0.16]	6 (0.07) [0.02, 0.14]
Suicidal behavior	0 (0.00) [0.00, 0.73]	0 (0.00) [0.00, 0.10]	4 (0.04) [0.01, 0.11]
Overall suicidal ideation and behavior	2 (0.40) [0.05, 1.44]	7 (0.20) [0.08, 0.41]	34 (0.37) [0.26, 0.52]

- There were 22 suicidal ideations (follow-up time–adjusted rate, 0.24), 6 suicide attempts (0.07), 3 completed suicides (0.03), and 1 additional suicide adjudicated as indeterminate

SIB, suicidal ideation and behavior.
[a]Cumulative events through the 52-week, controlled treatment period. [b]Includes events in the 52-week treatment period and the uncontrolled open-label extension. [c]Includes fatal event reported as intentional overdose that was adjudicated as indeterminate.

Suicidal Ideation and Behavior Rates in Psoriasis Studies

RESULTS (cont)

Table 3. Summary of Completed Suicides (Known and Unknown Cause)

Age, y/ Sex	Brodalumab dose	Clinical response (PASI score)	Clinical information
59/Male	210 mg	100	• 329 days after first dose of brodalumab • History of financial stressors (lost disability due to brodalumab response and unable to find work)
39/Male	210 mg	73	• 140 days after first dose of brodalumab • Informed investigator he had legal difficulties and was likely to be incarcerated • Family reported he killed himself, means unknown
56/Male	210 mg	100	• 845 days after first dose of brodalumab • Ongoing treatment for depression and anxiety • Described recent stress and isolation due to relocation
Indeterminate case			
56/Male	210 mg	100	• History of depression; on antidepressant and benzodiazepine • 97 days after first dose of brodalumab • Toxic levels of mixed opiates compatible with ingestion of poppy seed tea and methadone; therapeutic level of citalopram, elevated alprazolam, and alcohol • HADS baseline depression and anxiety score decreased from 15 to 2 and 14 to 6, respectively, 2 weeks before the event • Ruled indeterminate by C-CASA adjudication

C-CASA, Columbia classification algorithm of suicide assessment; HADS, hospital anxiety and depression scale; PASI, psoriasis area and severity index.

Results (cont)

- Two SIB events (suicide attempts) were reported in 1 patient treated with brodalumab during the 12-week induction phase (0.03%; 1/3066)
- Follow-up time–adjusted rates of SIB were greater in patients with a history of depression compared with those without (1.42 and 0.21 per 100 patient-years, respectively)
- Follow-up time–adjusted rates of SIB were greater in patients with a history of suicidality compared with those without (3.21 and 0.20 per 100 patient-years, respectively)

SIB, suicidal ideation and behavior.

Summary and Conclusions

- Median HADS anxiety and depression scores were reduced from baseline in patients with moderate-to-severe plaque psoriasis receiving brodalumab
- A higher patient satisfaction and quality of life was observed with brodalumab compared with placebo, as determined by DLQI response rate
- Rates of SIB at week 52 in patients treated with brodalumab were similar to those treated with the active comparator ustekinumab, and SIB rates did not increase with long-term treatment
- No pattern emerged between timing of the events and the initiation or withdrawal of brodalumab
- Controlled data do not suggest a causal relationship between brodalumab treatment and SIB

DLQI, dermatology life quality index; HADS, hospital anxiety and depression scale; SIB, suicidal ideation and behavior.

Tildrakizumab, a Selective Anti-IL-23 Monoclonal Antibody, Is Effective in Subjects With Chronic Plaque Psoriasis Who Do Not Adequately Respond to Etanercept

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Introduction

Background

- The IL-23/IL-17 inflammatory pathway is critical in psoriasis pathogenesis and has led to the development of treatments that target this pathway
- Tildrakizumab (TIL) is a high affinity, humanized, IgG1/κ monoclonal antibody targeting IL-23p19 that has demonstrated efficacy in patients with moderate-to-severe chronic plaque psoriasis[1,2]
- In reSURFACE 2, a phase 3 randomized controlled study evaluating tildrakizumab in patients with moderate-to-severe chronic plaque psoriasis, PASI 75 was achieved by 66%, 61%, 6%, and 48% by TIL 200 mg, TIL 100 mg, placebo (PBO), and etanercept (ETN) 50 mg, respectively at Week 12 ($P \leq 0.001$ TIL vs PBO; $P \leq 0.001$ TIL vs ETN) and 73%, 74%, and 54% of subjects on TIL 200 mg, TIL 100 mg, and etanercept (ETN) 50 mg, respectively, at Week 28 ($P \leq 0.001$ TIL vs ETN)

Objective

- Here, we evaluate ETN nonresponders (PASI <50) and partial responders (PASI ≥50 to <75) at Week 28 who were switched to TIL 200 mg until Week 52 of reSURFACE 2

Methods

Patients and endpoints:

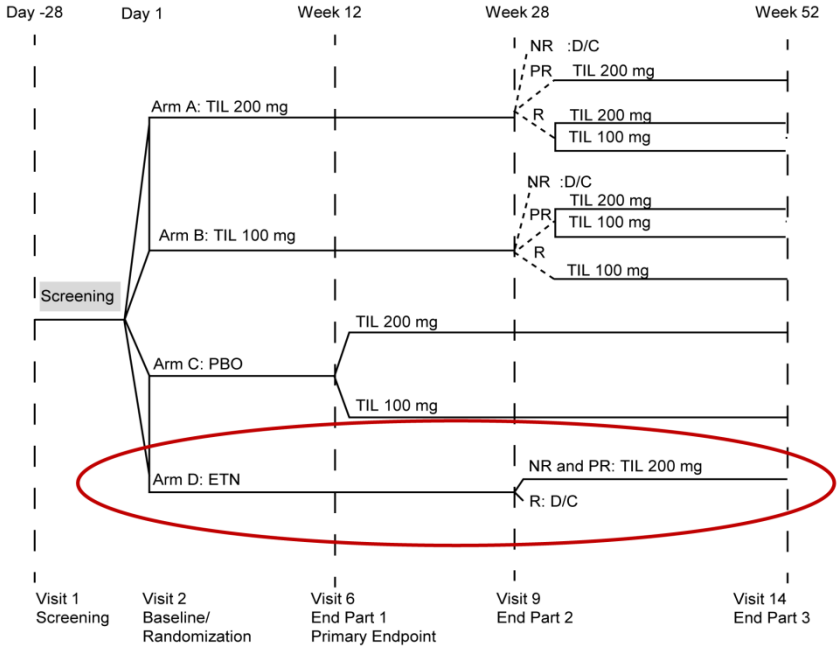
- Patients: ≥10% body surface area, ≥3 PGA, and PASI ≥12 participated in reSURFACE 2 (NCT01729754)
- Efficacy endpoints: % of patients with PASI 75, PASI 90, PASI 100, PGA score of 0 (clear) or 1 (minimal) with a ≥2-grade score reduction from baseline (PGA response) Week 28

Study design:

- **In Part 1 (Weeks 0-12)**, patients were randomized to TIL 200 mg, TIL 100 mg, placebo (PBO), or ETN 50 mg (2:2:1:2 ratio; TIL was administered subcutaneously at Weeks 0 and 4 and ETN administered twice weekly)
- **In Part 2 (Weeks 12-28)**, TIL and ETN patients remained on the same treatment (TIL administered at Week 16; ETN once weekly), while PBO patients were rerandomized to TIL 100 or 200 mg
- **In Part 3 (Weeks 28-52)**, patients on TIL 100 and 200 mg were further rerandomized; PASI 75 responders to ETN were discontinued, while partial responders (PASI ≥50 to <75) and nonresponders (PASI <50) were switched to TIL 200 mg (administered at Weeks 32, 36, and 48)

This analysis focuses on ETN partial and nonresponder patients and their response to TIL 200 mg over 20 weeks of treatment in Part 3

Study Design



Screening/ Washout	Base Study Treatment Period		
	Part 1 12 Weeks	Part 2 16 Weeks	Part 3 24 Weeks

D/C=discontinued; ETN=etanercept; NR=nonresponders; PBO=placebo; PR=partial responders; R=responders; TIL=tildrakizumab.

Results

Patients switched from ETN to TIL 200 mg

- 1090 patients entered the study: 314, 307, 156, and 313 received TIL 200 mg, TIL 100 mg, PBO, and ETN, respectively
- At Week 28, 120 ETN subjects (partial or nonresponders, PASI <75) switched to TIL 200 mg

Safety and tolerability

- Safety and tolerability of subjects who received ETN and then switched to TIL 200 mg at Week 28 are summarized in **Table 1**
- One death was due to sepsis (several months after being discontinued from the study; unrelated to study medication)

Table 1: Summary of AEs in part 3

	ETN to TIL 200 mg N=120
	n (%)
≥1 AE	62 (51.7)
Serious AEs	5 (4.2)
Discontinued due to AEs	1 (0.8)
Deaths	1 (0.8)
Most Common AEs	
Bronchitis	7 (5.8)
Nasopharyngitis	14 (11.7)
Upper Respiratory Tract Infection	6 (5.0)

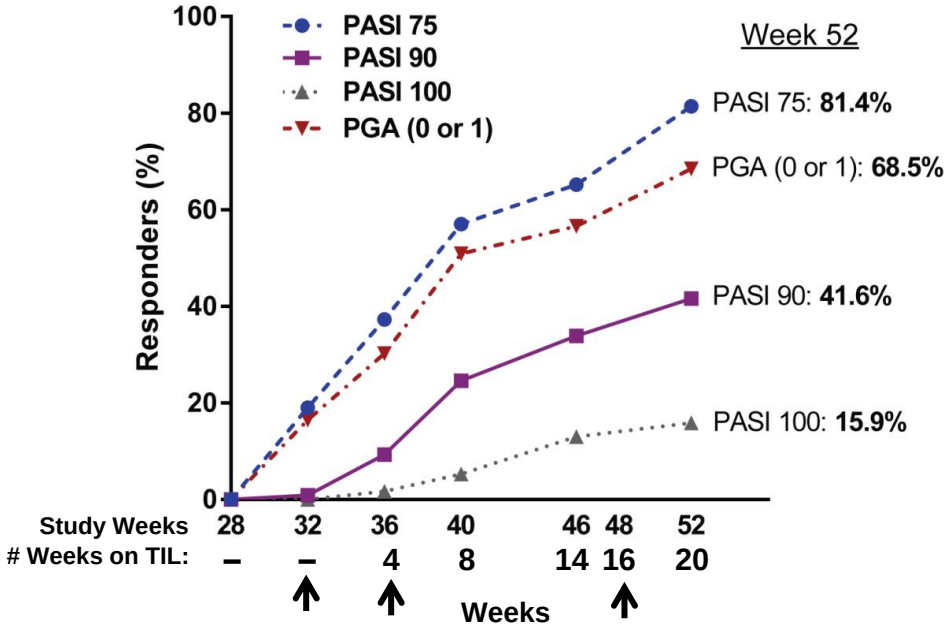
PASI 75, 90, 100, and PGA Responses

Efficacy

- Week 52 responses shown in **Figure 1** for PASI 75, 90, 100, and PGA (0 or 1) in patients who did not achieve PASI 75 with ETN, and were subsequently treated with TIL 200 mg for 20 weeks

- For comparison, during Parts 1 and 2 over 28 weeks of treatment with TIL 200 mg, responses were:
  - PASI 75: 74%
  - PGA response: 71%
  - PASI 90: 58%
  - PASI 100: 27%

Figure 1: Efficacy response rates in part 3 after rerandomization to TIL 200 mg in part 1 ETN patients not achieving PASI 75



Note: TIL administered at Weeks 32, 36, and 48.
Full analysis set population (All subjects who entered Part 3 and received at least 1 dose of Part 3 study treatment, based on the treatment assigned); no imputation of missing data

Summary and Conclusions

- Patients who did not achieve PASI 75 with etanercept by Week 28 were able to achieve clinically meaningful improvement in chronic plaque psoriasis upon switching treatment to tildrakizumab 200 mg for 20 weeks of treatment as measured by PASI 75, 90, 100, and PGA score of 0 or 1
- Tildrakizumab 200 mg was well tolerated in this subgroup of patients
- These results suggest that patients who are not successfully treated with etanercept may benefit from tildrakizumab, an anti-IL-23p19 antibody

References

1. Papp K, Thaçi D, Reich K, et al. Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial. *Br J Dermatol.* 2015;173(4):930-939.

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RAPID ONSET OF EFFICACY IN PATIENTS WITH PSORIASIS TREATED WITH BRODALUMAB VERSUS USTEKINUMAB: A POOLED ANALYSIS OF DATA FROM TWO PHASE 3 RANDOMIZED CLINICAL TRIALS (AMAGINE-2 AND AMAGINE-3)
(P-4978)

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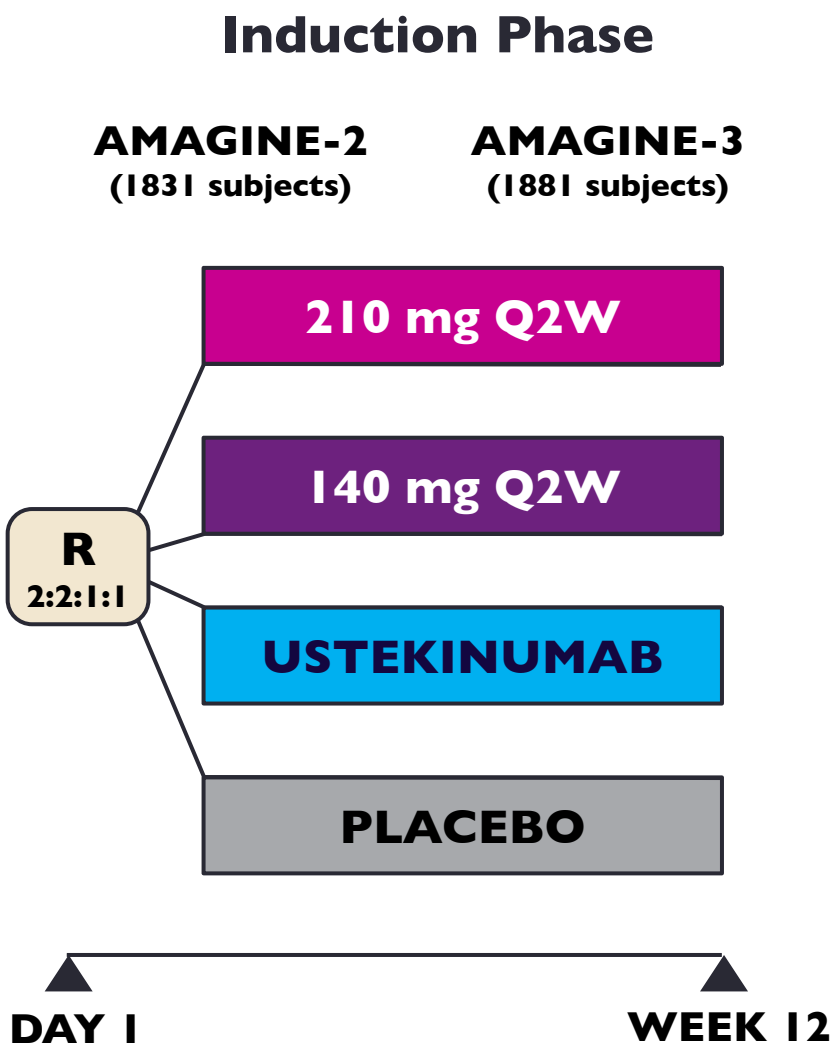
Sunday March 5, 4.45-4.50p

Statement of funding sources:Valeant Pharmaceuticals North America LLC.

Objectives and Methods

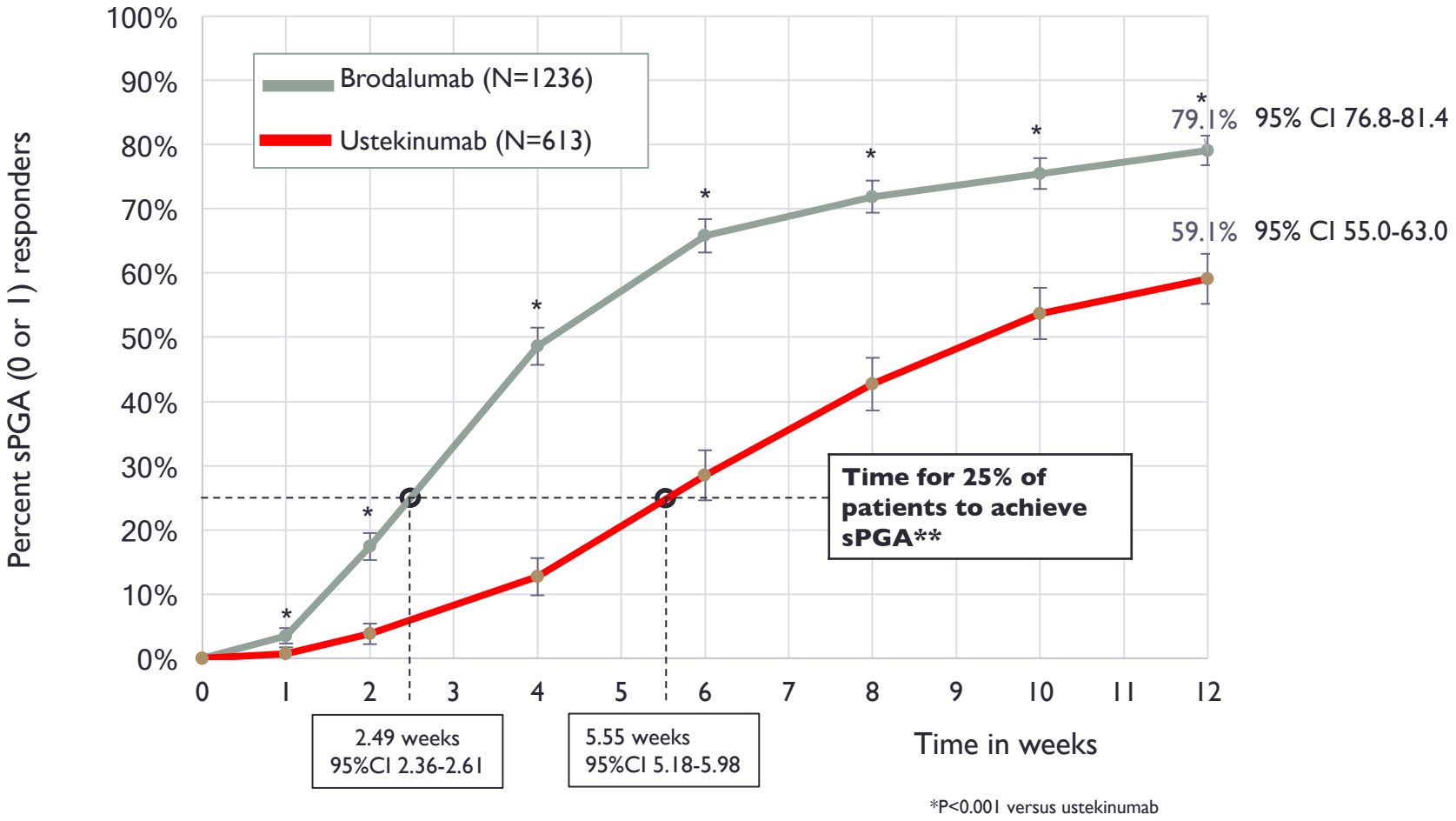
- To compare onset of response for brodalumab 210 mg Q2W and ustekinumab in the treatment of moderate-to-severe plaque psoriasis
- Two multicenter, randomized, double-blind studies in moderate-to-severe psoriasis (N=3712)
- Speed of response evaluated by assessing time taken to achieve static Physician's Global Assessment (sPGA) success (0/1), or Psoriasis Area and Severity Index (PASI) response (PASI 75) during the initial 12 week induction period of the studies



Results

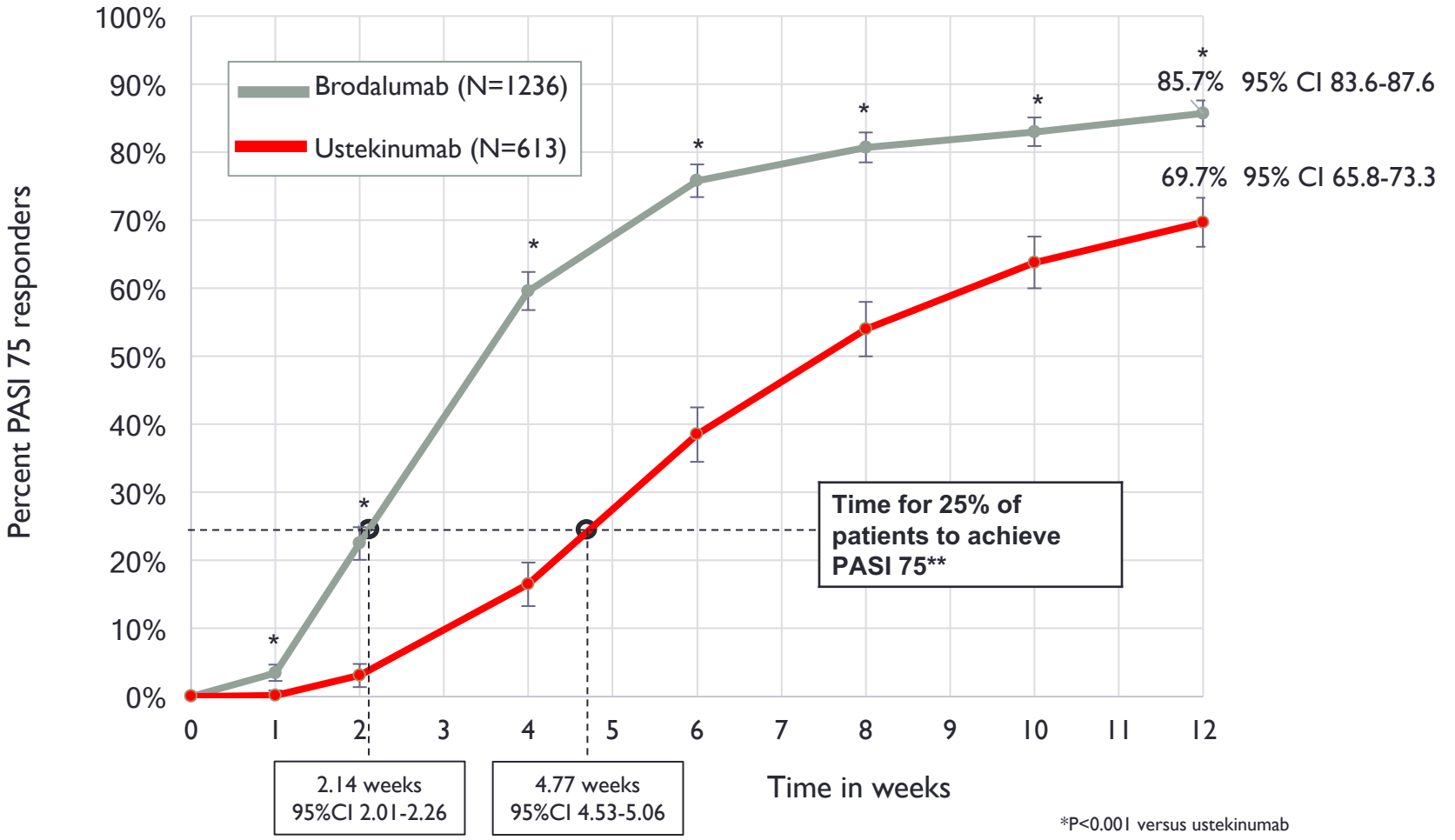
- At Week 12, 79.1% and 59.1% of subjects achieved sPGA success with brodalumab 210 mg Q2W and ustekinumab respectively. In addition, 85.7% and 69.7% of patients achieved PASI 75
- Statistically significant differences were seen from Week 1 ($P<0.001$), and maintained through to Week 12 for both sPGA success and PASI 75
- Forty-three patients (3.5%) treated with brodalumab achieved both sPGA success and PASI 75 as early as Week 1, compared with only 4 (0.7%) and one patient (0.2%) respectively treated with ustekinumab
- Time for 25% of patients to achieve sPGA and PASI 75 was 2.49 and 2.14 weeks respectively with brodalumab compared with 5.55 and 4.77 weeks with ustekinumab

Percent of patients achieving sPGA (NRI) success (0/1) in induction phase (baseline to week 12 pooled data, including 95% CI)



**Time for 25% of patients to achieve sPGA (0/1) NRI estimated from bootstrap samples with the use of linear interpolation between time points

Percent of patients achieving PASI 75 (NRI) in induction phase (baseline to week 12, pooled data, including 95% CI)



**Time for 25% of patients to achieve PASI 75 estimated from bootstrap samples with the use of linear interpolation between time points

Conclusions

- Brodalumab demonstrated a rapid onset of action with significantly more subjects achieving efficacy endpoints compared to ustekinumab as early as Week 1, and remained differentiated from ustekinumab through Week 12

- 25% of patients on brodalumab achieved at least PASI 75 and sPGA success around 2 weeks (2.5 and 2.1 weeks respectively). For ustekinumab it took as long as 5 weeks (5.6 and 4.8 weeks)

Seven-Year Interim Results from the ESPRIT 10-Year Postmarketing Surveillance Registry of Adalimumab for Moderate to Severe Psoriasis

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Presented at the 75th Annual Meeting of the American Academy of Dermatology, Orlando, FL, March 3-7, 2017

INTRODUCTION

- Adalimumab (ADA), a fully human, recombinant, monoclonal antibody directed against tumor necrosis factor-alpha (TNF-α), is indicated for the treatment of moderate to severe chronic plaque psoriasis in adult patients, who are candidates for systemic therapy or phototherapy.[1]
- ESPRIT is an ongoing, 10-year international, prospective observational registry evaluating the long-term safety and effectiveness of originator ADA (AbbVie) prescribed in in routine clinical practice according to local product labeling for adult patients with chronic plaque psoriasis (NCT00799877).[2]

OBJECTIVE

- To present safety, effectiveness, and patient-reported outcomes (PROs) over a 7-year period (26 September 2008 through 30 November 2015) from an interim analysis of data collected from the ESPRIT registry.

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METHODS

STUDY DESIGN AND PATIENTS

Enrollment:

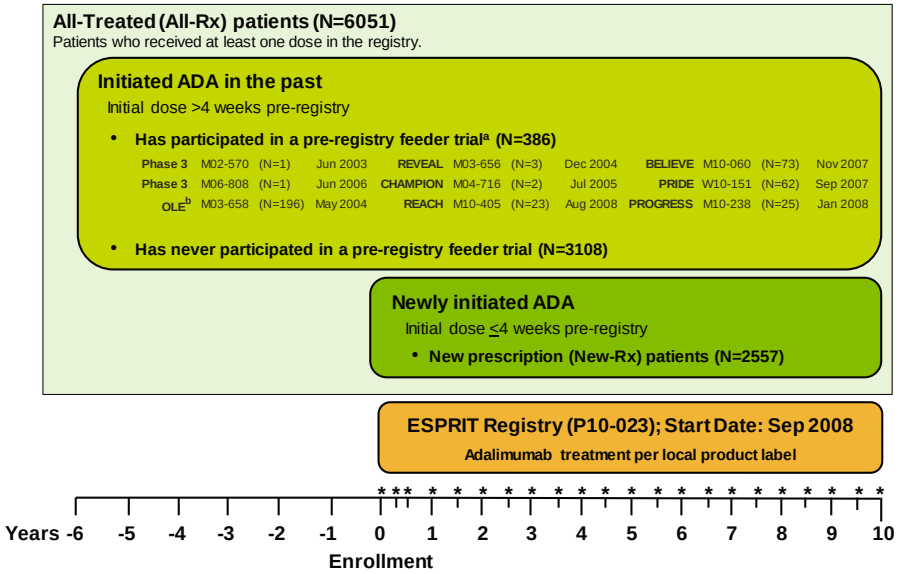
- Patient enrollment was initiated on 26 September 2008 and completed on 8 November 2012.
- As of 30 November 2015, 6066 patients were enrolled in the ESPRIT registry.
- Study sites were located in the United States, Canada, Austria, Czech Republic, Denmark, France, Germany, Greece, Ireland, Netherlands, Spain, Sweden, and United Kingdom.
- Treatment: ADA was dosed as recommended in the local product label.

Main Inclusion Criteria (Figure 1):

- Adult patients (≥ 18 years) with chronic plaque psoriasis who have been prescribed ADA according to local product labeling and meet one of the following criteria:
  - Previously initiated ADA therapy and continued on ADA with no more than 70 consecutive days off drug.
    - The initial ADA dose was received either in a pre-registry feeder clinical trial or from an existing prescription outside of a pre-registry feeder trial.
    - Source documentation of serious adverse events (SAEs), AEs of special interest, and dosing information since the initiation of therapy can be provided by the physician.
  - Newly initiated ADA therapy within 4 weeks of registry entry.

AbbVie Inc. funded this study and participated in the study design; study research; collection, analysis and interpretation of data; and writing, reviewing and approving of this publication. All authors had access to the data, and participated in the development, review, and approval, and in the decision to submit this publication.

Figure 1. Study Design And Patient Population of ESPRIT Observational Registry



a. Start dates are shown for clinical trials.
b. REVEAL and CHAMPION were among the feeder trials for the OLE; the number of patients in these trials were counted separately from OLE's 196 patients.

*Patients were evaluated 3 and 6 months post enrollment, then every 6 months for up to 10 years. Patients are followed at intervals determined by routine clinical practice or as recommended by national guidelines. Safety data are captured during the entire study period. Patients who discontinue registry drug are encouraged to remain in the registry.
ADA=adalimumab.

STATISTICAL ANALYSES

Populations (Figure 1):

- **All-treated (All-Rx) patient population**: Patients who received at least one dose of ADA in the registry.
- **New-prescription (New-Rx) patient population**: Patients who newly initiated ADA within 4 weeks prior to registry enrollment.
- New-Rx is a subgroup of All-Rx patient population.
- Descriptive statistics are presented for baseline patient demographics and disease characteristics.

ADA Exposure:

- "Overall exposure to ADA" (outside of and within the registry) was calculated as time from the initial (first ever) ADA dose to 14 days after the last ADA dose in the registry, excluding the total number of days of treatment interruption in the registry.
- "Registry exposure to ADA" (within the registry) was calculated as time from first ADA dose in registry to 14 days after the last ADA dose in registry, excluding the total number of days of treatment interruption in the registry.
- A treatment interruption (TI) is defined as >70 days without any ADA dose; TI starts at day 71 after ADA was stopped.

METHODS (CONTINUED)

Safety:

- All treatment-emergent adverse events (All-TEAEs) were events occurring from the date of initial (first ever) ADA dose through 70 days after the date of last ADA dose in the registry, excluding AEs occurring during TIs.
  - Incidence rates for All-TEAEs are reported as events per 100 patient years of overall exposure to ADA (E/100PY) and presented in subgroups of overall exposure to ADA.
  - In addition, the incidence of All-TEAEs is presented by time periods, i.e. the number of patients with new occurrence of the specific AE divided by the number of patients at risk.
    - Patients at risk had at least an overall exposure to ADA up to and including the respective time period and did not have the specific AE in any period before.

Standardized mortality ratio (SMR):

- SMR was calculated as the ratio of observed to expected treatment-emergent deaths using the 2006 country-specific World Health Organization (WHO) mortality rates.
- A SMR of <1.0 indicates that the observed number of deaths is lower than expected rate in an age-, sex-, and country-matched general population.

Effectiveness:

- Proportion of patients achieving Physician's Global Assessment (PGA) of "clear" or "minimal" were analyzed as observed during registry participation (patients were not necessarily receiving ADA at the time of assessment).

Patient-Reported Outcomes (US patients only):

- Change from baseline in Dermatology Life Quality Index (DLQI) and Work Productivity Activity Impairment (WPAI) scores were analyzed as observed during registry participation.

RESULTS

- This 7-year interim analysis used data collected from 6051 patients (2557 New-Rx patients, 42.3%), who were enrolled and dosed between 26 September 2008 and 30 November 2015.
- The majority of patients in ESPRIT were from sites in the United States (69.5%) and Canada (13.9%).
- 4242 (70.1%) All-Rx and 1652 (64.6%) New-Rx patients are continuing in the registry as of 30 November 2015.
  - Of those, 3070 (50.7%) All-Rx and 1061 (41.5%) New-Rx patients have not permanently discontinued ADA.
    - Of those, 2150 (35.5%) All-Rx and 674 (26.4%) New-Rx patients never interrupted ADA treatment for >70 days.
- 1809 (29.9%) All-Rx and 905 (35.4%) New-Rx patients discontinued from the registry; the most frequent reason for discontinuing was being lost to follow up (14.4%, All-Rx and 19.2, New-Rx) (**Table 1**).

Table 1. Reasons for Discontinuation from Registry and from Registry Drug (All-Rx and New-Rx Patient Population)

Reason for Discontinuation (in >1% patients)	All-Rx, N=6051 n (%)	New-Rx, N=2557 n (%)
From registry[a], any reason	1809 (29.9)	905 (35.4)
Lost to follow-up	874 (14.4)	491 (19.2)
Lack of efficacy	89 (1.5)	56 (2.2)
Withdrew consent	355 (5.9)	156 (6.1)
Death	70 (1.2)	25 (1.0)
Non-compliance	86 (1.4)	49 (1.9)
Other	333 (5.5)	116 (4.5)
From registry drug[b], any reason	2981 (49.3)	1496 (58.5)
AE	170 (2.8)	87 (3.4)
SAE or SAE of interest	101 (1.7)	40 (1.6)
Lost to follow-up	399 (6.6)	226 (8.8)
Lack of efficacy	1101 (18.2)	610 (23.9)
Intolerance	44 (0.7)	35 (1.4)
Withdrew consent	117 (1.9)	59 (2.3)
Other	445 (7.4)	220 (8.6)
Unknown reason	668 (11.0)	268 (10.5)

a. Reasons for registry discontinuations in ≤1% of patients were AE, intolerance, patient moved, SAE or SAE of interest, satisfactory improvement, pregnancy, or unknown reasons.
b. Reasons for registry drug discontinuations in ≤1% of patients were patient death, satisfactory improvement, or required additional therapy.
All-Rx=all-treated patient population; New-Rx=new prescription patient population; AE=adverse event; SAE=serious adverse event.

- Patient demographics and disease characteristics at registry entry are presented in **Table 2**.

Table 2. Patient Demographics and Disease Characteristics at Registry Entry (All-Rx and New-Rx Patient Population)

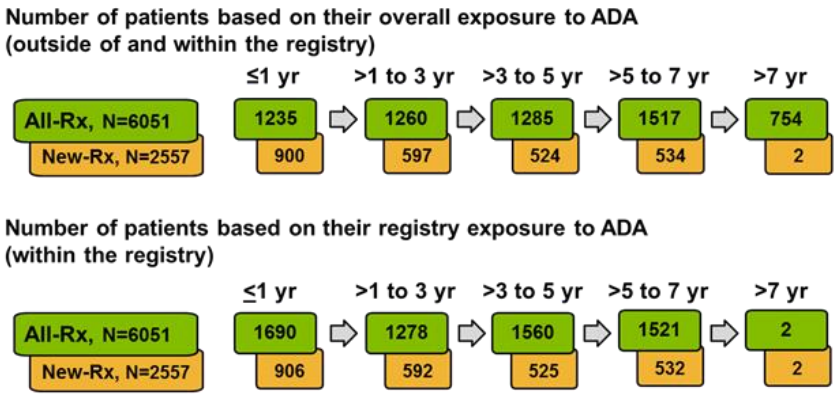
Demographic or Characteristic		All-Rx, N=6051	New-Rx , N=2557
Sex, n (%)	Male	3489 (57.7)	1380 (54.0)
	Female	2562 (42.3)	1177 (46.0)
Race[a], n (%)*	White	5268 (87.3)	2223 (87.1)
	Black	178 (2.9)	65 (2.5)
	Asian	259 (4.3)	106 (4.2)
	American Indian/ Alaska native	16 (0.3)	7 (0.3)
	Native Hawaiian or other pacific islander	40 (0.7)	25 (1.0)
	Other	253 (4.2)	115 (4.5)
	Multi-race	22 (0.4)	12 (0.5)
Psoriatic Arthritis, n (%)*		Not analyzed[b]	867 (34.0)[c]
Family history of psoriasis, n (%)*		Not analyzed[b]	1067 (41.9)[d]
PGA[e], n (%)*	Clear	731 (12.1)	53 (2.1)
	Minimal	1177 (19.5)	141 (5.5)
	Mild	1149 (19.1)	310 (12.2)
	Moderate	1781 (29.6)	1118 (44.0)
	Severe	973 (16.2)	749 (29.4)
	Very severe	213 (3.5)	172 (6.8)
Age, *years*, median (range)		47.0 (18–94)	46.0 (18–91)
Weight, *kg*, median (range)		87.0 (41–252)[f]	86.0 (41–218)[g]
BMI, *kg/m²*, median (range)		29.4 (16–77)[h]	29.4 (16–70)[i]
Duration of psoriasis[j], *years*, median (range)		Not analyzed[b]	13.4 (0–68)[k]

*Percentages calculated on non-missing values. [a]Missing data: All-Rx: n=15; New-Rx: n=4. [b]Not analyzed because not all data were captured in the registry database. [c]Missing data: New-Rx: n=7. [d]Missing data: New-Rx: n=9. [e]Many patients had received ADA prior to entering the registry, demonstrated by the number of patients entering the registry with a PGA of clear or minimal. Missing data: All-Rx: n=27; New-Rx: n=14. [f]N=5927; [g]N=2497; [h]N=5909; [i]N=2492; [k]N=2548. [j]Calculated at registry entry.
All-Rx=all-treated patient population; New-Rx=new prescription patient population; PGA=physician's global assessment; BMI=body mass index.

RESULTS (CONTINUED)

- Median duration of overall exposure to ADA was 1398 (14–4798) days and 714 (14–2581) days for All-Rx and New-Rx patient population, respectively.
- Median duration of registry exposure to ADA was 1132 (14-2581) days and 714 (14-2581) days for All-Rx and New-Rx patient population, respectively.
- The number of patients according to duration of overall exposure to ADA and registry exposure to ADA are shown in **Figure 2**.

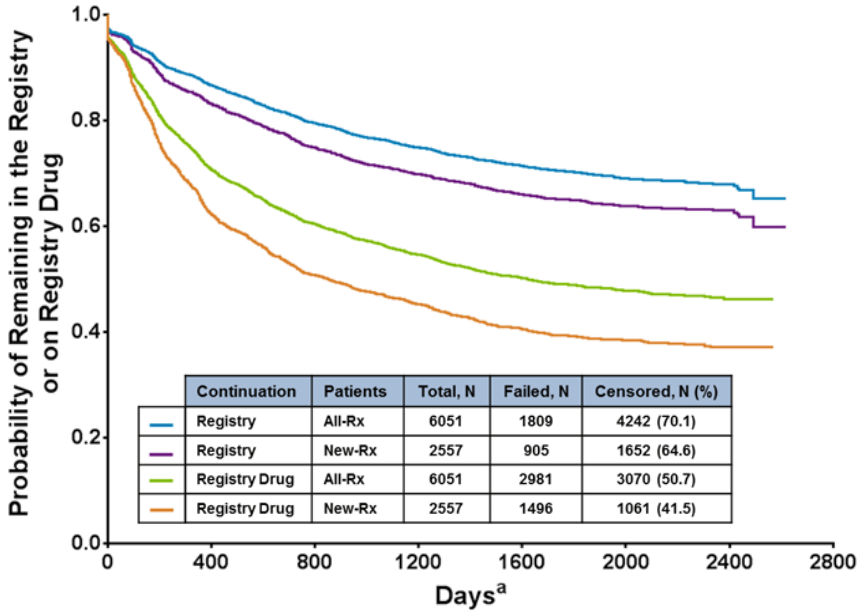
Figure 2. Number of Patients Based on Duration of ADA Exposure (All-Rx and New-Rx Patient Population)



ADA=adalimumab; All-Rx=all-treated patient population; New-Rx=new prescription patient population.

- The time to discontinuation from the registry and from registry drug in All-Rx and New-Rx patients are shown in **Figure 3**.

Figure 3. Time to Discontinuation from the Registry and from Registry Drug (ADA), (All-Rx and New-Rx Patient Population)



[a]Time of observation (first day to last day of registry participation) for time to registry discontinuation; Registry exposure to ADA for time to registry drug discontinuation.
ADA=adalimumab; All-Rx=all-treated patient population; New-Rx=new prescription patient population.

RESULTS (CONTINUED)

SAFETY

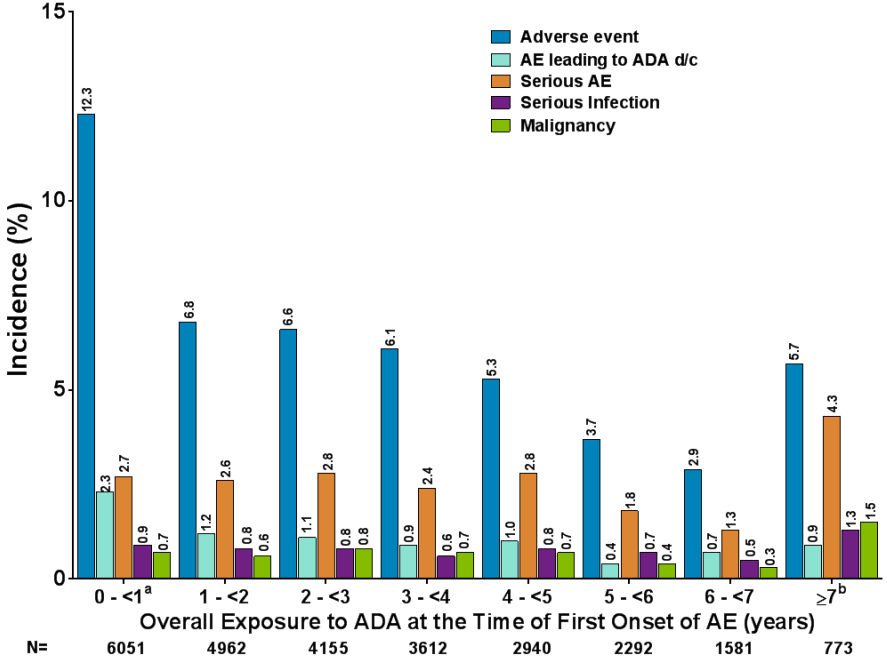
- An overview of incidence rates (E/100PY of overall exposure to ADA) of all treatment-emergent adverse events (All-TEAEs) in All-Rx patients by subgroups of overall exposure to ADA is presented in **Table 3**.
  - A majority of the rollover patients from feeder studies have overall exposure to ADA of >7 years and their AEs from feeder studies are included in the All-TEAE analyses.
- The incidence of All-TEAEs by time periods of overall exposure to ADA, i.e. the occurrence of new cases of a specific AE, in All-Rx patients remained stable over time and is shown in **Figure 4**.

Table 3. Incidence Rates of All-TEAE of Interest in Subgroups of Overall Exposure to ADA (All-Rx Patient Population)

		Subgroups of Overall Exposure to ADA					Overall All-Rx
		≤1 yr[a]	>1–3 yrs	>3–5 yrs	>5–7 yrs	>7 yrs[b]	
AE of Interest	N=	1235	1260	1285	1517	754	6051
E (E/100PY)	PY=	588.7	2359.7	5132.4	9195.5	6383.8	23660.1
AE		301 (51.1)	527 (22.3)	791 (15.4)	1207 (13.1)	2334 (36.6)	5160 (21.8)
AE leading to discontinuation of ADA		143 (24.3)	134 (5.7)	85 (1.7)	39 (0.4)	8 (0.1)	409 (1.7)
Serious AE		125 (21.2)	197 (8.3)	232 (4.5)	290 (3.2)	191 (3.0)	1035 (4.4)
Serious infection		40 (6.8)	52 (2.2)	53 (1.0)	58 (0.6)	44 (0.7)	247 (1.0)
Oral Candidiasis		1 (0.2)	3 (0.1)	2 (<0.1)	0	3 (<0.1)	9 (<0.1)
Active tuberculosis		2 (0.3)	2 (<0.1)	2 (<0.1)	0	0	6 (<0.1)
Opportunistic infection, other[c]		0	1 (<0.1)	1 (<0.1)	1 (<0.1)	0	3 (<0.1)
Malignancy		19 (3.2)	35 (1.5)	43 (0.8)	83 (0.9)	67 (1.0)	247 (1.0)
Congestive heart failure		2 (0.3)	0	5 (<0.1)	3 (<0.1)	1 (<0.1)	11 (<0.1)
Lupus-like reactions and systemic lupus		5 (0.8)	0	1 (<0.1)	1 (<0.1)	1 (<0.1)	8 (<0.1)
Demyelinating disorder		2 (0.3)	1 (<0.1)	1 (<0.1)	1 (<0.1)	0	5 (<0.1)
AE leading to death		8 (1.4)	12 (0.5)	7 (0.1)	2 (<0.1)	2 (<0.1)	31 (0.1)

[a]Intolerance to initial ADA therapy and subsequent discontinuations most likely occurred during the first year of ADA and a majority of these events were summarized as TEAEs within the ≤1 yr subgroup.
[b]The higher incidence of All-TEAEs in the subgroup with highest overall exposure to ADA (>7 years), which includes a majority of rollover patients from feeder studies, is likely due to closer AE documentation in feeder studies compared with registry AE collection and retroactive collection of AEs for patients who initiated ADA therapy outside of an AbbVie clinical trial before the registry.
[c]Excluding oral candidiasis and tuberculosis.
TEAE=treatment-emergent adverse event; ADA=adalimumab; All-Rx=all-treated patient population; AE=adverse event; E=event; PY=patient years; yr=year.

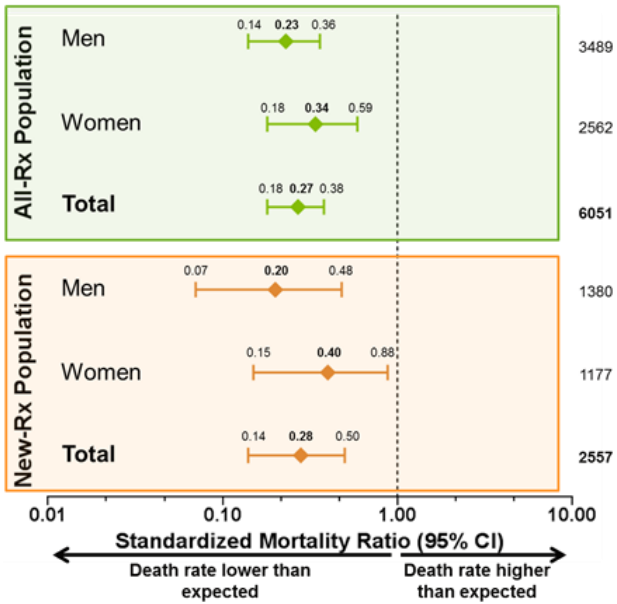
Figure 4. Incidence of All-TEAEs of Interest by Time Periods of Overall Exposure to ADA (All-Rx Patient Population)



[a]The AEs collected from rollover patients during feeder studies have most likely occurred in the first year of overall exposure to ADA.
[b]Patients with ≥7 years of overall exposure to ADA are a selected subgroup from the overall population who had longest exposure to ADA and potentially had a longer duration of disease.
N = number of patients who had at least an overall exposure to ADA up to and including the respective time period.
Incidence is defined as the number of patients with new occurrence of the specific AE divided by the number of patients at risk, i.e. patients who had at least an overall exposure to ADA up to and including the respective time period and who did not have the specific AE in any period before.
TEAE=treatment-emergent adverse event; All-Rx=all-treated patient population; AE=adverse event; ADA=adalimumab; d/c=discontinuation.

- Standardized mortality ratio was 0.27 (95%CI, 0.18–0.38) for All-Rx and 0.28 (95% CI, 0.14–0.50) for New-Rx, indicating that the observed number of deaths was below expected for age-, sex- and country-matched population (**Figure 5**).

Figure 5. Standardized Mortality Ratios (SMR), Overall and by Gender (All-Rx and New-Rx Patient Population)



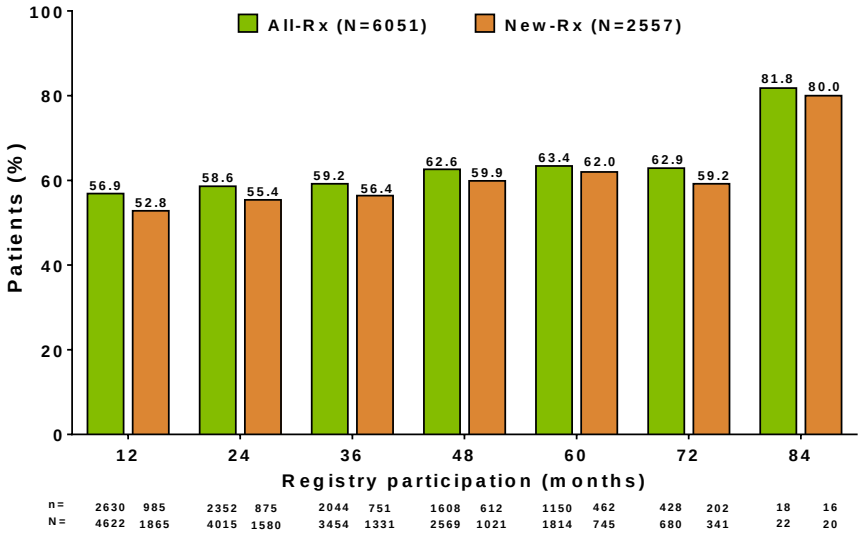
	N	PY	Expected deaths, n	Observed deaths, n
All-Rx Population – Men	3489	11175.7	78.6	18
All-Rx Population – Women	2562	6867.7	37.7	13
All-Rx Population – **Total**	**6051**	**18043.4**	**116.3**	**31**
New-Rx Population – Men	1380	4015.0	24.5	5
New-Rx Population – Women	1177	2689.8	14.9	6
New-Rx Population – **Total**	**2557**	**6704.8**	**39.4**	**11**

All-Rx=all-treated patient population; New-Rx=new prescription patient population; PY=patient years; CI=confidence intervals.

EFFECTIVENESS

- 56.9–81.8% of All-Rx and 52.8–80.0% of New-Rx patients achieved PGA "clear" or "minimal" during years 1–7 of registry participation (**Figure 6**).

Figure 6. Proportion of Patients (as Observed) Achieving PGA "Clear" or "Minimal" (All-Rx and New-Rx Patient Population)

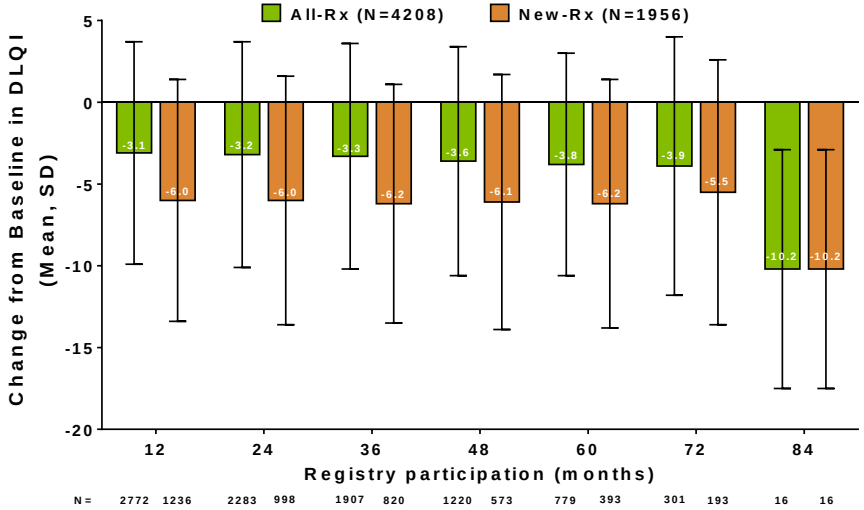


PGA=physician's global assessment; All-Rx=all-treated patient population; New-Rx=new prescription patient population.

PATIENT-REPORTED OUTCOMES (US patients only)

- Improvement in DLQI scores and WPAI subscores from baseline were maintained through the first 7 years of registry participation (**Figures 7** and **8**).

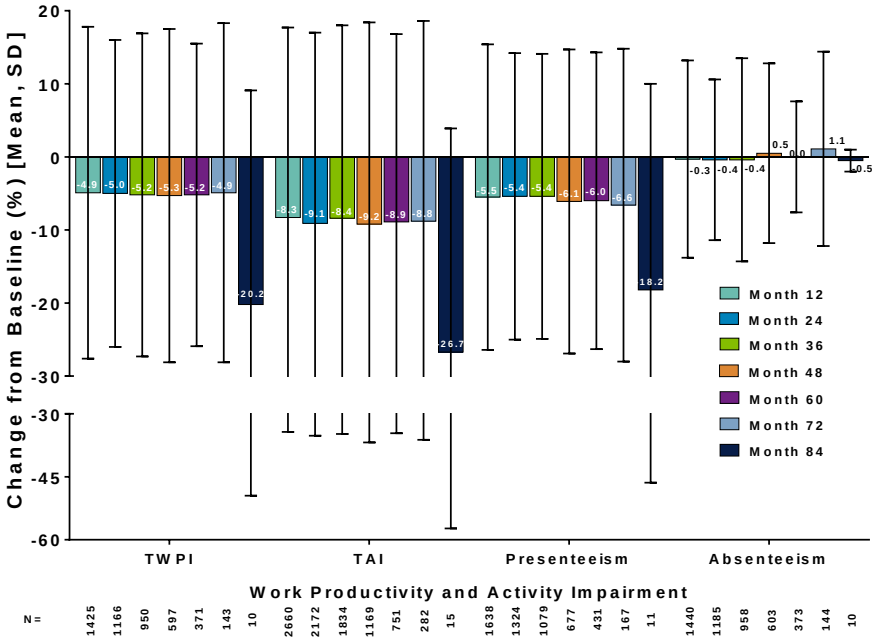
Figure 7. Change from Baseline (as Observed) in DLQI Scores[a] (All-Rx and New-Rx Patient Population)



[a]Decrease in DLQI score denotes improvement.
DLQI=dermatology life quality index; All-Rx=all-treated patient population; New-Rx=new prescription patient population.

RESULTS (CONTINUED)

Figure 8. Change from Baseline (as Observed) in WPAI Subscores[a] (All-Rx Patient Population)[b]



[a]Decrease in WPAI subscores denotes improvement.
[b]New-Rx patients showed maintained improvement in WPAI subscores similar to All-Rx patients (data not shown).
WPAI=work productivity and activity impairment; TWPI=total work productivity impairment; TAI=total activity impairment; presenteeism=impairment while working; All-Rx=all-treated patient population; New-Rx=new prescription patient population.

CONCLUSION

- In this 7-year interim analysis, no new safety signals were observed and safety was consistent with the known safety profile of ADA.
- The number of treatment-emergent deaths in the registry was below the expected rate for comparable general population.
- As-observed effectiveness of ADA and improvement from baseline in PROs were maintained through 84 months.

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ACKNOWLEDGEMENTS & DISCLOSURES

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The Efficacy of Certolizumab Pegol over 4 Years in Psoriatic Arthritis Patients With and Without Concomitant Use of DMARDs

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Background and Objective

BACKGROUND

- In addition to peripheral and axial arthritis, and psoriatic skin disease, patients with psoriatic arthritis (PsA) may experience extra articular manifestations (EAMs), including dactylitis and enthesitis
- In the RAPID-PsA trial (NCT01087788), patients with PsA treated with certolizumab pegol (**CZP**, a PEGylated Fc-free anti-TNF), showed rapid improvements in both joint and skin manifestations of the disease,[1] which were maintained over 4 years' treatment[2]
- As CZP may be used in the treatment of PsA either alongside non-biologic DMARDs or as a monotherapy, here we assess long-term efficacy of CZP on joint, skin and extra-articular manifestations in these two populations

OBJECTIVE

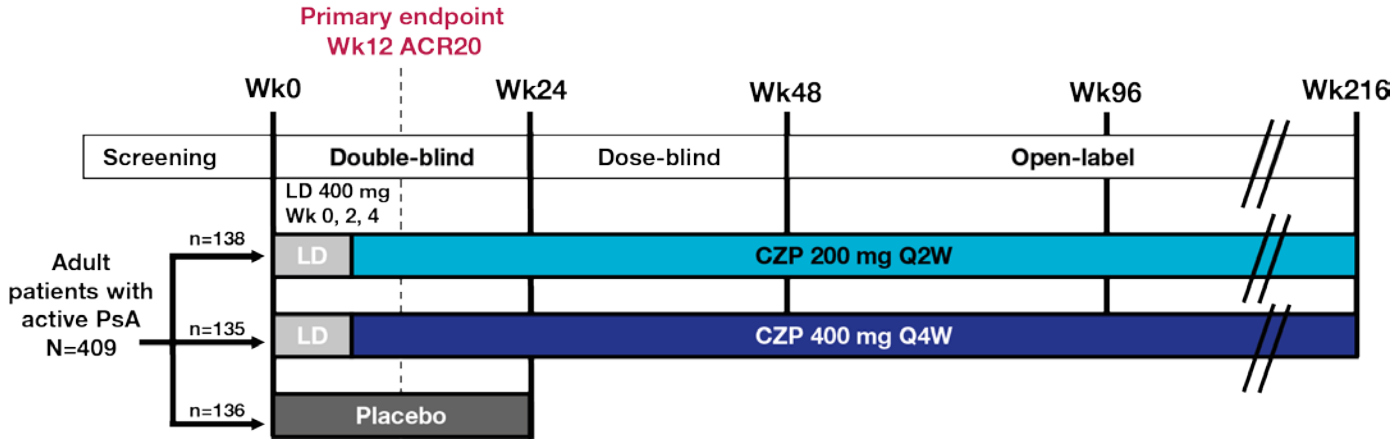
To report the efficacy of CZP with and without concomitant DMARD use on symptoms of PsA, including effects on EAMs.

1. Mease, P. *et al.* Ann Rheum Dis 2014;73:48–55
2. Mease, P. *et al*. Ann Rheum Dis 2016;75(Suppl2):608

DMARD: disease modifying anti-rheumatic drug

Methods: Study Design

- RAPID-PsA (NCT01087788) was a phase III, multicenter, randomized, double-blind, parallel-group, placebo-controlled study that investigated the efficacy of CZP in patients with PsA
- The primary clinical (ACR20 response at Week 12)[1] and radiographic (change from baseline in mTSS at Week 24)[2] endpoints have already been reported



INCLUSION

- ≥18 years of age
- Diagnosis of adult onset PsA of ≥6 months' duration, defined by CASPAR criteria
- Active psoriatic skin lesions or history of psoriasis
- Active arthritis (≥3 TJC, ≥3 SJC, and either ESR ≥ 28 mm/h or CRP >7.9 mg/L)
- Previous failure with ≥1 DMARD

EXCLUSION

- Previous treatment with >1 anti-TNF
- Primary failure with prior anti-TNF
- Diagnosis of other inflammatory arthritis
- Evidence of latent/active tuberculosis unless prophylactic treatment had begun ≥4 weeks prior to baseline

1. Mease, P. *et al*. Ann Rheum Dis 2014;73:48–55
2. van der Heijde, D. *et al*. Ann Rheum Dis 2014;73:233–237

CRP: C-Reactive protein; ESR: erythrocyte sedimentation rate; LD: loading dose; SJC: swollen joint count; TJC: tender joint count

Methods: Study Assessment and Statistical Analyses

- Data are presented for all patients originally randomized to **CZP 200 mg Q2W** or **CZP 400 mg Q4W**, and are shown for patients with (**DMARD+**) and without (**DMARD-**) DMARD use at baseline
- Outcomes assessed include:
  - ACR20 response
  - Enthesitis: Leeds Enthesitis Index (LEI; range: 0–6) in patients with LEI >0 at baseline
  - Dactylitis: Leeds Dactylitis Index (LDI; calculated as: sum of dactylitic digits, where each digit score = ratio of circumference of affected vs opposite digit multiplied by tenderness score [0: non-tender; 1: tender]) in patients with at least 1 digit affected and with a difference in circumference ≥10% at baseline compared to the opposite digit
  - Psoriasis: Psoriasis Severity Index (PASI) score, and patients achieving a PASI75 response, for patients with baseline skin involvement (≥3% body surface area [BSA] affected by psoriasis)
- Data are shown as observed case (OC) and with imputation (NRI for missing categorical data and LOCF for missing continuous measures)
- Safety data are presented for the Safety Set - all patients treated with ≥1 dose of CZP at any stage of the 216-week study period

ACR20: American College of Rheumatology score 20; CZP: certolizumab pegol; DMARD: disease modifying anti-rheumatic drug; LOCF: last observation carried forward; NRI: non-responder imputation.

Results: Baseline Characteristics

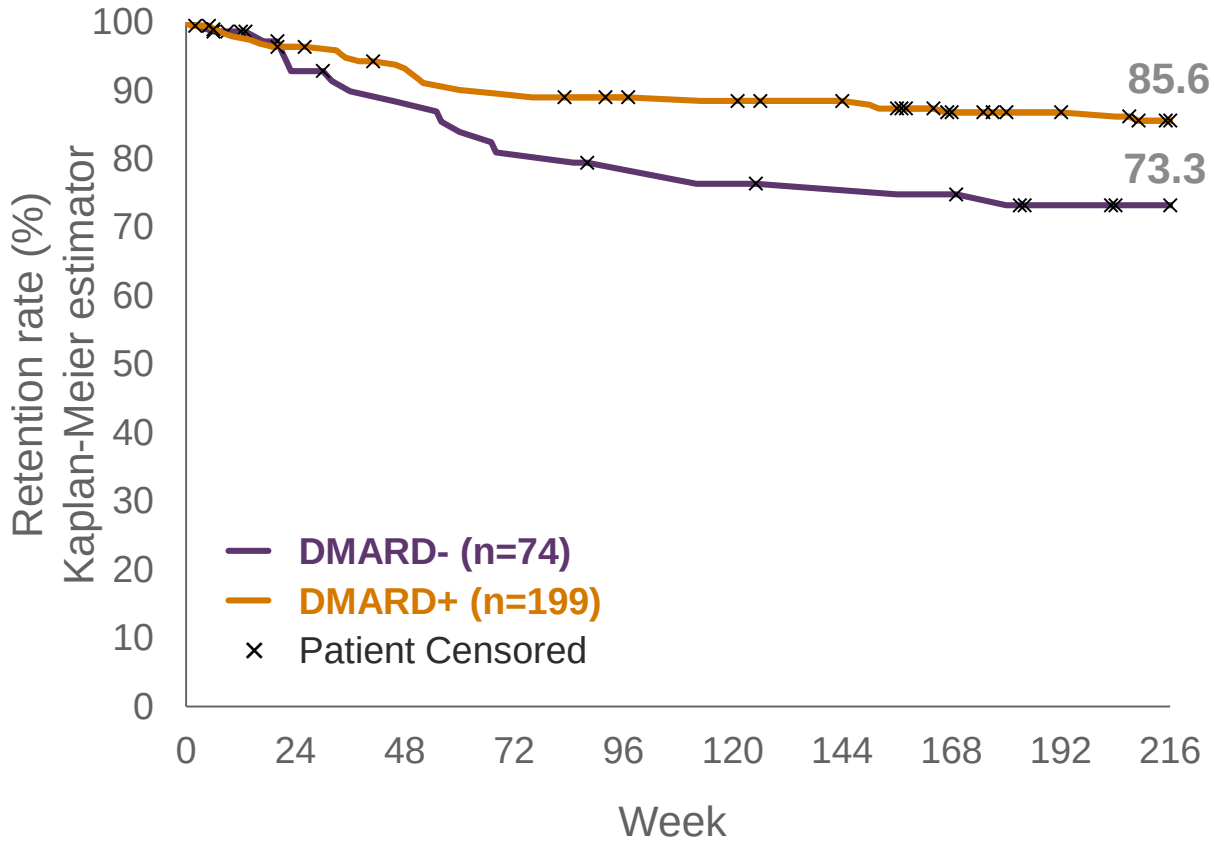
- A total of 409 patients were randomized, of whom 273 received CZP from Week 0

	DMARD- (n=74)	DMARD+ (n=199)
Demographics		
Age, years, mean (SD)	45.9 (12.4)	48.4 (11.2)
Female, n (%)	41 (55.4)	106 (53.3)
Weight, kg, mean (SD)	84.5 (18.7)	85.6 (18.0)
Prior medication		
1 prior non-biologic DMARD, n (%)	42 (56.8)	91 (45.7)
≥2 prior non-biologic DMARDs, n (%)	26 (35.1)	107 (53.8)
Prior anti-TNF, n (%)	23 (31.1)	31 (15.6)
Disease characteristics		
Tender joint count (0–68 joints), mean	21.5	20.2
Swollen joint count (0–66 joints), mean	11.7	10.4
HAQ-DI (range 0–3), mean	1.40	1.28
Patients with psoriasis BSA ≥3%, n (%)	53 (71.6)	113 (56.8)
Psoriasis BSA, mean (SD)	13.3 (12.8)	11.4 (12.2)
Extra-articular manifestations		
Patients with enthesitis, n (%)	47 (63.5)	125 (62.8)
LEI, mean (SD)	2.7 (1.6)	3.1 (1.6)
Patients with dactylitis, n (%)	20 (27.0)	47 (23.6)
LDI, mean (SD)	59.7 (49.1)	54.3 (65.3)

Dactylitis defined as at least 1 digit affected and with a difference in circumference ≥10% and marked as tender. BSA: Body Surface Area; DMARD: disease modifying anti-rheumatic drug; HAQ-DI: Health Assessment Questionnaire Disability Index; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index.

Results: Withdrawals to Week 216 for Week 0 CZP Patients both With and Without Concomitant DMARD Use

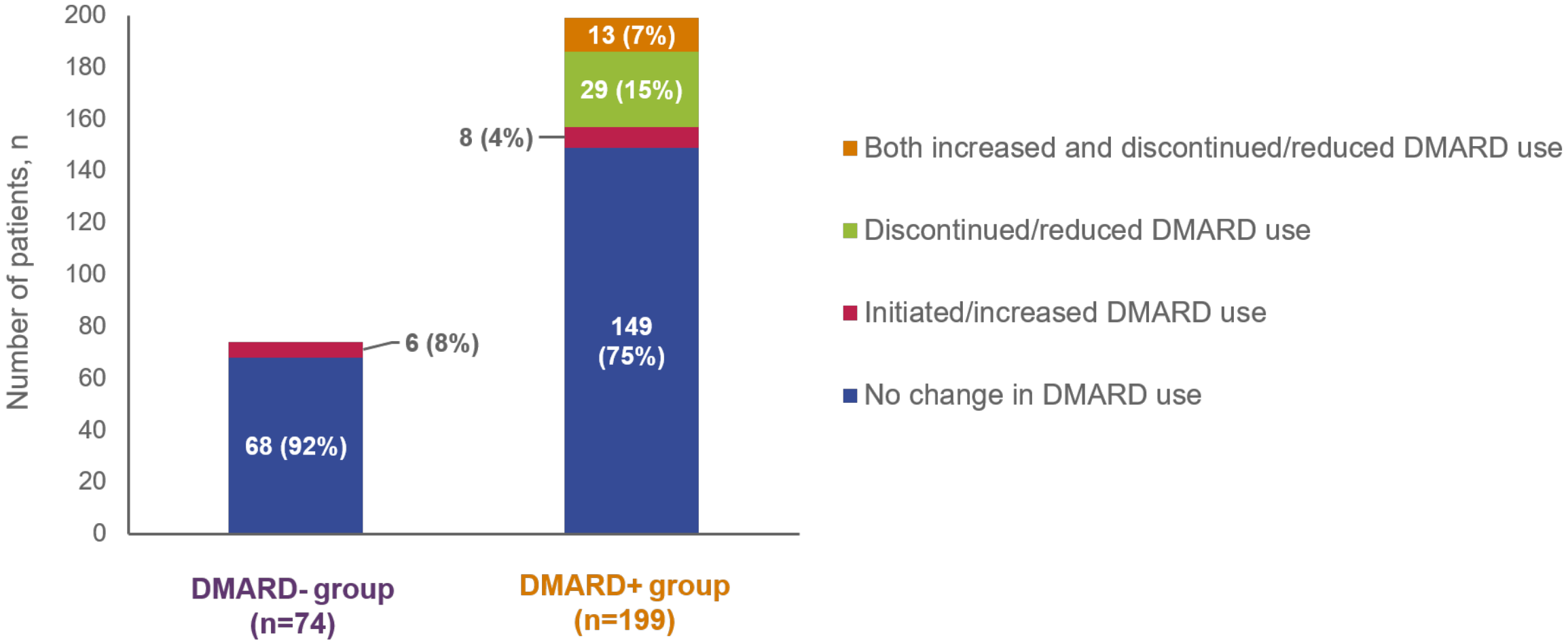
Withdrawals due to lack of efficacy or adverse event



Patients withdrawing from the study		
Reason for withdrawal	**DMARD- n (%)**	**DMARD+ n (%)**
Any reason	32 (43.2)	58 (29.1)
Adverse event	14 (18.9)	22 (11.1)
Lack of efficacy	4 (5.4)	5 (2.5)
Protocol violation	1 (1.4)	1 (0.5)
Lost to follow-up	5 (6.8)	4 (2.0)
Consent withdrawn	7 (9.5)	18 (9.0)
Other	1 (1.4)	8 (4.0)

Censored patients (each represented by an individual cross) are those who withdrew due to reasons other than lack of efficacy or adverse event, and those lost to follow-up. Censored patients do not contribute to the retention rate estimate. CZP: certolizumab pegol; DMARD: disease modifying anti-rheumatic drug.

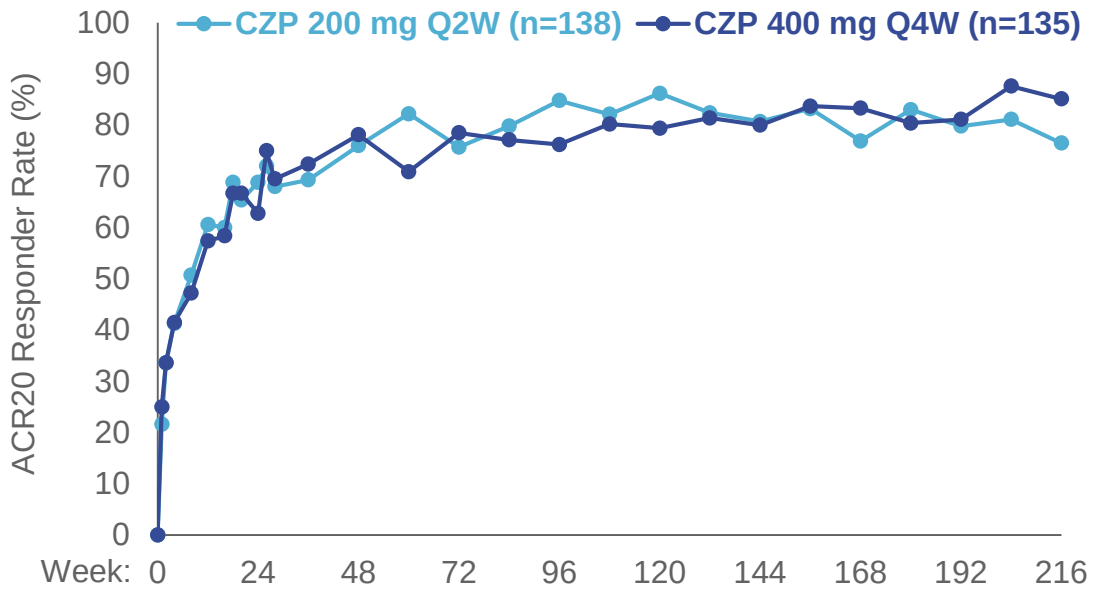
Results: Use of DMARDs in CZP-Treated Patients at Baseline and Throughout the 4-Year Study



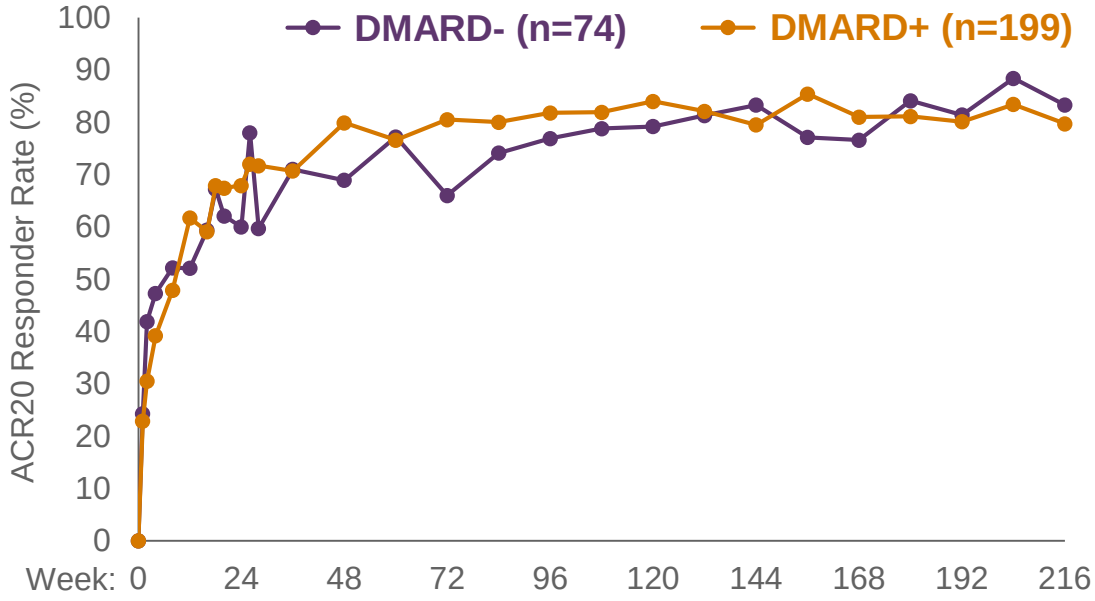
CZP: certolizumab pegol; DMARD: disease modifying anti-rheumatic drug.

Results: ACR20 Responses with CZP Treatment were Maintained to Week 216 in Patients both With and Without Concomitant Use of DMARDs (Observed Case)

By CZP Dose



By Concomitant DMARD Use



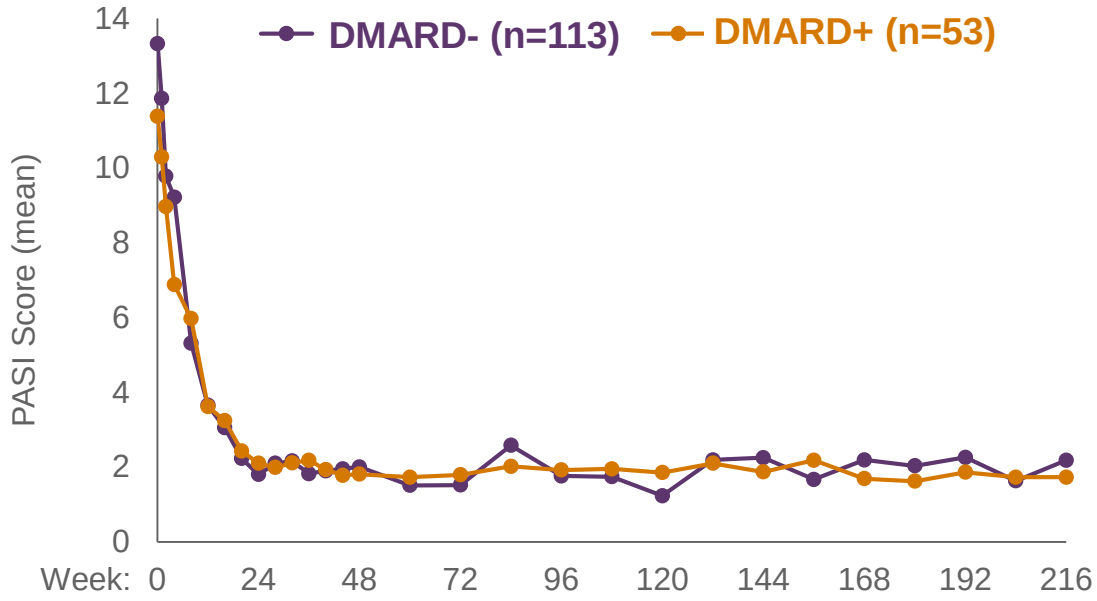
CZP Dose	ACR 20 Responder Rate, %			
	Week 96		Week 216	
	OC	NRI	OC	NRI
200 mg Q2W	84.8 [n=112]	68.8	76.5 [n=98]	54.3
400 mg Q4W	76.2 [n=105]	59.3	85.1 [n=87]	54.8

CZP Dose Combined	ACR 20 Responder Rate, %			
	Week 96		Week 216	
	OC	NRI	OC	NRI
DMARD-	76.9 [n=52]	54.1	83.3 [n=42]	47.3
DMARD+	81.8 [n=165]	67.8	79.7 [n=143]	57.3

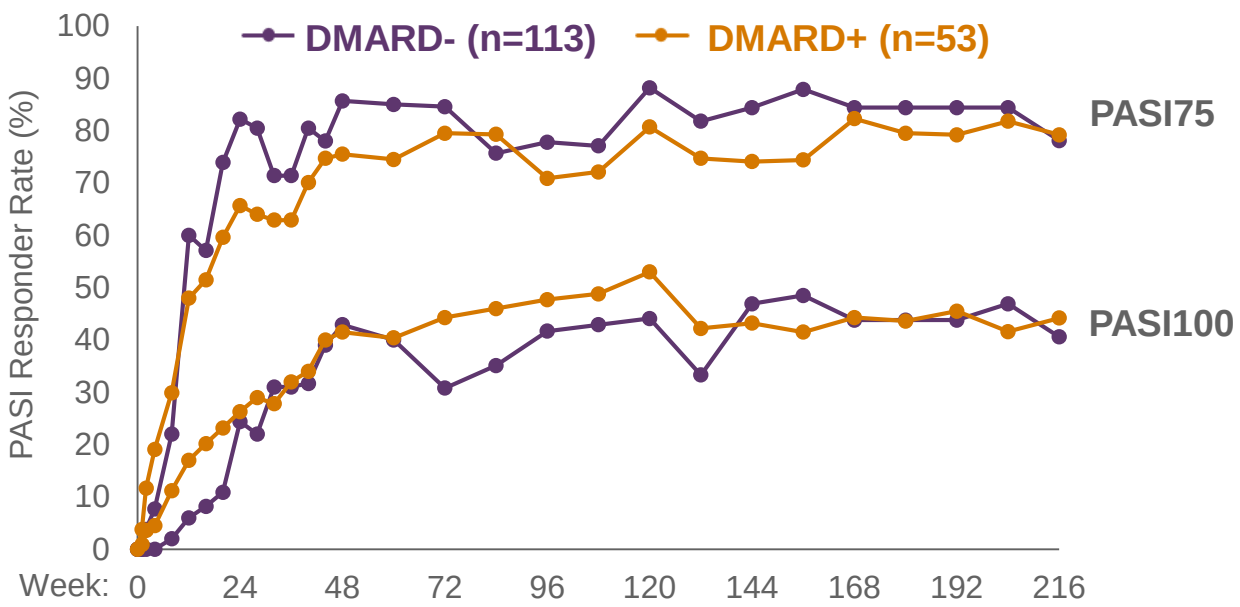
ACR20: American College of Rheumatology score 20; CZP: certolizumab pegol; DMARD: disease modifying anti-rheumatic drug; NRI: non-responder imputation; OC: observed case; Q2W: every 2 weeks; Q4W: every 4 weeks.

Results: Improvements in Psoriasis with CZP Treatment were Maintained to Week 216 in Patients both With and Without Concomitant Use of DMARDs (Observed Case)

PASI Score



PASI Responder Rate



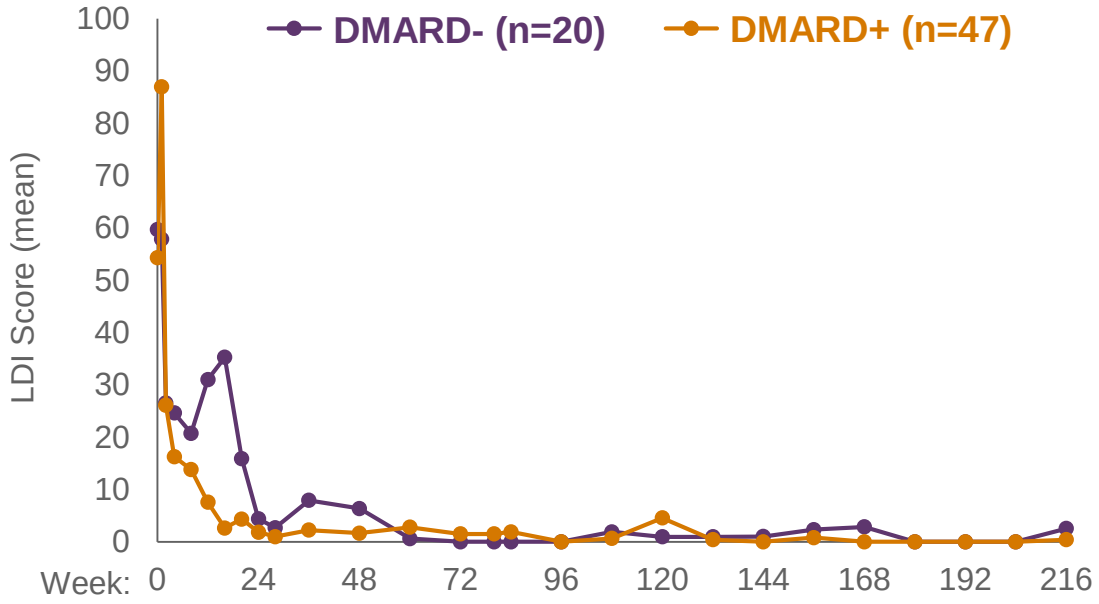
CZP Dose Combined	PASI Score, mean (SD)		
	Week 0	Week 216	
	OC	OC	LOCF
DMARD-	13.3 (12.8) [n=53]	2.2 (3.3) [n=32]	3.2 (7.8)
DMARD+	11.4 (12.2) [n=112]	1.7 (6.4) [n=77]	2.3 (6.1)

	PASI75 Responder Rate, %				PASI100 Responder Rate, %			
	Week 96		Week 216		Week 96		Week 216	
	OC	NRI	OC	NRI	OC	NRI	OC	NRI
DMARD-	77.8 [n=36]	52.8	78.1 [n=32]	47.2	41.7 [n=36]	28.3	40.6 [n=32]	24.5
DMARD+	70.9 [n=86]	54.0	79.2 [n=77]	54.0	47.7 [n=86]	36.3	44.2 [n=77]	30.1

CZP: certolizumab pegol; DMARD: disease modifying anti-rheumatic drug; LOCF: last observation carried forward; OC: observed case; PASI: Psoriasis Severity Index; PASI75: 75% reduction in Psoriasis Severity Index; PASI100: 100% reduction in Psoriasis Severity Index.

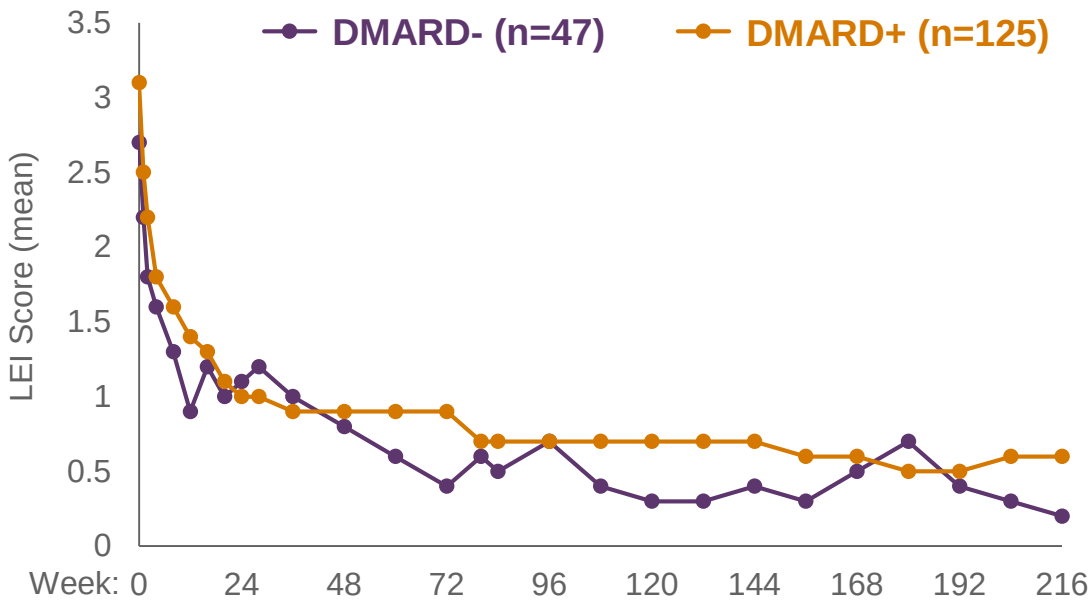
Results: Improvements in Extra-Articular Manifestations with CZP Treatment were Maintained to Week 216 in Patients both With and Without Concomitant Use of DMARDs (Observed Case)

Dactylitis



CZP Dose Combined	LDI Score, mean (SD)		
	Week 0	Week 216	
	OC	OC	LOCF
DMARD-	59.7 (49.1) [n=20]	2.5 (9.8) [n=15]	3.7 (11.3)
DMARD+	54.3 (65.3) [n=47]	0.4 (2.3) [n=34]	4.3 (13.5)

Enthesitis



CZP Dose Combined	LEI Score, mean (SD)		
	Week 0	Week 216	
	OC	OC	LOCF
DMARD-	2.7 (1.6) [n=47]	0.2 (0.5) [n=24]	0.9 (1.7)
DMARD+	3.1 (1.6) [n=125]	0.6 (1.2) [n=86]	0.8 (1.5)

CZP: certolizumab pegol; DMARD: disease modifying anti-rheumatic drug; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; LOCF: last observation carried forward; OC: observed case.

Results: Safety Profile of All CZP-Treated Patients to Week 216

Safety

- Patients in the Safety Set (n=393) had total CZP exposure of 1,321 patient-years
- The serious adverse event rate per 100 patient-years was 11.9
- No new safety signal was identified from Week 96 to Week 216, and no further death was reported for this period
- The 6 deaths occurring in RAPID-PsA were reported previously[1] and include:
  - 2 cardiac disorders (1 unlikely to be related and 1 unrelated to CZP)
  - 1 sudden death (unrelated to CZP)
  - 1 infection (related to CZP)
  - 1 case each of breast cancer (unlikely related to CZP) and lymphoma (possibly related to CZP)

Treatment-Emergent Adverse Events (TEAEs)

	All CZP* (N=393) n (%) [ER]
Any TEAE	**367 (93.4) [257.9]**
Mild	**336 (85.5)**
Moderate	**261 (66.4)**
Severe	**71 (18.1)**
Drug-related TEAEs	**199 (50.6)**
Serious TEAEs	**100 (25.4) [11.9]**
Infections and infestations	**23 (5.9) [2.3]**
Withdrawals due to TEAEs	**54 (13.7)**
Deaths	**6 (1.5)**

1. Mease P. *et al.* RMD Open 2015;1(1):e000119.

*Safety data are presented for the Safety Set (all patients treated with ≥1 dose of CZP, including placebo patients re-randomized to CZP). CZP: certolizumab pegol; ER: event rate per 100 patient-years; TEAE: treatment emergent adverse event.

Summary and Conclusion

SUMMARY

- PsA patients treated with CZP over 4 years demonstrated sustained improvements in the joint, skin and extra articular manifestations of their disease, in the RAPID-PsA trial
- Among patients completing the open-label period of the study, those treated with CZP monotherapy exhibited similar long-term improvements in PsA symptoms to those patients with concomitant DMARD use at baseline

CONCLUSION

PsA patients treated with CZP for 4 years, both with and without concomitant DMARD use, exhibited similar and sustained improvements in the joint, skin and extra articular manifestations of their disease

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