Τι μάθαμε από την κλινική πράξη: η θέση της απρεμιλάστης στην αντιμετώπιση της ψωρίασης

Αικατερίνη Πατσατσή
Καθηγήτρια Δερματολογίας – Αφροδισιολογίας ΑΠΘ
Ειδικό Ιατρείο Ψωρίασης
Β΄Κλινική Δερματικών & Αφροδισίων Νόσων ΑΠΘ
Νοσοκομείο Παπαγεωργίου

Απρεμιλάστη: Θεραπευτικές ενδείξεις

Ψωρίαση

Η Απρεμιλάστη ενδείκνυται για τη θεραπεία της μέτριας έως σοβαρής χρόνιας κατά πλάκας ψωρίασης σε ενήλικες ασθενείς οι οποίοι δεν ανταποκρίθηκαν, ή έχουν κάποια αντένδειξη, ή εμφάνισαν μη ανοχή σε άλλη συστηματική θεραπεία, συμπεριλαμβανομένης της κυκλοσπορίνης, της μεθοτρεξάτης ή του ψωραλενίου και της υπεριώδους ακτινοβολίας A (PUVA).

Ψωριασική αρθρίτιδα

Η Απρεμιλάστη, ως μονοθεραπεία ή σε συνδυασμό με Τροποποιητικά της Νόσου Αντιρρευματικά Φάρμακα (DMARDs), **ενδείκνυται για τη θεραπεία της ενεργού ψωριασικής αρθρίτιδας (ΨΑ) σε ενήλικες ασθενείς** οι οποίοι είχαν ανεπαρκή ανταπόκριση ή εμφάνισαν μη ανοχή σε προηγούμενη θεραπεία με DMARD

Νόσος Behçet

Η Απρεμιλάστη ενδείκνυται για τη θεραπεία των στοματικών ελκών που σχετίζονται με τη νόσο Behçet (BD) σε ενήλικες ασθενείς οι οποίοι είναι υποψήφιοι για συστηματική θεραπεία**.**

Η Απρεμιλάστη στη θεραπεία της ψωρίασης

- Χρησιμοποιείται από το 2016 – σημαντική η καταγεγραμμένη εμπειρία

- Έχει πλέον τη θέση της στη θεραπευτική της μέτριας ψωρίασης και των ειδικών μορφών της

Από την επέκταση των εγκριτικών μελετών

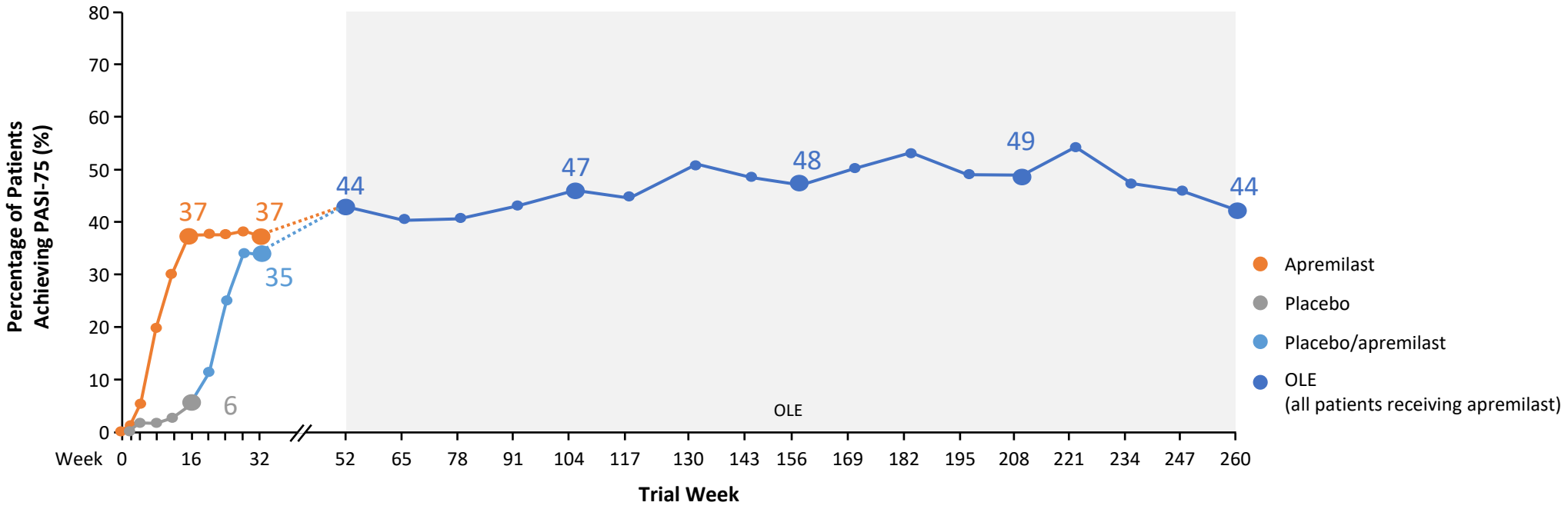
Απρεμιλάστη στην αντιμετώπιση της ψωρίασης

Αποτελεσματικότητα και Διάρκεια της απάντησης

Διατήρηση PASI 75 στην πενταετία

- Patients with moderate to severe PsO experienced sustained PASI-75 response rates through 5 years with apremilast

Proportion of Patients Achieving PASI-75 Through 260 Weeks*,†
(Data as Observed; FAS)



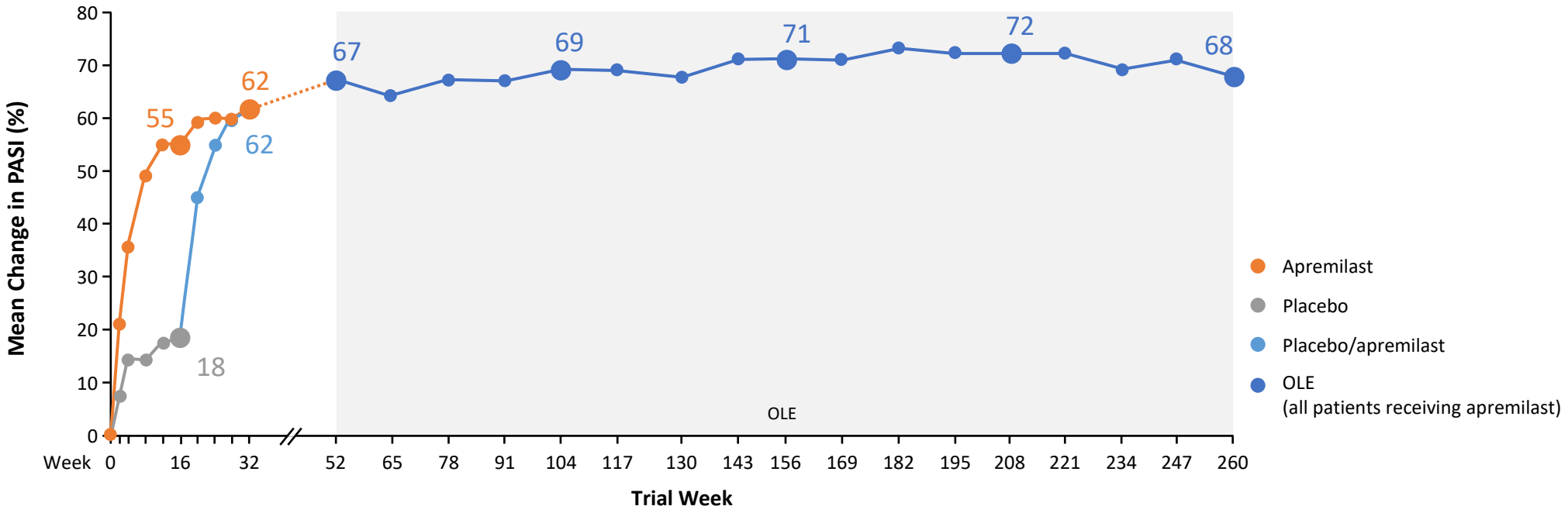
Placebo, N	282	247	216					
Apremilast, N	562	501	425	486	312	215	157	125

*Consider OLE study limitations when interpreting results. The OLE is not blinded, not controlled, and includes self-selection bias; †Randomized treatment withdrawal phase (weeks 32–52) where additional PsO therapies, including topicals and/or phototherapy, could have been added to PASI-75 nonresponders.
ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; FAS = full analysis set; OLE = open-label extension; PASI-75 = 75% reduction in psoriasis area and severity index score; PsO = psoriasis.
Data on file, Amgen.

Διατήρηση της βελτίωσης του PASI Score στην πενταετία

- Patients with moderate to severe PsO experienced sustained improvements in PASI score through 5 years with apremilast

Mean Change in PASI Through 260 Weeks*,†,‡
(Data as Observed; FAS)



Placebo, N	282	247	216					
Apremilast, N	562	501	425	486	312	215	157	125

*Consider OLE study limitations when interpreting results. The OLE is not blinded, not controlled, and includes self-selection bias; †Randomized treatment withdrawal phase (weeks 32–52) where additional PsO therapies, including topicals and/or phototherapy, could have been added to PASI-75 nonresponders; ‡Baseline mean PASI scores: placebo, 19; apremilast, 19.
ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; FAS = full analysis set; OLE = open-label extension; PASI = psoriasis area and severity index; PASI-75 = 75% reduction in psoriasis area and severity index score; PsO = psoriasis.
Data on file, Amgen.

Από την επέκταση των εγκριτικών μελετών

Απρεμιλάστη στην αντιμετώπιση ειδικών εντοπίσεων ψωρίασης

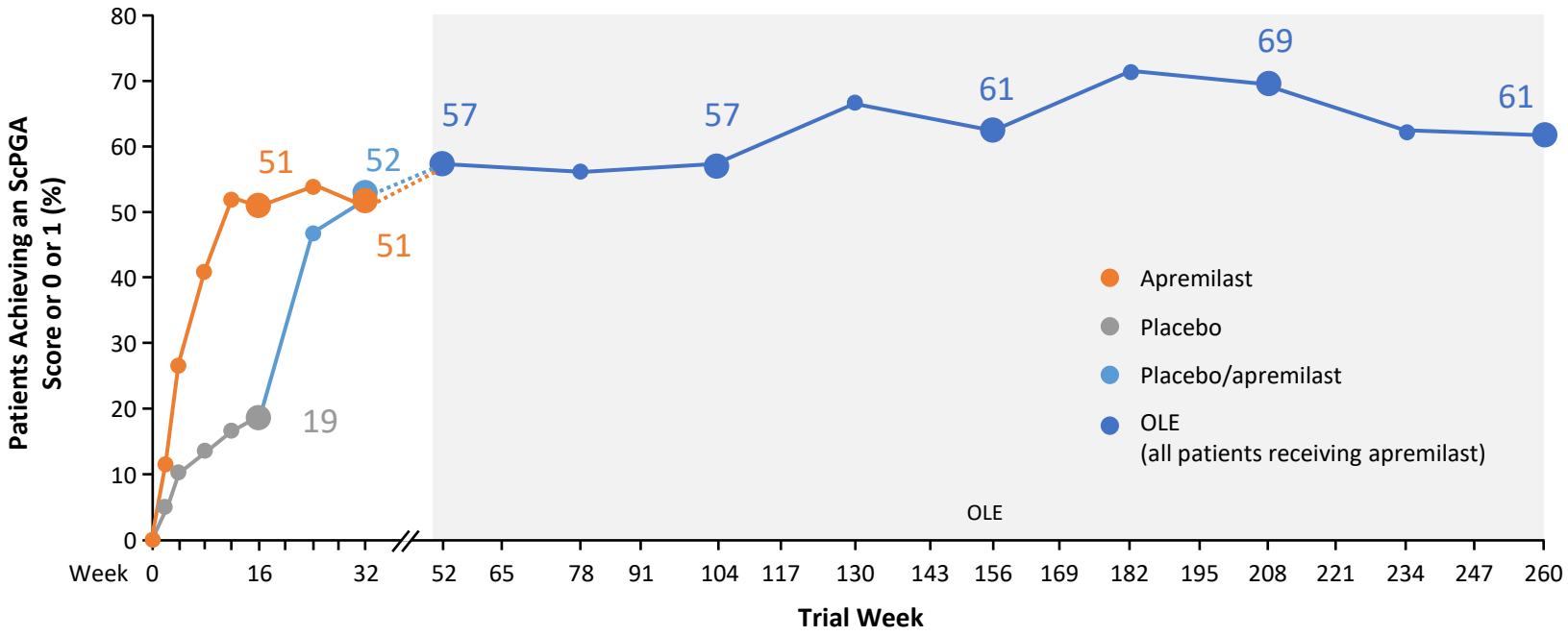
Αποτελεσματικότητα και Διάρκεια της απάντησης

Διατήρηση της υψηλής αποτελεσματικότητας στην ψωρίαση του τριχωτού σε βάθος πενταετίας

- Patients with moderate to severe PsO sustained scalp responses through 5 years with apremilast[1,2]

Scalp

Proportion of Patients Achieving ScPGA Responses Through 260 Weeks[1,*,†,‡]
(Data as Observed; FAS)



Placebo, N	189	162	137					
Apremilast, N	374	328	274	308	191	132	99	125

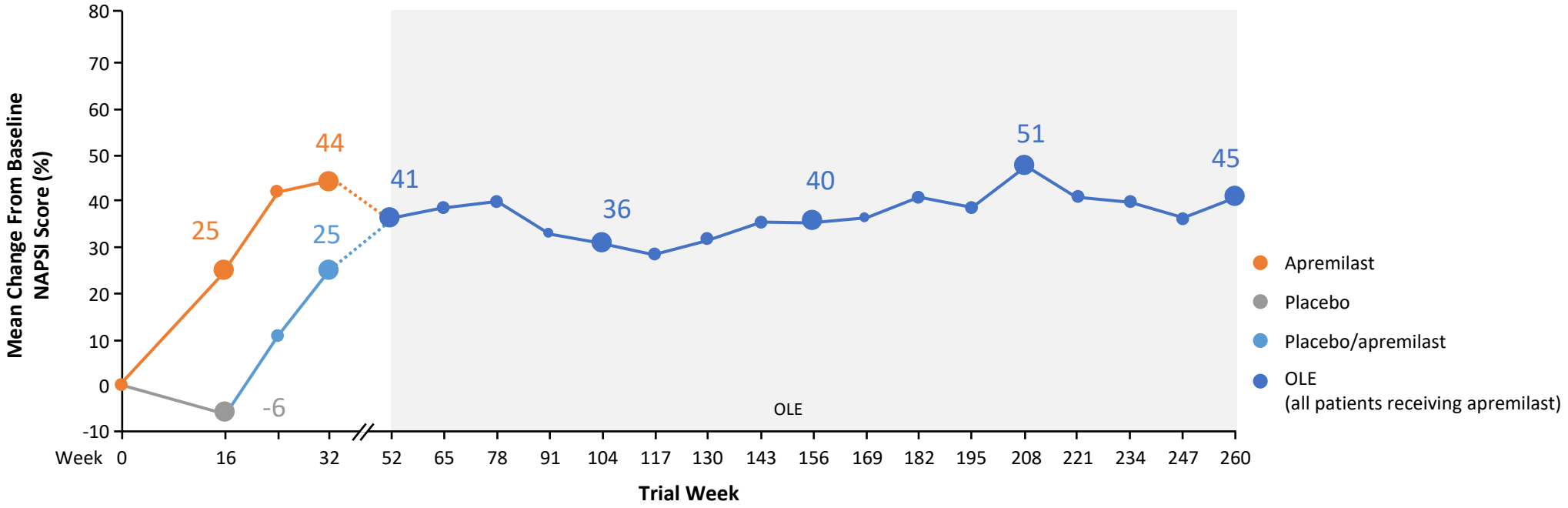
*OLE phase: pooled treatment arms reflect post hoc analysis. Consider OLE study limitations when interpreting results. The OLE is not blinded, not controlled, and includes inherent self-selection bias; †Randomized treatment withdrawal phase (weeks 32–52) where additional PsO therapies, including topicals and/or phototherapy, could have been added to PASI-75 nonresponders; ‡Baseline ScPGA ≥ 3.
ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; FAS = full analysis set; OLE = open-label extension; PASI-75 = 75% reduction in psoriasis area and severity index score; PsO = psoriasis; RWE = real-world evidence; ScPGA = scalp physician's global assessment.
1. Data on file, Amgen; 2. Papp K, et al. *J Am Acad Dermatol*. 2015;73:37-49.

Διατήρηση της αποτελεσματικότητας στην ψωρίαση των ονύχων σε βάθος πενταετίας

- Patients with moderate to severe PsO experienced sustained improvements in NAPSI score through 5 years with apremilast[1,2]

Nail

Mean Percent Change in NAPSI Scores Through 260 Weeks[1,*,†,‡]
(Data as Observed; FAS)



Placebo, N	0	170	145					
Apremilast, N	0	318	275	315	192	131	99	82

*OLE phase: pooled treatment arms reflect post hoc analysis. Consider OLE study limitations when interpreting results. The OLE is not blinded, not controlled, and includes inherent self-selection bias; †Randomized treatment withdrawal phase (weeks 32–52) where additional PsO therapies, including topicals and/or phototherapy, could have been added to PASI-75 nonresponders. ‡In patients with nail PsO at baseline (NAPSI score ≥ 1; 66.1% [558/844]).
ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; FAS = full analysis set; NAPSI = Nail Psoriasis Severity Index; OLE = open-label extension; PASI-75 = 75% reduction in psoriasis area and severity index score; PsO = psoriasis.
1. Data on file, Amgen; 2. Papp K, et al. *J Am Acad Dermatol*. 2015;73:37-49.

Από την επέκταση των εγκριτικών μελετών

Απρεμιλάστη στον κνησμό της ψωρίασης

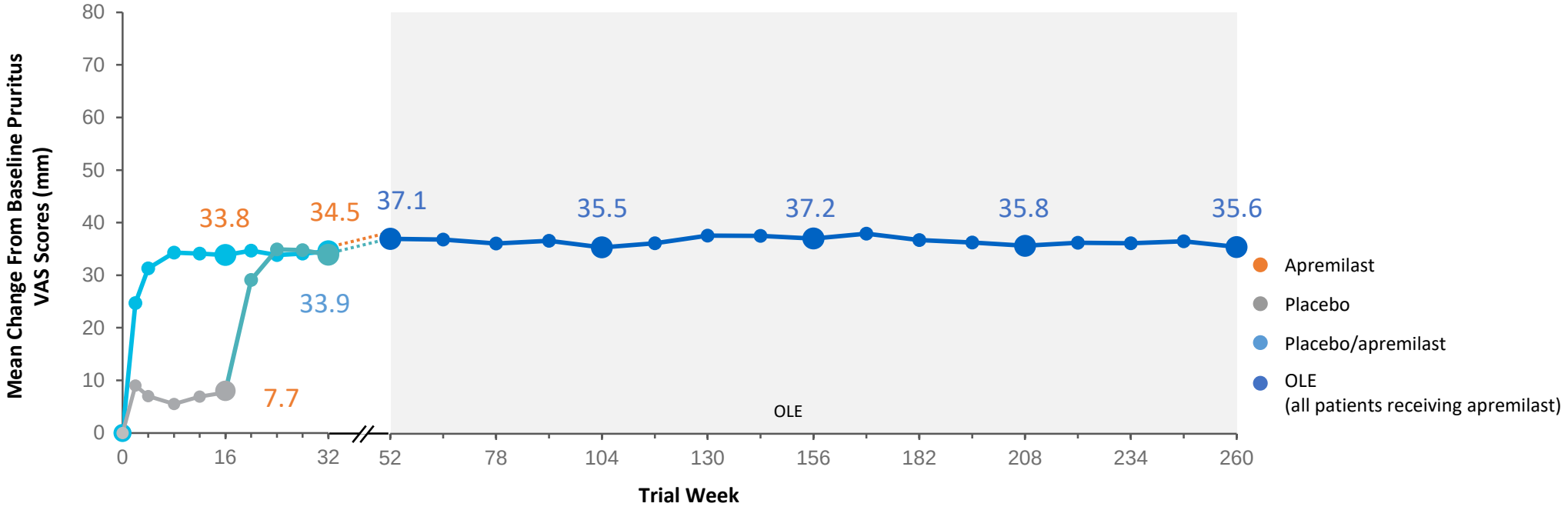
Αποτελεσματικότητα και Διάρκεια της απάντησης

Διατήρηση της ύφεσης του κνησμού σε βάθος πενταετίας

- Patients with moderate to severe PsO experienced sustained improvements in pruritus through 5 years with apremilast[1,2]

Itch

Mean Change in Baseline Pruritus VAS Scores Through 260 Weeks[1,*,†,‡]
(Data as Observed; FAS)



Placebo, N	282	248	216					
Apremilast, N	562	500	424	487	314	215	158	126

*OLE phase: pooled treatment arms reflect post hoc analysis. Consider OLE study limitations when interpreting results. The OLE is not blinded, not controlled, and includes inherent self-selection bias; †Randomized treatment withdrawal phase (weeks 32–52) where additional PsO therapies, including topicals and/or phototherapy, could have been added to PASI-75 nonresponders; ‡Pruritus was measured on a 100-mm VAS. baseline mean pruritus VAS scores (mm): placebo, 65.2; apremilast, 66.2.
ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; FAS = full analysis set; OLE = open-label extension; PASI-75 = 75% reduction in psoriasis area and severity index score; PsO = psoriasis; VAS = visual analog scale.
1. Data on file, Amgen; 2. Papp K, et al. *J Am Acad Dermatol*. 2015;73:37-49.

Από την επέκταση των εγκριτικών μελετών

Απρεμιλάστη και βελτίωση της ποιότητας ζωής

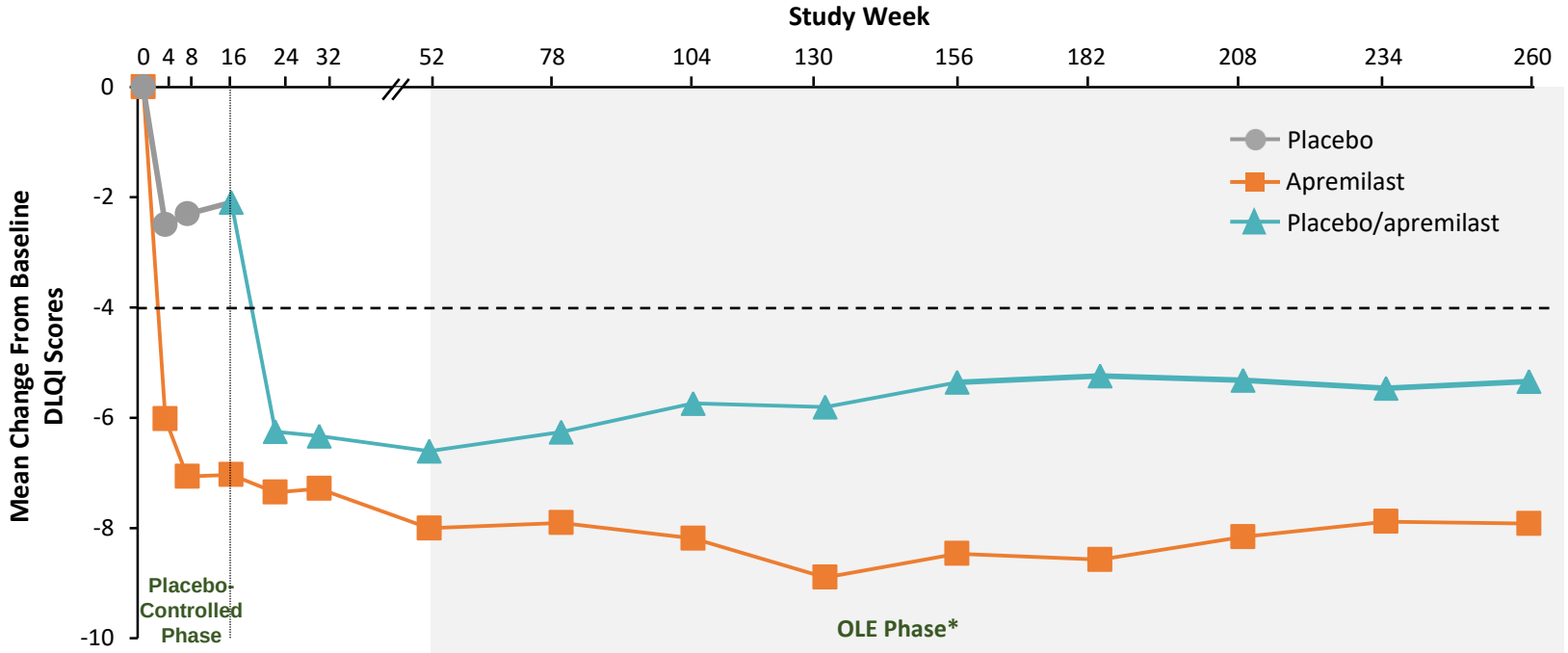
Αποτελεσματικότητα και Διάρκεια της απάντησης

Διατήρηση της βελτίωσης της ποιότητας ζωής σε βάθος πενταετίας

- Patients with moderate to severe PsO experienced sustained improvements in mean DLQI scores through 5 years with apremilast[1-3]

DLQI

Mean Change in Baseline DLQI Scores Through 260 Weeks[1,*,†,‡]
(Data as Observed; FAS)



Placebo, N	282	247	216	162	100	62	58	50	43	41
Apremilast, N	562	500	422	326	213	153	131	107	95	85

*OLE phase. Consider OLE study limitations when interpreting results. The OLE is not blinded, not controlled, and includes inherent self-selection bias; †Randomized treatment withdrawal phase (weeks 32–52) where additional PsO therapies, including topicals and/or phototherapy, could have been added to PASI-75 nonresponders; ‡Baseline mean DLQI scores: placebo, 12.1; apremilast 30 mg BID, 12.7.
BID = twice daily; DLQI = Dermatology Life Quality Index; ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; FAS = full analysis set; MCID = minimal clinically important difference; OLE = open-label extension; PASI-75 = 75% reduction in psoriasis area and severity index score; PsO = psoriasis.
1. Data on file, Amgen; 2. Papp K, et al. *J Am Acad Dermatol*. 2015;73:37-49; 3. Basra MKA, et al. *Dermatology.* 2015;230:27-33.

Μελέτη EMBRACE

Απρεμιλάστη σε ασθενείς με περιορισμένη νόσο

Efficacy and Safety of Apremilast in Patients With Limited Skin Involvement, Plaque Psoriasis in Special Areas, and Impaired Quality of Life: Results From the EMBRACE Randomized Trial

TRIAL OBJECTIVE[9]

- **To evaluate the impact on QoL, efficacy, and safety of APR 30 mg BID in patients with limited skin involvement with plaque PsO manifestations in special areas and impaired QoL**

Primary Endpoint: DLQI* response of ≥ 4-point reduction from baseline at week 16

Other Endpoints

Secondary endpoints	◆ Reduction from baseline in DLQI at week 16 ◆ Percentage change from baseline in affected BSA ◆ Proportion of patients achieving PASI < 3 ◆ Reduction from baseline in itch NRS ◆ Reduction from baseline in skin discomfort/pain VAS ◆ Achievement of PBI ≥ 1†
Exploratory endpoint	◆ Improvements in manifestations of plaque PsO in special areas
Ad hoc analysis	◆ Change from baseline in mean DLQI at week 16‡
Safety assessments	◆ TEAEs through week 16

*The DLQI is a 10-item questionnaire with a score range of 0 (best QoL) to 30 (worst QoL).[10] †The PBI evaluates patient-perceived benefit of treatment on a scale ranging from 0 (no benefit) to 4 (maximum benefit).[11]
‡DLQI at week 16 was categorized (worse [score increase], no change [0- to 1-point decrease], small [2- to 5-point decrease], moderate [6- to 10-point decrease], very large [11- to 20-point decrease], extremely large [21- to 30-point decrease]) and stratified by baseline score.

BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS[9]

- Baseline demographics and clinical characteristics were similar between the treatment groups in the EMBRACE study
- The most common special area affected was visible locations (26.7%), followed by the scalp (24.5%), nails (21.7%), genitals (15.5%), and palmoplantar areas (11.6%)

% Male*

58.8%

Mean Age*

49

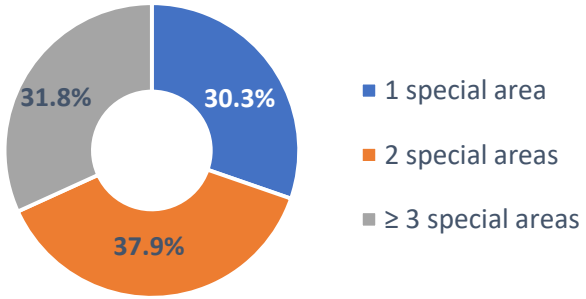
years

Mean Duration of Plaque PsO*

17

years

Special Areas Affected*,†



Baseline Demographics and Clinical Characteristics

Patients	PBO (n = 92)	APR (n = 185)
Age, mean (SD), years	50.9 (13.7)	47.4 (14.3)
Male, n (%)	57 (62)	106 (57)
BMI, mean (SD), kg/m^2	29.4 (5.7)	28.1 (5.6)
Duration of plaque PsO, mean (SD), years	18.4 (13.4)	16.3 (13.1)
Presence of plaque PsO, n (%)		
Visible locations	24 (26)	50 (27)
Dorsal hand‡	14 (58)	31 (62)
Face‡	11 (46)	26 (52)
Hairline‡	15 (63)	21 (42)
Neck‡	4 (17)	11 (22)
Scalp	23 (25)	45 (24)
Nails	20 (22)	40 (22)
Genitals	15 (16)	28 (15)
Palmoplantar areas	10 (11)	22 (12)
Number of special areas, mean	2.1	2.1
DLQI, mean (SD)	18.5 (4.9)	18.1 (4.9)
PASI, mean (SD)	6.8 (2.0)	6.8 (1.9)
BSA, mean (SD), %	7.3 (4.3)	7.0 (3.5)

*Overall population. †Special areas include scalp, nails, palms, soles, genitals, or visible locations such as the face, neck, hairline, or dorsal hand. ‡Percentages are based on the number of patients with PsO in visible locations (PBO: n = 24; APR: n = 50).

Efficacy and Safety of Apremilast in Patients With Limited Skin Involvement, Plaque Psoriasis in Special Areas, and Impaired Quality of Life: Results From the EMBRACE Randomized Trial

The phase 4 EMBRACE study evaluated the impact on QoL, efficacy, and safety of APR in patients with PsO with limited skin involvement, PsO manifestations in special areas, and impaired QoL

Significantly greater proportions of patients treated with APR (73.3%) vs PBO (41.3%) achieved the primary endpoint of DLQI response (≥ 4-point reduction) at week 16 ($P < 0.0001$)

Significantly greater improvement in BSA ($P = 0.0085$) and PASI < 3 ($P = 0.0328$) was observed with APR treatment compared with PBO at week 16

Significantly greater improvements with APR vs PBO in itch NRS score (–2.5 vs –0.9; $P < 0.0001$) and skin discomfort/pain VAS score (–21.5 vs –5.4; $P = 0.0003$) were also observed

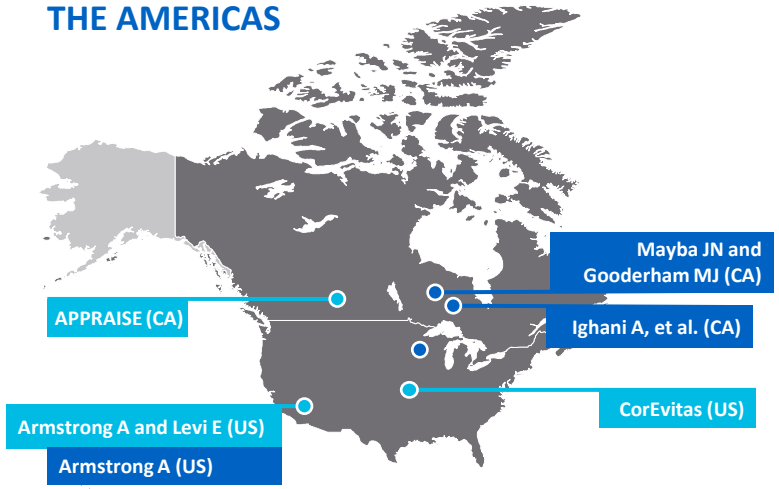
The most common TEAEs (APR vs PBO) were diarrhea (33.0% vs 6.6%), nausea (20.0% vs 5.5%), and headache (20.0% vs 5.5%)

Common TEAEs and the overall safety profile were consistent with the known safety profile of APR

Απρεμιλάστη και Δεδομένα Πραγματικού Κόσμου

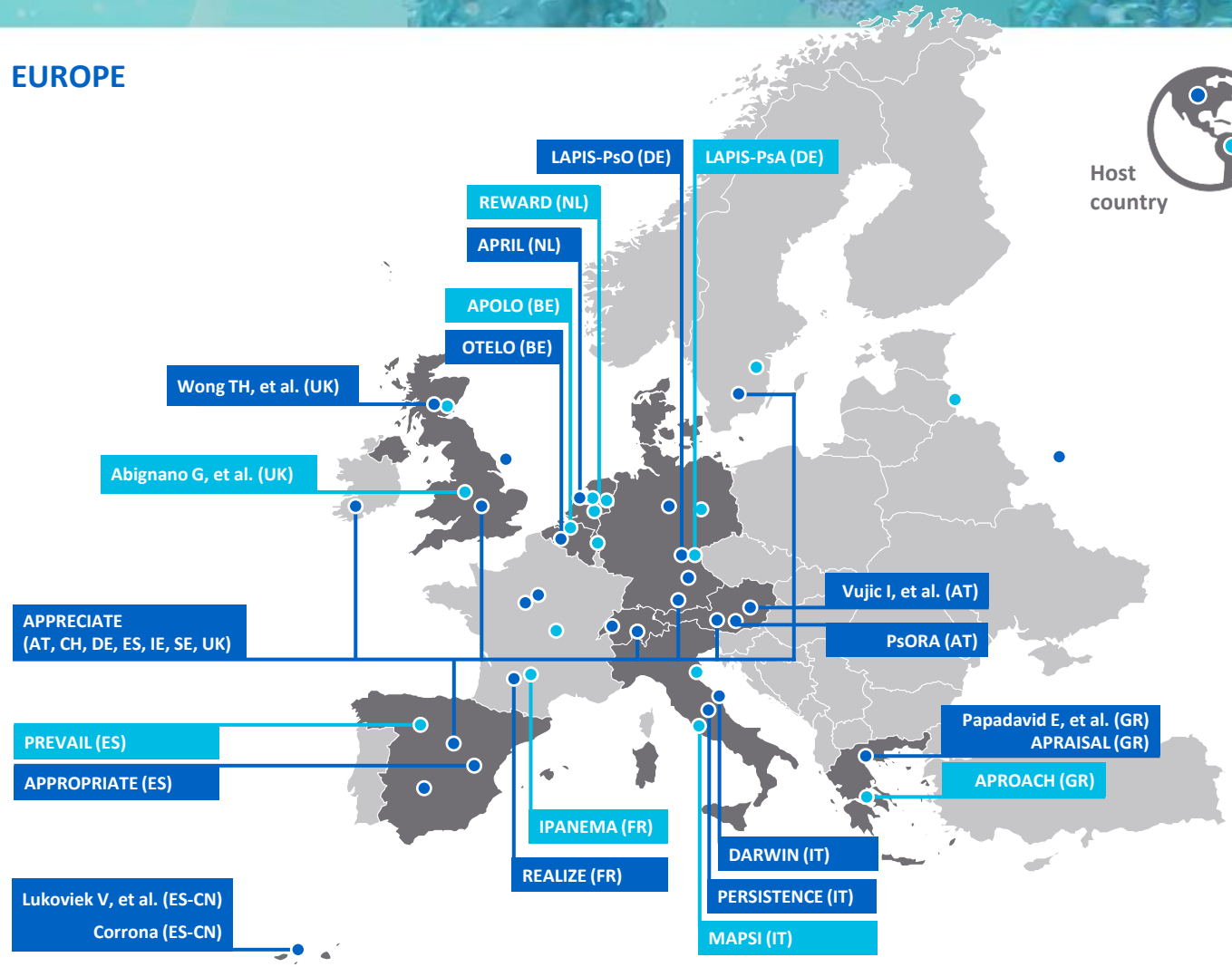
Δεδομένα Πραγματικού κόσμου από διάφορα κέντρα σε όλο τον κόσμο

THE AMERICAS



AUSTRALIA/OCEANIA

EUROPE



APOLO = Study of the Real-life Management of Psoriatic Arthritis Patients Treated With Apremilast in Belgium; APPRAISE = Study to Evaluate the Real-World Effectiveness, Safety and Tolerability of Treatment With Apremilast in Psoriatic Arthritis Patients Followed in Canadian Routine Care; APPRECIATE = Apremilast Clinical Treatment Experience in Psoriasis; APPROPRIATE = Study to Evaluate the Benefits for the Patient Associated With the Treatment of Plaque Psoriasis With Apremilast After Other Systemic Treatment in Conditions of Clinical Practice in Spain; APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; APRIL = Observational Study of Apremilast in Patients With Psoriasis in the Netherlands; APROACH = Apremilast in Psoriatic Arthritis in Real-life Clinical Practice in Greece; AT = Austria; AU = Australia; BE = Belgium; CA = Canada; CH = Switzerland; DARWIN = Study to Describe the Characteristics of Patients Treated With Apremilast for Plaque Psoriasis in Italian Routine Clinical Practice; DE = Germany; ES = Spain; ES-CN = Canary Islands, Spain; FR = France; GR = Greece; IE = Ireland; IT = Italy; LAPIS-PsA = Long-term Documentation on the Use of Apremilast in Patients With Psoriatic Arthritis in Practice Conditions; LAPIS-PsO = Long-term Documentation of the Utilization of Apremilast in Patients With Plaque Psoriasis Under Routine Conditions; MAPSI = Management of Psoriatic Arthritis Across Italy; NE = the Netherlands; OTELO = Study of the Real-life Management of Psoriasis Patients Treated With Apremilast in Belgium; PREVAIL = Study to Evaluate the Use of Apremilast in Patients With Psoriatic Arthritis, Naive to Biological Treatment; PsA = psoriatic arthritis; PsO = psoriasis; PsORA = Psoriasis Registry Austria; REALIZE = Study to Assess Benefits of Apremilast in Patients With Moderate to Severe Chronic Plaque Psoriasis Followed by Dermatologists Under Real Life Settings in France; REWARD = Study of Apremilast Use and Effectiveness in Patients With Psoriatic Arthritis in the Netherlands; RWE = real-world evidence; SE = Sweden; UK = United Kingdom; US = United States.

Μελέτες Παρατήρησης της απρεμιλάστης (συνθήκες πραγματικού κόσμου) σε ασθενείς με ψωρίαση κατά πλάκες

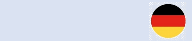
	CorEvitas PsO Registry[1,2]	APPRECIATE[3,4]	LAPIS-PsO[5,6]	APPROPRIATE[7]	APRAISAL[8]
Location(s)					
Study design	Prospective, observational registry study	Retrospective observational cohort study	Prospective, observational cohort study	Prospective, observational cohort study	Prospective, observational cohort study
Study population	Plaque PsO	Plaque PsO	Plaque PsO	Plaque PsO	Plaque PsO
Disease severity	Moderate to severe	Mild, moderate, severe	Moderate to severe	Moderate to severe	Moderate
Sources of data	Provider and patient questionnaires	Medical records, patients, physicians	Patients, physicians	Patient	Patient
Number of study participants	92	480*	389	153	302
Primary outcome measures	Number of patients with AEs or SAEs	PBI score up to 6 ± 1 months†	DLQI score ≤ 5 or DLQI improvement by ≥ 5 points vs baseline at ≈ 4 months	Percentage of subjects achieving PBI ≥ 1	Percentage of patients with moderate plaque PsO treated with apremilast who will achieve a DLQI total score ≤ 5
Primary completion date	2023 (estimated)	2021	2018	2020	2019

*Additional countries and patients were added to APPRECIATE after the initial survey; †The global score index is calculated on a weighted base and ranges from 0 (no benefit) to 4 (maximum benefit), with a PBI value ≥ 1 considered the minimum clinically relevant benefit and PBI ≥ 3 considered a high benefit.
AEs = adverse events; APPRECIATE = Apremilast Clinical Treatment Experience in Psoriasis; APPROPRIATE = Study to Evaluate the Benefits for the Patient Associated With the Treatment of Plaque Psoriasis With Apremilast After Other Systemic Treatment in Conditions of Clinical Practice in Spain; APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; DLQI = Dermatology Life Quality Index; LAPIS-PsO = Long-term Documentation of the Utilization of Apremilast in Patients With Plaque Psoriasis Under Routine Conditions; PBI = patient benefit index; PsO = psoriasis;
SAEs = serious adverse events.

1. Merola JF, et al. Poster presented at: 77th Annual Meeting of the American Academy of Dermatology; March 1-5, 2019; Washington, DC. Poster 9718; 2. ClinicalTrials.gov. clinicaltrials.gov/ct2/show/NCT02707341. Accessed July 14, 2022; 3. Augustin M, et al. *J Eur Acad Dermatol Venereol*. 2021;35:123-134; 4. ClinicalTrials.gov. clinicaltrials.gov/ct2/show/NCT02740218. Accessed July 14, 2022; 5. Reich K, et al. Poster presented at: 77th Annual Meeting of the American Academy of Dermatology; March 1-5, 2019; Washington, DC; Poster 9837; 6. ClinicalTrials.gov. clinicaltrials.gov/ct2/show/NCT02626793. Accessed July 14, 2022; 7. ClinicalTrials.gov. clinicaltrials.gov/ct2/show/NCT03539419. Accessed July 14, 2022; 8. ClinicalTrials.gov. clinicaltrials.gov/ct2/show/NCT03059953. Accessed July 14, 2022.

Δημογραφικά Χαρακτηριστικά

Bold text highlights the greatest variation from RCTs

Key patient demographics	CorEvitas[1,†]	APPRECIATE[2,3]	LAPIS-PSO[4]	APPROPRIATE[5]	APRAISAL[6]
Patients, n[‡]	92	480[‡‡]	253	75	100
Location					
Age, years	**52.7 ± 14.6**	**51.3**	51.1 ±13.3	52.7	49.9
Female, %	43	**46.3**	**46.6**	45.3	29.0
Body weight, kg	(BMI 30.1)	—	(BMI 28.5)	(BMI 28.8)	(Obese 41.0)
Co-therapy with apremilast, n (%)	—	—	—	—	—
Key disease characteristics	**CorEvitas**	**APPRECIATE**	**LAPIS- PSO**	**APPROPRIATE**	**APPRAISAL**
Chronic plaque PsO, %	100	100	100[§]	—	100
PASI, mean	**6.3 ± 5.2**	**11.5**	15.1	8.3	11.7 (median)
BSA, mean %	**13.4**	—	21.8 ±18.6	—	15.0 (median)
DLQI, mean (min–max)	**6.8 ± 5.1**	11.4	14.1 ± 5.9	10.6	12.0 (median)
History of PsA, % or n (%)	**41 (46)**	—	–	—	7 (7.0)
Pruritus VAS, mm or NRS	—	—	56.2 mm ± 26.1	—	—
PGA, 0–4 scale, mean	—	—	3.1	—	—
NAPSI score for target nail, mean**	—	—	4.1 ± 2.3	—	—
Previous therapy experience, n (%)	**CorEvitas**	**APPRECIATE**	**LAPIS- PSO**	**APPROPRIATE**	**APPRAISAL**
Biologic-naive	47 (51)	408 (85)	253 (100)	—	100 (100)
Biologic-exposed	45 (49)	72 (15.0)	0	—	0
Prior systemic[††]/biologic naive	—	50 (10.4)	—	—	67.0 (67.0)
Prior systemic[††]/biologic exposure	—	430 (89.6)	—	75 (100)	—

*RWE patient demographic data presented for illustrative purposes and not intended for comparative efficacy assessment; [†]Formerly known as the Corrona PsA/SpA Registry; [‡]Patients receiving apremilast and n reflects the randomized population; the number of patients in categories below may vary because of the available data; [§]Inclusion criteria based on EU indication; **Among patients with NAPSI ≥ 1; [††]"Systemic" includes systemic therapies or phototherapy; [‡‡]Additional countries and patients were added to APPRECIATE after the initial survey.

APPRECIATE = Apremilast Clinical Treatment Experience in Psoriasis; APPROPRIATE = Study to Evaluate the Benefits for the Patient Associated With the Treatment of Plaque Psoriasis With Apremilast After Other Systemic Treatment in Conditions of Clinical Practice in Spain; APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; BMI = body mass index; BSA = body surface area; DLQI = Dermatology Life Quality Index; EU = European Union; LAPIS-PSO = Long-term Documentation of the Utilization of Apremilast in Patients With Plaque Psoriasis Under Routine Conditions; NAPSI = Nail Psoriasis Severity Index; NRS = numeric rating scale; PGA = physician's global assessment; PsA = psoriatic arthritis; PsO = psoriasis; RCTs = randomized controlled trials; RWSs = real-world studies; RWE = real-world evidence; SpA = spondyloarthritis; VAS = visual analog scale.

1. Merola JF, et al. Poster presented at: 77th Annual Meeting of the American Academy of Dermatology; March 1-5, 2019; Washington, DC. Poster 9718; 2. ClinicalTrials.gov. clinicaltrials.gov/ct2/history/NCT02740218. Accessed August 7, 2020; 3. Augustin M, et al. *J Eur Acad Dermatol Venereol*. 2021;35:123-134; 4. Reich K, et al. Dermatol Ther (Heidelb). 2022;12:203-221; 5. de la Cueva Dobao P, et al. Poster presented at: American Academy of Dermatology Virtual Meeting Experience 2020; June 12-14, 2020. Poster 17817; 6. Ioannides D, et al. *J Eur Acad Dermatol Venereol*. 2021;35:1838-1848.

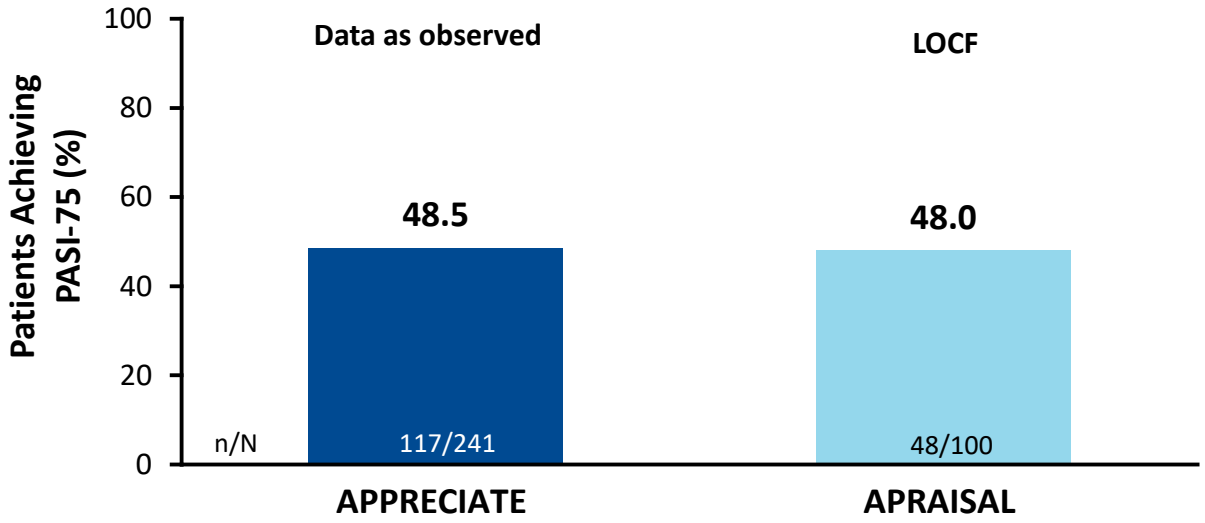
Οι μισοί περίπου ασθενείς με απρεμιλάστη πέτυχαν PASI-75 την εβδομάδα 24 σε συνθήκες πραγματικού κόσμου

- In RWE, almost half of patients receiving apremilast achieved PASI-75 responses at Week 24, including those who were biologic-naive with moderate plaque PsO in the APRAISAL study[1,2]

Baseline Characteristics

	APPRECIATE[1]	APRAISAL[2]
Patient population	Apremilast users of all disease severities	Biologic-naive with moderate Plaque PsO
Age, mean, years	51.3	49.9
Female, %	46.3	29.0
PASI, mean	12.5	11.7
Prior treatment, % Phototherapy Conventional systemics Biologics	56.3 68.3 15.0	11.0 67.0 0

Patients Achieving PASI-75 at Week 24 in RWE[1,2,*]



*This includes patients with PASI-75 response or PASI-50 to -75 response with DLQI ≤ 5; based on an analysis in patients with both PASI and DLQI scores available.
APPRECIATE = Apremilast Clinical Treatment Experience in Psoriasis; APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; DLQI = Dermatology Life Quality Index; LOCF = last observation carried forward; PASI = psoriasis area and severity index; PASI-50 = 50% reduction in psoriasis area and severity index score; PASI-75 = 75% reduction in psoriasis area and severity index score; PsO = psoriasis; RCT = randomized controlled trial; RWE = real-world evidence.

1. Augustin M, et al. *J Eur Acad Dermatol Venereol*. 2021;35:123-134; 2. Ioannides D, et al. *J Eur Acad Dermatol Venereol*. 2021;35:1838-1848.

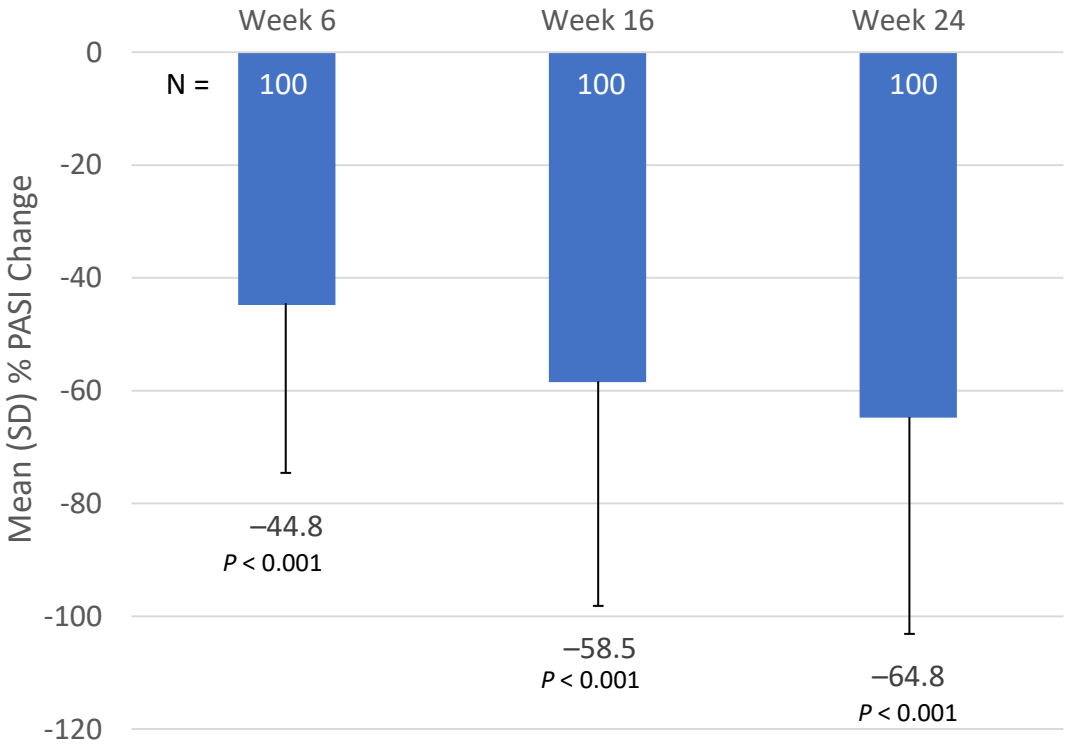
Improvement in PASI Score Was Observed Following Treatment With Apremilast and Was Maintained Through Week 24 in RWE

- Among **biologic-naive** patients with **moderate** PsO, mean improvement in PASI scores from apremilast initiation were maintained through 24 weeks in the APRAISAL study

Baseline Characteristics

	APRAISAL N = 100
Age, mean years	49.9
Female, %	29.0
PASI, median	11.7

Mean PASI Change From Baseline in APRAISAL Study at 24 Weeks* (LOCF)



*Error bars represent SD.
APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; LOCF = last observation carried forward; PASI = psoriasis area and severity index; PsO = psoriasis; RWE = real-world evidence; SD = standard deviation.
Ioannides D, et al. *J Eur Acad Dermatol Venereol*. 2021;35:1838-1848.

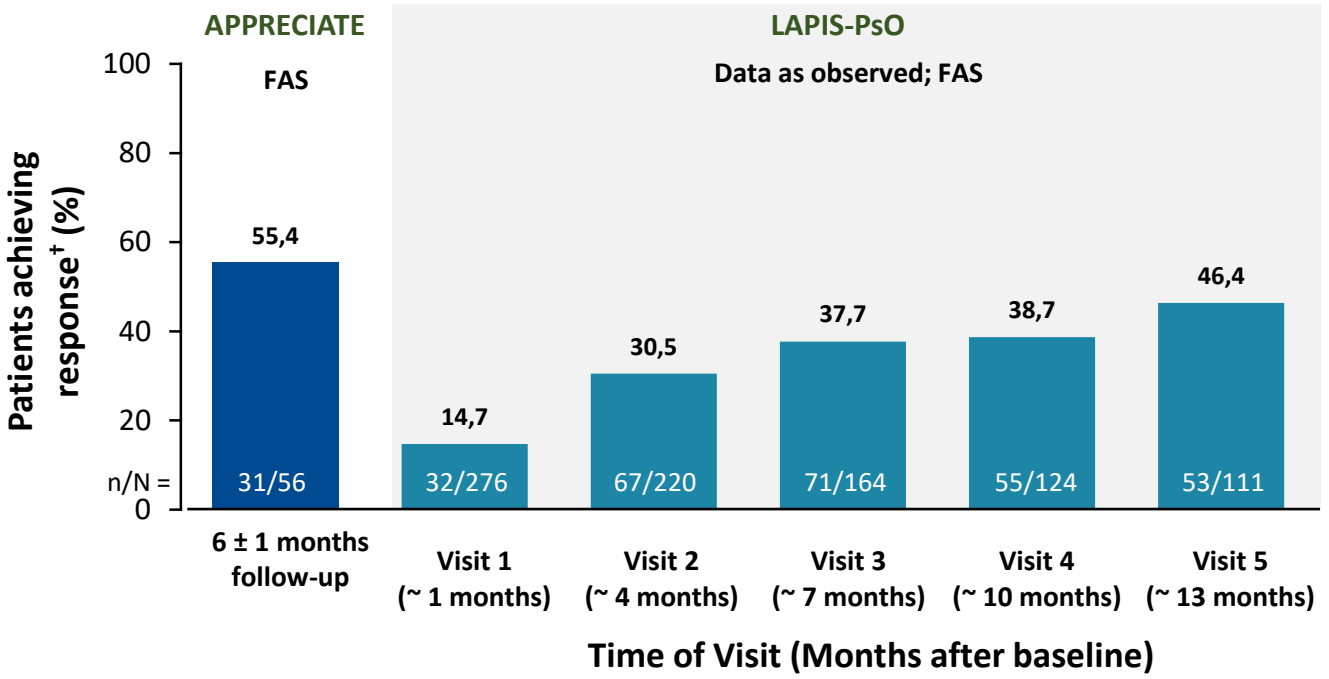
PGA Responses Were Achieved Following Treatment With Apremilast in RWE

- About 50% of patients in both APPRECIATE and LAPIS-PsO achieved PGA responses following apremilast treatment[1,2]

Baseline Characteristics

	APPRECIATE (UK, DE, SE)[1]	LAPIS-PsO[2]
Patient population	Apremilast users of all disease severities	Moderate to severe plaque PsO
Age, years	52.4	51.1
Female, %	57.7	46.6
PGA score, mean	2.8	3.1

Patients Achieving PGA Response* in RWE[1,2]



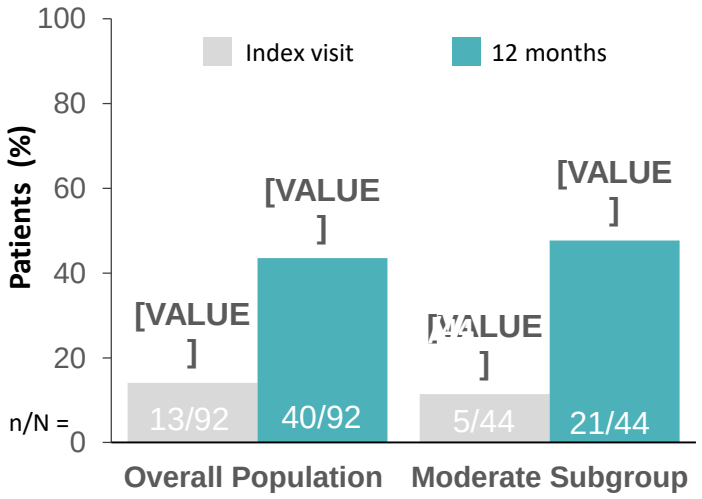
*sPGA response is considered an sPGA score of 0 (clear) or 1 (almost clear) with a ≥ 2-point reduction from baseline.
APPRECIATE = Apremilast Clinical Treatment Experience in Psoriasis; DE = Germany; FAS = full analysis set; LAPIS-PsO = Long-term Documentation of the Utilization of Apremilast in Patients With Plaque Psoriasis Under Routine Conditions; PGA = physician's global assessment; PsO = psoriasis; RWE = real-world evidence; SE = Sweden; sPGA = static physician's global assessment; UK = United Kingdom.
1. Kleyn E, et al. Poster presented at: Psoriasis From Gene to Clinic, 8th International Congress; November 30 to December 2, 2017; London, United Kingdom. Poster FC21; 2. Reich K, et al. Poster presented at: 77th Annual Meeting of the American Academy of Dermatology; March 1-5, 2019; Washington, DC. Poster 9837.

Η αποτελεσματικότητα της απρεμιλάστης σε ασθενείς με μέτρια ψωρίαση είναι παρόμοια στα διάφορα registries

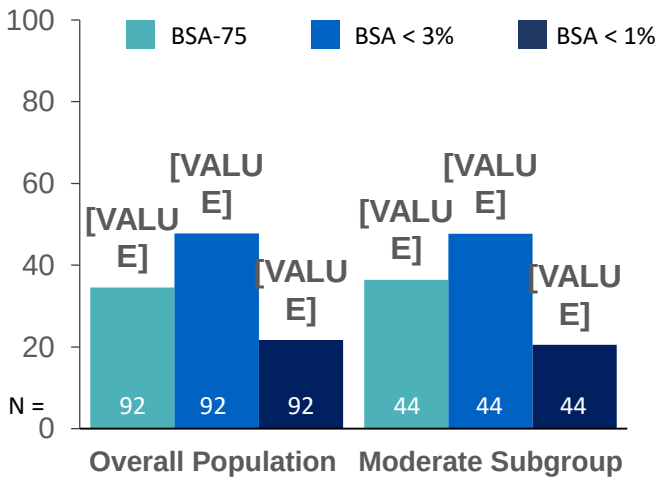
- This descriptive analysis of real-world data from the CorEvitas PsO Registry* suggests that 12-month effectiveness of apremilast in patients with moderate plaque PsO is similar to that among all patients initiating apremilast[1]

Data From the CorEvitas* PsO Registry: 12-month Effectiveness[1]

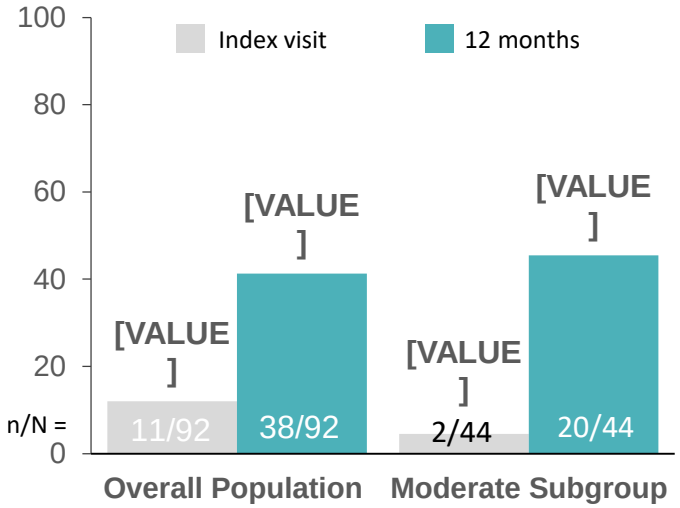
Proportion of Patients With IGA Score of 0 or 1



Proportions of Patients Achieving BSA Treatment Targets at 12 Months†



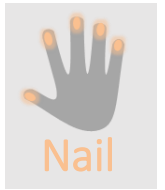
Proportion of Patients Maintaining or Achieving IGAxBSA ≤ 3

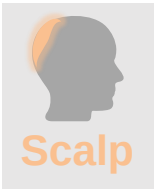


*Formerly known as Corrona PsA/SpA Registry;[2] †Adapted from NPF treatment targets.[1]
BSA = body surface area; BSA-75 = 75% reduction in body surface area; IGA = investigator's global assessment; IGAxBSA = the product of IGA and BSA; NPF = National Psoriasis Foundation; PsA = psoriatic arthritis; PsO = psoriasis; SpA = spondyloarthritis.
1. Adapted from Merola JF, et al. Poster presented at: 77th Annual Meeting of the American Academy of Dermatology; March 1-5, 2019; Washington, DC. Poster 9718; 2. National Psoriasis Foundation. www.psoriasis.org/corevitas-psoriasis-patient-registry/. Accessed July 15, 2022.

Η αποτελεσματικότητα στις ειδικές εντοπίσεις και στον κνησμό

- Among biologic-naive patients with moderate PsO in LAPIS-PsO, patients receiving apremilast achieved scalp, nail, palmoplantar, and itch responses

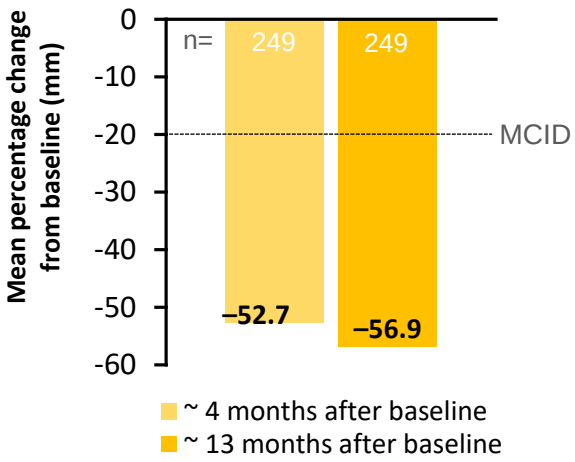




Patients Achieving Responses at Month 4 and Month 13 After Initiating Apremilast in LAPIS-PsO (FAS, LOCF)

	Scalp* ScPGA 0–1	Nail† NAPSI 0	Palmoplantar‡ PPPGA 0–1
~ 4 months after baseline	53.2% (108/203)	26.3% (31/118)	62.7% (42/67)
~ 13 months after baseline	54.7% (111/203)	35.6% (42/118)	71.6% (48/67)

Itch
VAS



*Baseline ScPGA > 0; †Baseline NAPSI > 0; ‡Baseline PPPGA > 0.
FAS = full analysis set; LAPIS-PsO = Long-term Documentation of the Utilization of Apremilast in Patients With Plaque Psoriasis Under Routine Conditions; LOCF = last observation carried forward; MCID = minimal clinically important difference; NAPSI = Nail Psoriasis Severity Index; PPPGA = palmoplantar psoriasis physician's global assessment; PsO = psoriasis; RCT = randomized controlled trial; RWE = real-world evidence;
ScPGA = scalp physician's global assessment; VAS = visual analog scale.
Reich K, et al. *Dermatol Ther (Heidelb)*. 2022;12:203-221.

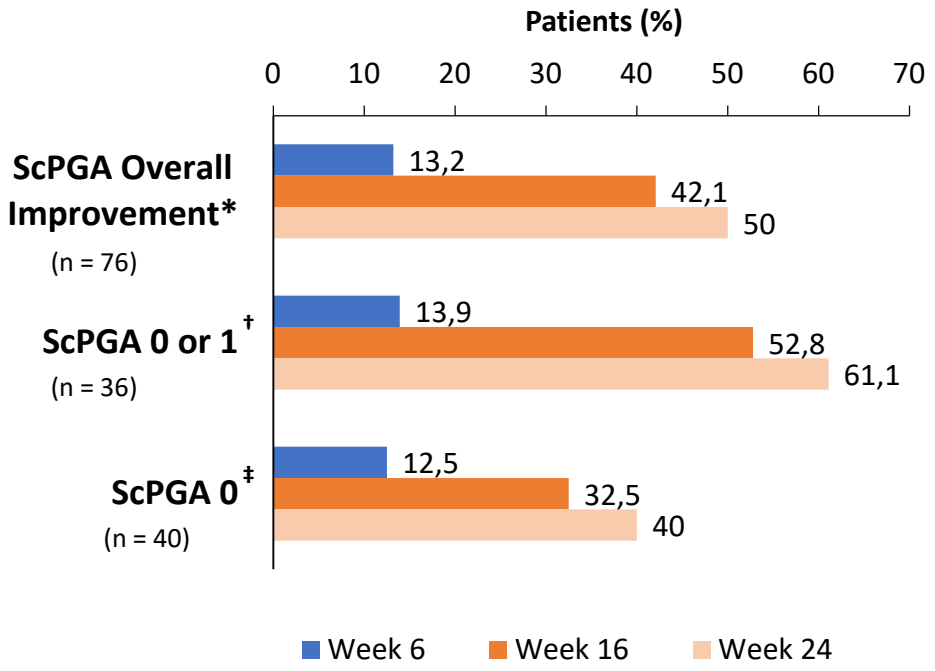
Ελληνικά Δεδομένα: Βελτίωση στην ψωρίαση τριχωτού και στην ψωριασική ονυχία

- Among **biologic-naive** patients with **moderate** PsO, improvements in scalp and palmoplantar PsO were observed at week 24 following treatment with apremilast in APRAISAL

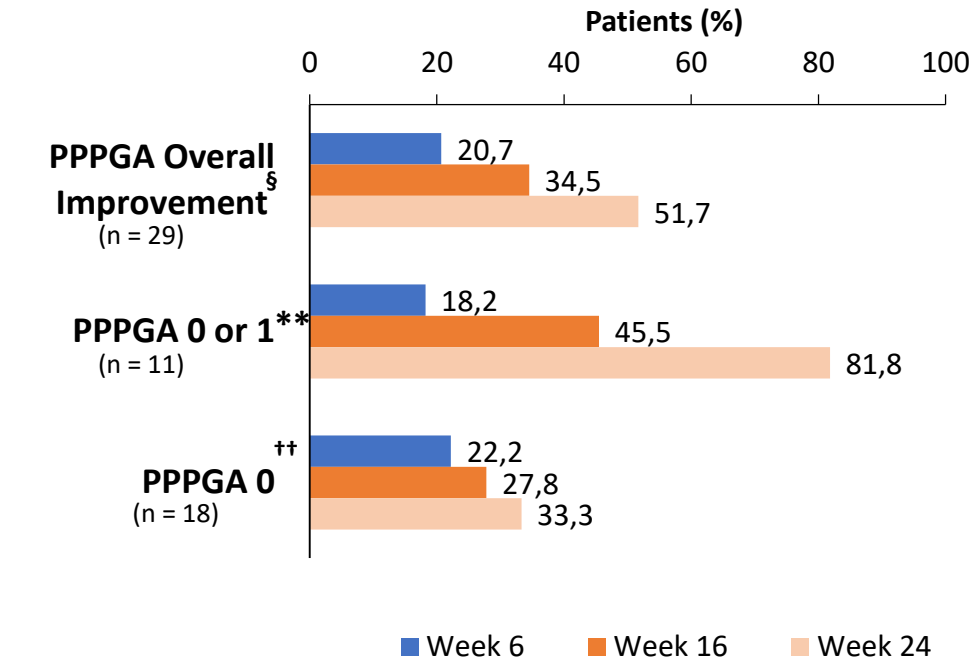
Palms & Soles

Scalp

Scalp PsO Improvement in APRAISAL (LOCF)



Palmoplantar PsO Improvement in APRAISAL (LOCF)



*Patients with baseline ScPGA ≥ 1; †Patients with baseline ScPGA ≥ 3; ‡Patients with baseline ScPGA 1 or 2; §Patients with baseline PPPGA ≥ 1; **Patients with baseline PPPGA ≥3; ††Patients with baseline PPPGA 1 or 2.
APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; LOCF = last observation carried forward; PPPGA = palmoplantar psoriasis physician's global assessment; PsO = psoriasis; RCT = randomized controlled trial; RWE = real-world evidence; ScPGA = scalp physician's global assessment.
Adapted from Ioannides D, et al. *J Eur Acad Dermatol Venereol.* 2021;35:1838-1848.

Βελτίωση στην ψωρίαση τριχωτού, την ψωρίαση παλαμών / πελμάτων και την ψωριασική ονυχία σε όσους δεν πέτυχαν PASI-75

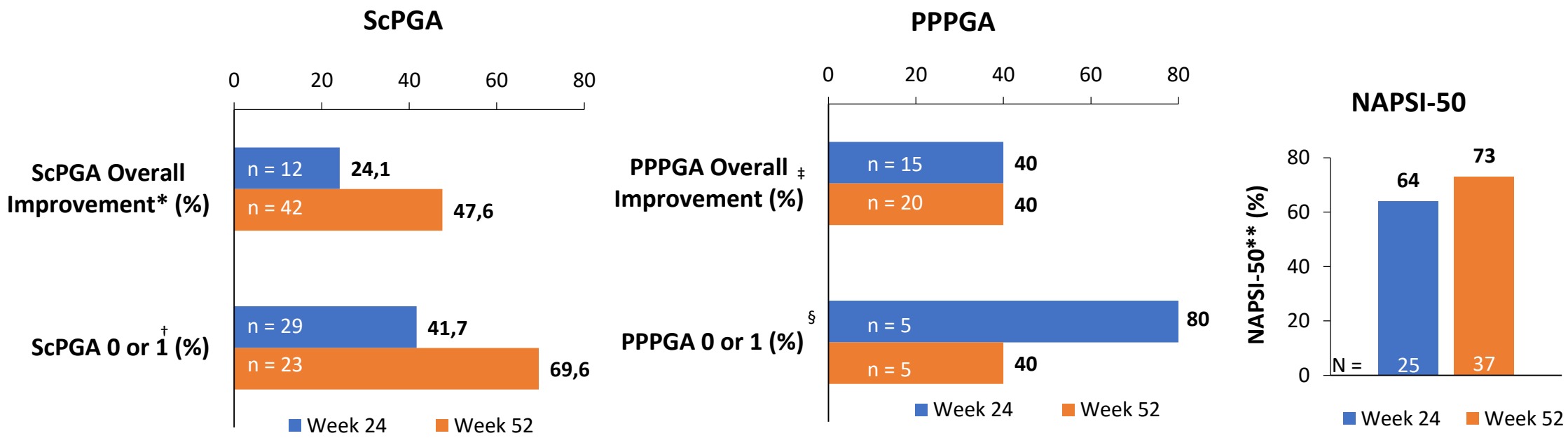
- Among **biologic-naive** patients with **moderate** PsO who did not achieve PASI-75 responses, improvements in scalp PsO, palmoplantar PsO, and nail disease were still observed at Weeks 24 and 52 following treatment with apremilast in APRAISAL

Palms & Soles

Scalp

Nail

Improvement in Scalp, Palmoplantar, and Nail Disease in PASI-75 Nonachievers Receiving Apremilast[1,2]
(Data as Observed)

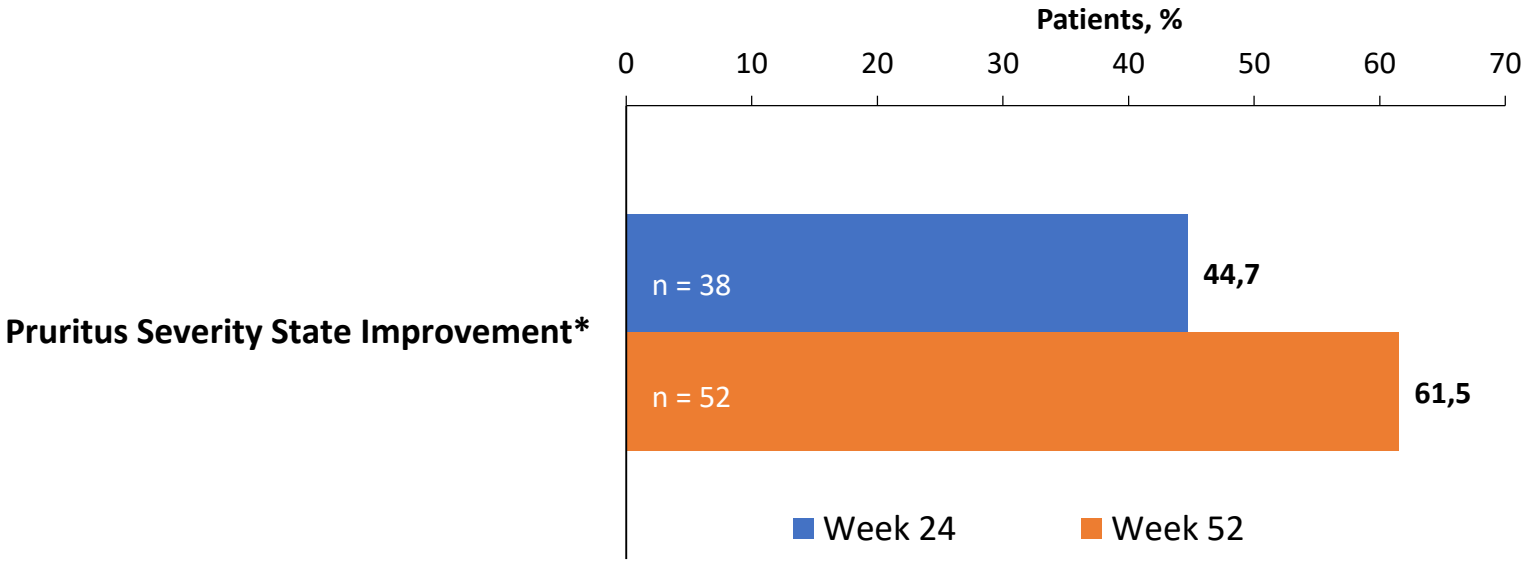


*ScPGA overall improvement was defined as achievement of ScPGA score 0 or 1 among patients with ScPGA score ≥ 3 at baseline or ScPGA score of 0 among patients with ScPGA score 1 or 2 at baseline; †Among patients with baseline ScPGA score ≥ 3; ‡PPPGA overall improvement is defined as achievement of PPPGA score 0 or 1 among patients with PPPGA score ≥ 3 at baseline or PPPGA score of 0 among patients with PPPGA score of 1 or 2 at baseline; §Among patients with baseline PPPGA score ≥ 3; **NAPSI-50 was evaluated among patients with baseline NAPSI ≥ 1.
APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; NAPSI = Nail Psoriasis Severity Index; NAPSI-50 = ≥ 50% reduction from baseline in Nail Psoriasis Severity Index score; PASI-75 = 75% reduction in psoriasis area and severity index score; PPPGA = palmoplantar psoriasis physician's global assessment; PsO = psoriasis; ScPGA = scalp physician's global assessment.
1. Ioannides D, et al. Poster presented at: American Academy of Dermatology Virtual Meeting Experience 2020; June 12-14, 2020. Poster 13643; 2. Papakonstantis M, et al. Poster presented at: 80th Annual Meeting of the American Academy of Dermatology; March 25-29, 2022; Boston, MA. Poster 27480.

Βελτίωση του κνησμού σε όσους δεν πέτυχαν PASI-75

- Among **biologic-naive** patients with **moderate** PsO, improvements in pruritus were observed in PASI-75 non-achievers at Weeks 24 and 52 following treatment with apremilast in APRAISAL[1,2]

Improvement in Pruritus at Week 24 and Week 52 in PASI-75 Nonachievers[1,2,*]
(Data as Observed)



*Pruritus severity was assessed using a 10-cm horizontal pruritus VAS (continuous rating scale), with scores ranging from 0 (no itch) to 10 (worst imaginable itch). Pruritus severity states were defined as follows: 0 points = no pruritus; 1– < 4 points = mild pruritus; 4– < 7 points = moderate pruritus; 7– < 9 points = severe pruritus; and ≥ 9 points = very severe pruritus. Pruritus severity state improvement was defined as improvement by ≥ 1 severity state (eg, from moderate pruritus to mild pruritus). Improvement was analyzed among patients with baseline VAS ≥ 1.
APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; PASI-75 = 75% reduction in psoriasis area and severity index score; PsO = psoriasis; VAS = visual analog scale.
1. Ioannides D, et al. Poster presented at: American Academy of Dermatology Virtual Meeting Experience 2020; June 12-14, 2020. Poster 13643; 2. Papakonstantis M, et al. Poster presented at: 80th Annual Meeting of the American Academy of Dermatology; March 25-29, 2022; Boston, MA. Poster 27480.

Δεδομένα πραγματικού κόσμου για τη βελτίωση της ποιότητας ζωής

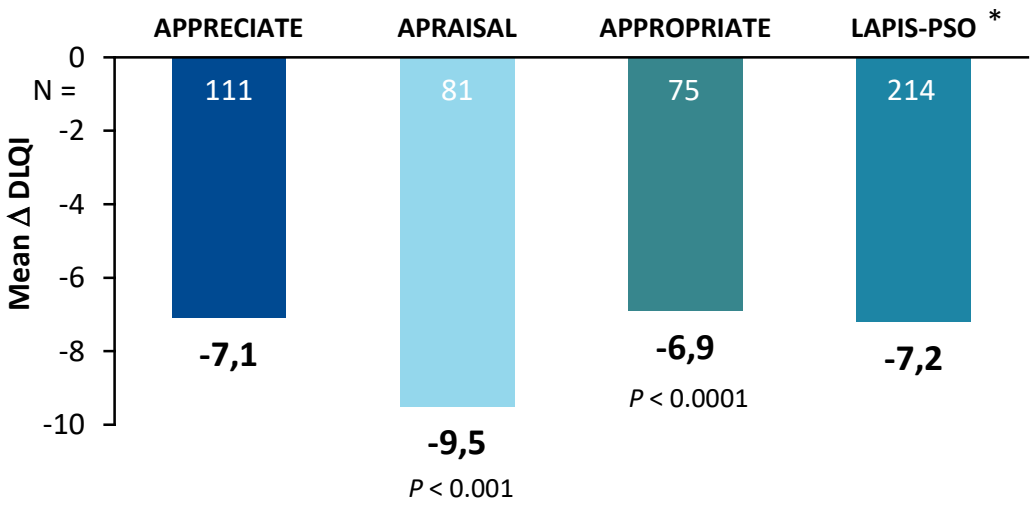
- Improvements in DLQI were observed following treatment with apremilast in:
  - Biologic and/or systemic experienced patients with **moderate to severe PsO** (APPRECIATE)[1]
  - **Biologic naive** patients with **moderate PsO** (APRAISAL) **moderate to severe** PsO (APPROPRIATE and LAPIS-PsO)[1,2]

DLQI

Baseline Characteristics

	APPRECIATE[1]	APRAISAL[2]	APPROPRIATE[3]	LAPIS-PsO[4,*]
Patient population	Apremilast users of all disease severities	Biologic-naive with moderate plaque PsO	First time apremilast users with moderate to severe plaque PsO	Moderate to severe plaque PsO
Age, years	51.3	49.9	52.7	51.1
Female, %	46.3	29.0	45.3	46.6
DLQI, mean	12.8	13.6	10.6	14.1

Mean Change in DLQI From Baseline at ~Week 24[1–4]
(Data as Observed)



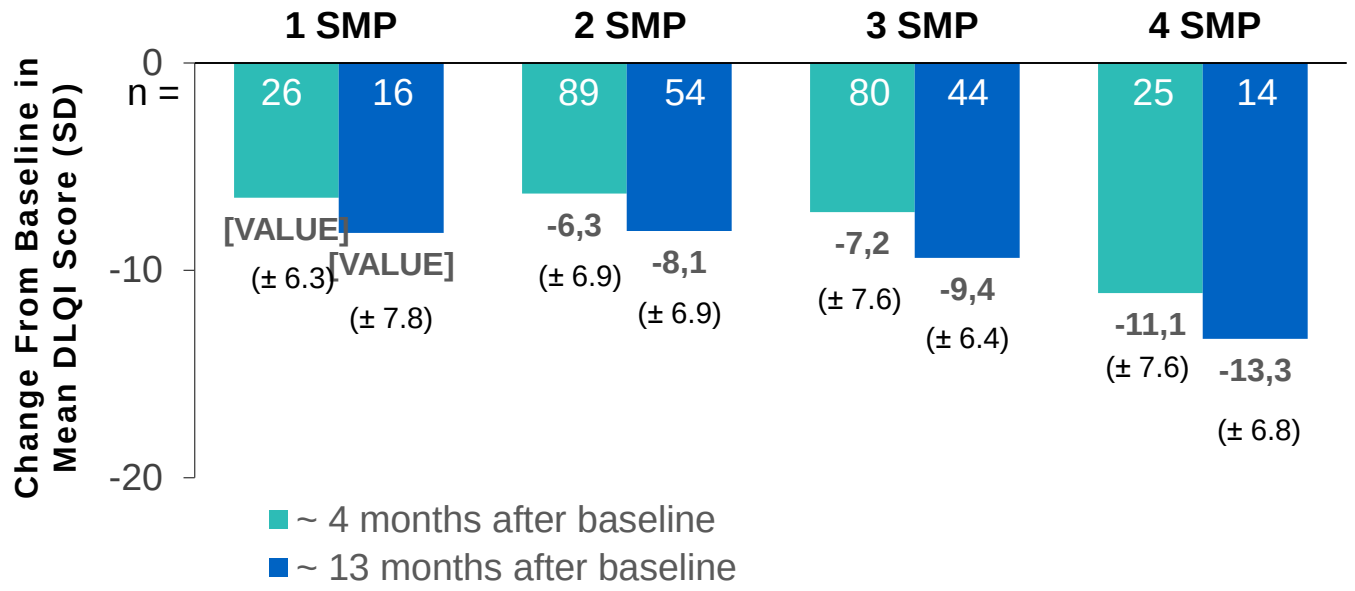
*Change in DLQI from LAPIS-PsO was assessed at about 4 months postbaseline.
APPRECIATE = Apremilast Clinical Treatment Experience in Psoriasis; APPROPRIATE = Study to Evaluate the Benefits for the Patient Associated With the Treatment of Plaque Psoriasis With Apremilast After Other Systemic Treatment in Conditions of Clinical Practice in Spain; APRAISAL = Apremilast in Moderate Psoriasis in Real Life Clinical Practice; DLQI = Dermatology Life Quality Index;
LAPIS-PsO = Long-term Documentation of the Utilization of Apremilast in Patients With Plaque Psoriasis Under Routine Conditions; PsO = psoriasis; RCT = randomized controlled trial; RWE = real-world evidence.
1. Augustin M, et al. *J Eur Acad Dermatol Venereol.* 2021;35:123-134; 2. Ioannides D, et al. *J Eur Acad Dermatol Venereol.* 2021;35:1838-1848; 3. de la Cueva Dobao P, et al. Poster presented at:
American Academy of Dermatology Virtual Meeting Experience 2020; June 12-14, 2020. Poster 17817; 4. Reich K, et al. Poster presented at: 77th Annual Meeting of the American Academy of Dermatology; March 1-5, 2019; Washington, DC. Poster 9837.

DLQI Improved the Most in Patients With Higher Numbers of PsO Manifestations and Symptoms

- Among **biologic-naive** patients with **moderate to severe PsO**, patients with higher numbers of manifestations in special areas and/or special symptoms at baseline experienced greater improvements in DLQI with apremilast than patients with fewer special areas and/or symptoms in the LAPIS-PsO Study

DLQI

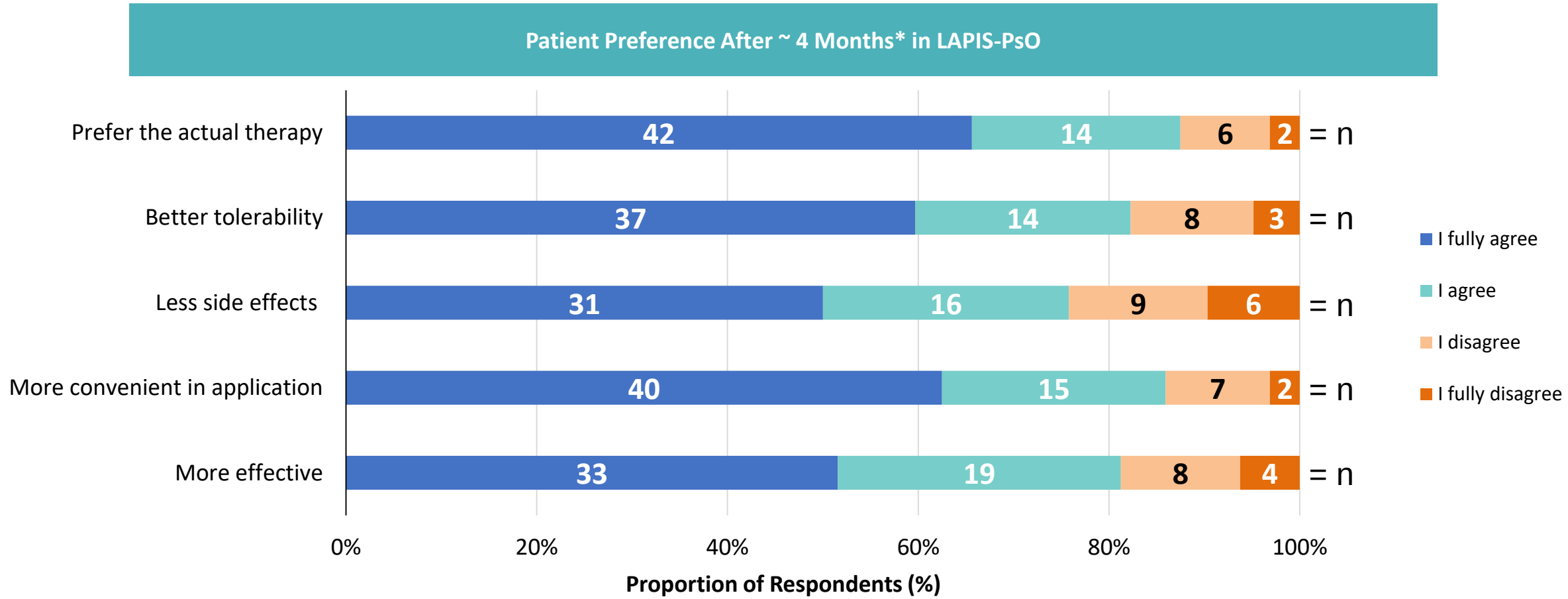
Mean Change in DLQI Score From Baseline in LAPIS-PsO*,†



*SMP included itch, scalp involvement, nail involvement, and palmoplantar involvement; †Visit 2 was ~ 4 months after baseline visit and visit 5 was ~ 52 weeks after baseline visit.
DLQI = Dermatology Life Quality Index; LAPIS-PsO = Long-term Documentation of the Utilization of Apremilast in Patients With Plaque Psoriasis Under Routine Conditions; PsO = psoriasis; SD = standard deviation; SMP = specific manifestations and symptoms of psoriasis.
Reich K, et al. Poster presented at: 29th Congress of the European Academy of Dermatology and Venereology; October 29-31, 2020.

Προτίμηση σε σχέση με προηγούμενες θεραπείες

- Among **biologic-naive** patients with **moderate to severe PsO** initiating apremilast, the majority of patients preferred apremilast over their previous systemic therapy



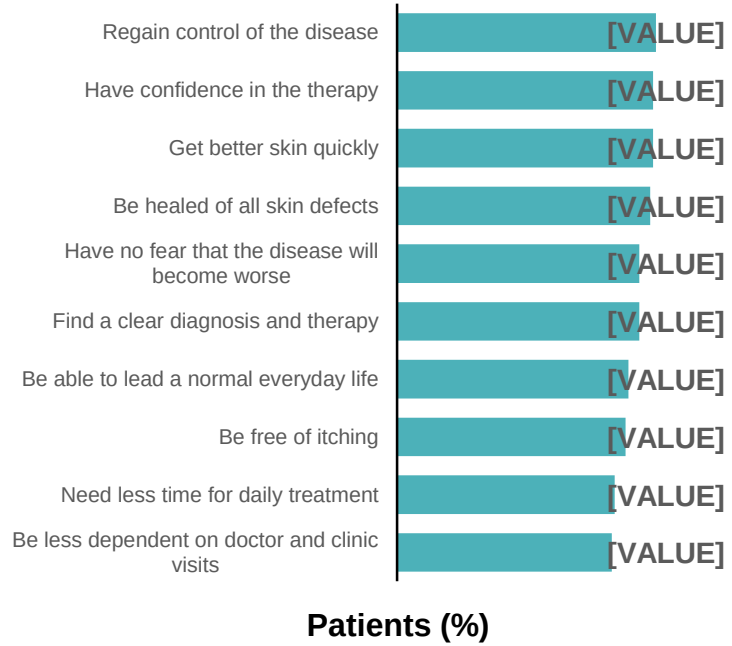
*Q1: In comparison to previous, systemic therapies, the actual therapy is more effective. Q2: In comparison to previous, systemic therapies, the actual therapy is more convenient in application.
Q3: In comparison to previous, systemic therapies, the actual therapy has fewer side effects; Q4: In comparison to previous, systemic therapies, the actual therapy is better tolerated. Q5: In comparison to previous, systemic therapies, I prefer the actual therapy.
LAPIS-PsO = Long-term Documentation of the Utilization of Apremilast in Patients With Plaque Psoriasis Under Routine Conditions; PsO = psoriasis.
Adapted from Reich K, et al. Oral abstract presented at: 75th Annual Meeting of the American Academy of Dermatology; March 3-7, 2017; Orlando, FL. Oral abstract 5137.

Απρεμιλάστη και ανάγκες των ασθενών

- The majority of patients achieved benefit in the domains identified as their greatest needs with apremilast treatment

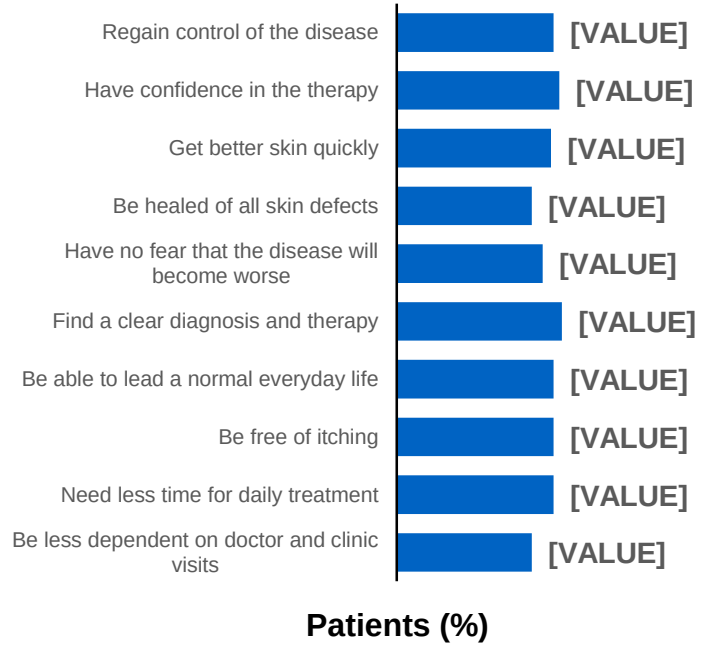
PNQ*

Top 10 Needs of Patients Identified by PNQ†

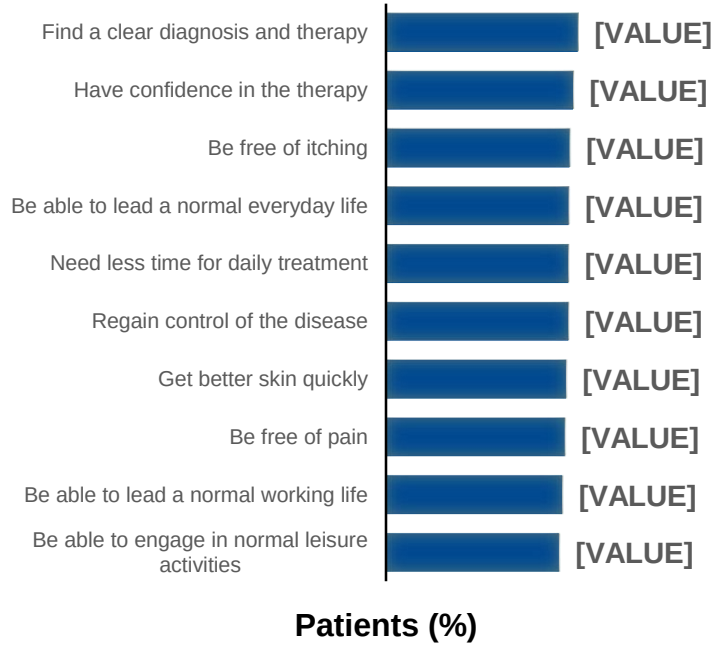


PBQ*

Benefit of Apremilast for Top 10 Needs Identified by PNQ‡



Top 10 Benefits Overall of Apremilast Identified by PBQ‡



*Patients enrolled in this study completed the PBI for skin diseases, which consists of PNQ and PBQ and was conducted 6 ± 1 months after apremilast initiation. Although the PNQ and PBQ are typically completed before and after treatment, both the PNQ and PBQ were completed by the patient at study inclusion (ie, 6 ± 1 months after apremilast initiation) owing to the retrospective study design of APPRECIATE; †Top 10 needs of patients, as identified in the PNQ. FAS, N = 480; the number of patients with data available may vary. Possible answers include 0 = not at all/does not apply to me, 1 = somewhat, 2 = moderately, 3 = quite, and 4 = very. The top 10 needs of patients (according to those who answered that the need is "quite" or "very" important) out of 25 needs on the PNQ are presented. Percentage calculation excludes missing answers; ‡Apremilast benefits were determined by the PNQ. FAS, N = 480; the number of patients with data available may vary. Patients responded to the prompt: "Apremilast has helped me to…" with possible answers: 0 = not at all/does not apply to me, 1 = somewhat, 2 = moderately, 3 = quite, and 4 = very. The benefits are defined as positive responses, including answers of "quite" or "very." Percentage calculation excluded missing and "does not apply to me" answers.
APPRECIATE = Apremilast Clinical Treatment Experience in Psoriasis; APR = apremilast; FAS = full analysis set; PBI = patient benefit index; PBQ = patient benefit questionnaire; PNQ = patient needs questionnaire;
PsO = psoriasis.
Adapted from Klein TM, et al. *Dermatol Ther (Heidelb)*. 2022;12:81-95.

Προφίλ ασφάλειας

- In a long-term follow-up of patients in phase 3 trials (ESTEEM 1 and 2 and PALACE 1–4), apremilast demonstrated an acceptable safety profile and was generally well tolerated for up to 5 years in patients with moderate to severe plaque PsO and patients with active PsA
- During the apremilast-exposure period, incidence of AEs, severe AEs, SAEs, and AEs leading to withdrawal did not increase with increasing exposure
- Most AEs were predominantly mild or moderate in severity and did not lead to discontinuations during the placebo-controlled and apremilast-exposure periods

Overview of AEs in the Pooled Population

	Placebo-Controlled Period* Weeks 0–16 or 24				Apremilast-Exposure Period† Weeks 0 to ≥ 260	
	Placebo (n = 1,089*) 344.3 pt-yrs		Apremilast (n = 1,504*) 520.1 pt-yrs		Apremilast (n = 2,157*) 5,163.1 pt-yrs	
Patients	n (%)	EAIR/ 100 pt-yrs	n (%)	EAIR/ 100 pt-yrs	n (%)	EAIR/ 100 pt-yrs
≥ 1 AE	553 (50.8)	242.8	980 (65.2)	378.8	1824 (84.6)	155.2
≥ 1 severe AE	40 (3.7)	11.8	66 (4.4)	12.9	256 (11.9)	5.3
≥ 1 SAE	35 (3.2)	10.3	37 (2.5)	7.2	298 (13.8)	6.3
AE leading to drug withdrawal	43 (3.9)	12.6	87 (5.8)	16.9	259 (12.0)	5.0
AE leading to death	1 (0.1)	0.3	1 (0.1)	0.2	8 (0.4)	0.2

*Patients as initially randomized at week 0 who received ≥ 1 dose of study medication during the placebo-controlled period (0 to 16 or 24 weeks); †The apremilast-exposure period (0 to ≥ 260 weeks) includes all patients who received apremilast regardless of when apremilast exposure started (week 0, week 16, or week 24). Apremilast exposure is based on each patient's total exposure to apremilast, defined as the time interval between the dates of the first and last doses of apremilast, through December 2017.
AEs = adverse events; EAIR = exposure-adjusted incidence rate; ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; PALACE = Psoriatic Arthritis Long-term Assessment of Clinical Efficacy;
PsA = psoriatic arthritis; PsO = psoriasis; pt-yrs = patient-years; SAEs = serious adverse events.
Callis-Duffin K, et al. Poster presented at: American Academy of Dermatology Virtual Meeting Experience 2020; June 12–14, 2020. Poster 15114.

The Incidence Rates of the Most Common AEs Did Not Increase With Increased Exposure to Apremilast Through 5 Years

- The EAIR/100 patient-years for the most commonly reported AEs did not increase with increased exposure to apremilast
- During the apremilast-exposure period, most cases of diarrhea and nausea were mild or moderate in severity, occurred during the first 2 weeks of apremilast exposure, and generally resolved in 1 month; low rates of discontinuation of apremilast because of diarrhea (1.5%) and nausea (1.7%) were observed

Most Commonly Reported AEs in the Pooled Population

	Placebo-Controlled Period* Weeks 0–16 or 24				Apremilast-Exposure Period† Weeks 0 to ≥ 260	
	Placebo (n = 1,089) 344.3 pt-yrs		Apremilast (n = 1,504) 520.1 pt-yrs		Apremilast (n = 2,157) 5,163.1 pt-yrs	
Most Common ARs (≥ 5%)‡	n (%)	EAIR/ 100 pt-yrs	n (%)	EAIR/ 100 pt-yrs	n (%)	EAIR/ 100 pt-yrs
Nausea	56 (5.1)	16.8	246 (16.4)	54.4	361 (16.7)	8.1
Diarrhea	45 (4.1)	13.5	234 (15.6)	51.7	372 (17.2)	8.4
Headache	41 (3.8)	12.2	119 (7.9)	24.4	218 (10.1)	4.6
URTI	46 (4.2)	13.6	107 (7.1)	21.3	376 (17.4)	8.5
Nasopharyngitis	47 (4.3)	13.9	85 (5.7)	16.8	320 (14.8)	7.1

*Patients as initially randomized at week 0 who received ≥ 1 dose of study medication during the placebo-controlled period (0 to 16 or 24 weeks); †The apremilast-exposure period (0 to ≥ 260 weeks) includes all patients who received apremilast regardless of when apremilast exposure started (week 0, week 16, or week 24). Apremilast exposure is based on each patient's total exposure to apremilast, defined as the time interval between the dates of the first and last doses of apremilast, through December 2017; ‡ARs occurring in ≥ 5% of patients in any treatment group during the placebo-controlled period.

AEs = adverse events; ARs = adverse reactions; EAIR = exposure-adjusted incidence rate; ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; PALACE = Psoriatic Arthritis Long-term Assessment of Clinical Efficacy; PsA = psoriatic arthritis; PsO = psoriasis; pt-yrs = patient-years; URTI = upper respiratory tract infection.

Callis-Duffin K, et al. Poster presented at: American Academy of Dermatology Virtual Meeting Experience 2020; June 12–14, 2020. Poster 15114.

Δεν απαιτείται εργαστηριακή παρακολούθηση

- Overall, markedly abnormal laboratory parameters were infrequent, transient, and comparable between the placebo and apremilast groups during the placebo-controlled period and EAIRs remained low during the apremilast-exposure period

Select Marked Laboratory Abnormalities in the Pooled Population*

	Placebo-Controlled Period Weeks 0–16 or 24				Apremilast-Exposure Period Weeks 0 to ≥ 260	
	Placebo (n = 1,089)* 344.4 pt-yrs		Apremilast (n = 1,504)* 520.1 pt-yrs		Apremilast (n = 2,157)† 5,163.1 pt-yrs	
Laboratory Parameter*	n/m (%)	EAIR/ 100 pt-yrs	n/m (%)	EAIR/ 100 pt-yrs	n/m (%)	EAIR/ 100 pt-yrs
ALT > 3 × ULN, U/L	4/1,070 (0.4)	1.2	9/1,481 (0.6)	1.7	38/2,127 (1.8)	0.7
AST > 3 × ULN, U/L	7/1,069 (0.7)	2.0	5/1,480 (0.3)	1.0	39/2,126 (1.8)	0.8
Creatinine > 1.7 × ULN, µmol/L	1/1,070 (0.1)	0.3	2/1,481 (0.1)	0.4	18/2,127 (0.8)	0.4
Bilirubin >1.8 × ULN, µmol/L	1/1,070 (0.1)	0.3	4/1,481 (0.3)	0.8	14/2,127 (0.7)	0.3
Hemoglobin A_{1C} > 9%	4/846 (0.5)	1.4	4/1,255 (0.3)	0.9	23/1,893 (1.2)	0.5
Cholesterol > 7.8 mmol/L†	26/1,043 (2.5)	7.8	25/1,439 (1.7)	4.9	84/2,090 (4.0)	1.7
Neutrophils < 1.0 × 10^9/L	3/1,067 (0.3)	0.9	2/1,474 (0.1)	0.4	17/2,123 (0.8)	0.3
Lymphocytes < 0.8 × 10^9/L	32/1,067 (3.0)	9.5	27/1,474 (1.8)	5.3	111/2,123 (5.2)	2.2
Leukocytes < 1.5 × 10^9/L	0/1,068 (0.0)	0.0	0/1,476 (0.0)	0.0	0/2,125 (0.0)	0.0
Platelets < 75 × 10^9/L	0/1,066	0.0	0/1,475 (0.0)	0.0	3/2,125 (0.1)	0.1

*Patients as initially randomized at week 0 who received ≥ 1 dose of study medication during the placebo-controlled period (0 to 16 or 24 weeks); †The apremilast-exposure period (0 to ≥ 260 weeks) includes all patients who received apremilast regardless of when apremilast exposure started (week 0, week 16, or week 24). Apremilast exposure is based on each patient's total exposure to apremilast, defined as the time interval between the dates of the first and last doses of apremilast, through December 2017.
ALT = alanine aminotransferase; AST = aspartate aminotransferase; EAIRs = exposure-adjusted incidence rates; ESTEEM = Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; PALACE = Psoriatic Arthritis Long-term Assessment of Clinical Efficacy; PsA = psoriatic arthritis; PsO = psoriasis; pt-yrs = patient-years; ULN = upper limit of normal.
Callis-Duffin K, et al. Poster presented at: American Academy of Dermatology Virtual Meeting Experience 2020; June 12-14, 2020. Poster 15114.

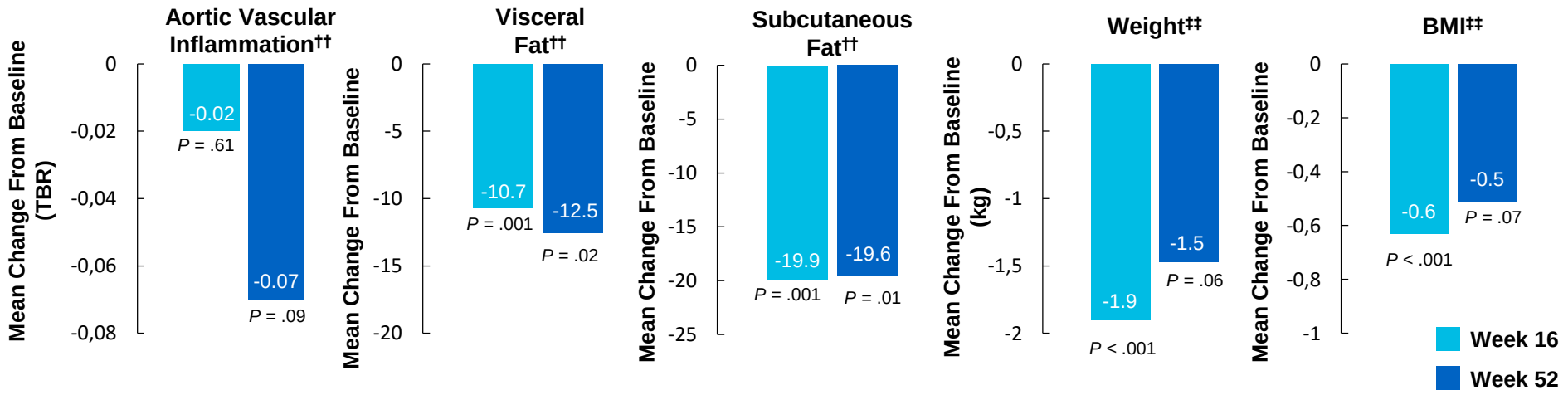
Apremilast Had a Neutral Association With Aortic Vascular Inflammation and Was Associated With Reductions in Visceral and Subcutaneous Fat

- This phase 4, open-label, nonrandomized clinical trial conducted in the US included 70 adult patients diagnosed with moderate to severe chronic plaque PsO*
- Patients could not have received biologics within 90 days of baseline†, oral PsO therapies within 30 days‡, or UV-B phototherapy/laser therapy or topical prescription PsO treatment within 14 days of baseline§
- Apremilast had a neutral association with aortic vascular inflammation and was associated with weight loss
- Patients experienced a 5%–6% reduction in SC and visceral fat at 16 weeks of treatment, which was maintained through 52 weeks of treatment
  - Reduction in visceral fat, a metabolically active fat that promotes metabolic and atherosclerotic disease

Baseline Characteristics

Age in years, mean (SD)	47.5 (14.6)
Male, n (%)	54 (77.1)
Race, n (%)	
Black or African American	4 (5.7)
White	58 (82.9)

Changes in Aortic Vascular Inflammation and Adiposity**



*The VIP-A clinical trial included adult patients (≥ 18 years) who had a diagnosis of moderate to severe chronic plaque PsO (≥ 6 months before randomization), ≥ 10% BSA involvement, PASI score ≥ 12 at baseline, stable disease for > 2 months before screening and baseline, and were in general good health. †Patients could not have received ustekinumab within 180 days of baseline. ‡Patients could not have received oral PsO therapies or investigational agents within 30 days or 5 half-lives, whichever was longer, of baseline. §With the exception of hydrocortisone, 2.5%, for the face and intertriginous areas. **_P_ value is from a paired _t_ test. ††Included patients with PET/CT data at Week 16 (N = 57) and Week 52 (N = 38). ‡‡Included patients with weight and BMI data at Week 16 (N = 60) and Week 52 (N = 39).

BSA = body surface area; BMI = body mass index; PASI = Psoriasis Area and Severity Index; PET/CT = positron emission tomography/computed tomography; PsO = psoriasis; SC = subcutaneous; SD = standard deviation; TBR = target-to-background ratio; US = United States; UV-B = ultraviolet B; VIP-A = Vascular Inflammation in Psoriasis- Apremilast.

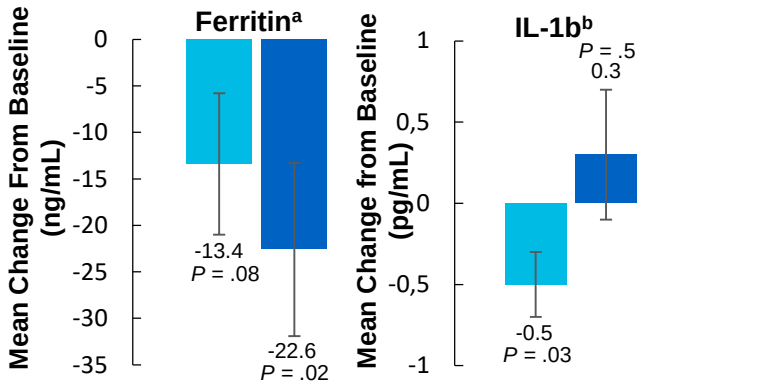
Gelfand JM, et al. *JAMA Dermatol*. Published online September 21, 2022.

Apremilast Had Potentially Beneficial Effects Across Most Markers of Inflammation, Adipose Dysfunction, and Metabolism

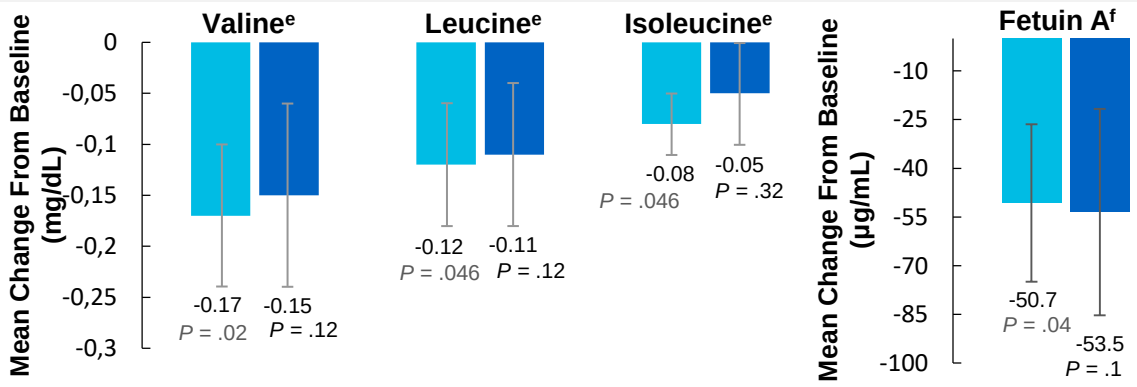
- Apremilast was associated with reductions versus baseline in IL-1b, fetuin A, BCAA, valine, leucine, and isoleucine at Week 16 and ferritin, β-OHB, acetone, and ketone bodies at Week 52
- There was an increase in levels of ApoA1 but a reduction in CEC at Week 52

Changes in Blood-Based Biomarkers of Inflammation and Lipoprotein Characterization*

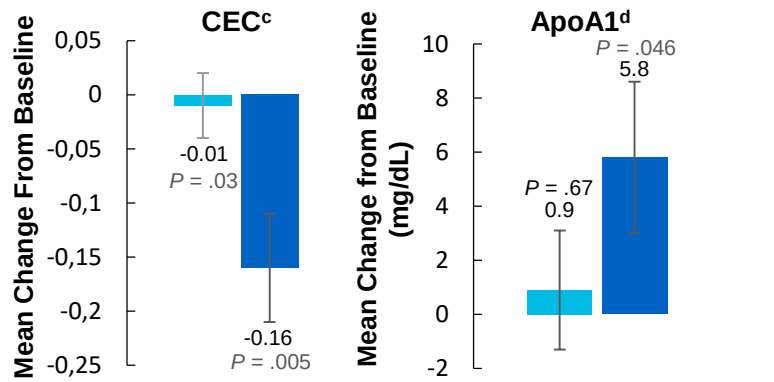
Markers of Inflammation

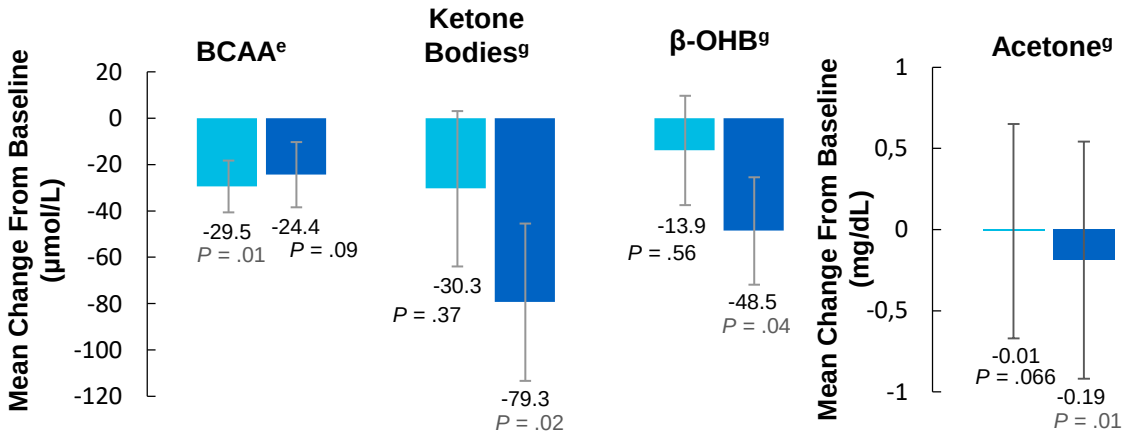


Markers of Adipose Dysfunction and General Metabolism



Lipid Function & Metabolism





Week 16†
Week 52‡

Clinical Association

[a]Acute phase reactant and marker of inflammation and cellular damage

[b]Pro-inflammatory cytokine causally linked to CVD

[c]Reduction in CEC could be negatively associated with atheroprotective effects of HDL-C

[d]Considered atheroprotective

[e]Incident CV risk

[f]Diabetes risk

[g]Implicated in CVD, including HF

*P value is from a paired *t* test. †N = 57-59. ‡N = 37-38.

ApoA1 = apolipoprotein A-1; BCAA = branched-chain amino acids; β-OHB = β-hydroxybutyrate; CEC = cholesterol efflux capacity; CV = cardiovascular; CVD = cardiovascular disease; HDL-C = high-density lipoprotein cholesterol; HF = heart failure; IL = interleukin; PsO = psoriasis; VIP-A = Vascular Inflammation in Psoriasis- Apremilast.

Gelfand JM, et al. *JAMA Dermatol*. Published online September 21, 2022.

Συμπερασματικά από τα δεδομένα πραγματικού κόσμου για την απρεμιλάστη

Improvements in Skin-related Scores

- The percentage of patients achieving **PASI-75** in a real-word setting ranged from ~40%–70%, and effectiveness of apremilast in patients with moderate plaque PsO was similar to that of all patients initiating apremilast[1–3]

Improvements in bothersome manifestations of PsO

- Apremilast was also **effective in improving specific or bothersome manifestations of PsO** such as scalp, nail, and palmoplantar involvement and itch[4–7]

Clinically meaningful PROs

QoL

- Patients who received apremilast in clinical practice showed substantial improvements in **DLQI**[1,6,8]

Patient Satisfaction

- Most patients agreed that apremilast was able to treat symptoms of PsO, and 50-75% of patients achieved a **clinically meaningful PBI score**[2,6,8,9]

Real-World Safety and Efficacy

- RWE supports a consistent safety and tolerability profile of apremilast[10,11]

DLQI = Dermatology Life Quality Index; PASI-75 = 75% reduction in psoriasis area and severity index score; PBI = patient benefit index; PROs = patient-reported outcomes; PsO = psoriasis; QoL = quality of life; RWE = real-world evidence.

1.Kleyn E, et al. Psoriasis From Gene to Clinic, 8th International Congress; November 30 to December 2, 2017; London, United Kingdom. Poster FC21; 2. Wong TH, et al. *Clin Exp Dermatol*. 2017;42:675-676; 3. Merola JF, et al. Poster presented at: 77th Annual Meeting of the American Academy of Dermatology; March 1-5, 2019; Washington, DC. Poster 9718; 4. Papadavid E, et al. *J Eur Acad Dermatol Venereol*. 2018;32:1173-1179; 5. Vujic I, et al. *J Eur Acad Dermatol Venereol.* 2018;32:254-259; 6. Ioannides D, et al. American Academy of Dermatology Virtual Meeting Experience 2020; June 12-14, 2020. Poster 13643; 7. Reich K, et al. Poster presented at: 50th German Dermatological Society Conference; May 1-4, 2019; Berlin, Germany. Poster P115; 8. Augustin M, et al. *J Eur Acad Dermatol Venereol*. 2021;35:123-134; 9. Reich K, et al. Poster presented at: 75th Annual Meeting of the American Academy of Dermatology; March 3-7, 2017; Orlando, FL. Poster 5137; 10. Reich K, et al. *Dermatol Ther (Heidelb).* 2022;12:203-221; 11. Ioannides D, et al. *J Eur Acad Dermatol Venereol*. 2021;35:1838-1848.

Ασφάλεια Απρεμιλάστης
μέσα από τις Ευρωπαϊκές κατευθυντήριες οδηγίες

DOI: 10.1111/jdv.16926 JEADV

GUIDELINES

EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris – Part 2: specific clinical and comorbid situations

Heart disease: How should psoriasis patients with ischaemic heart disease and/or congestive heart failure be managed?

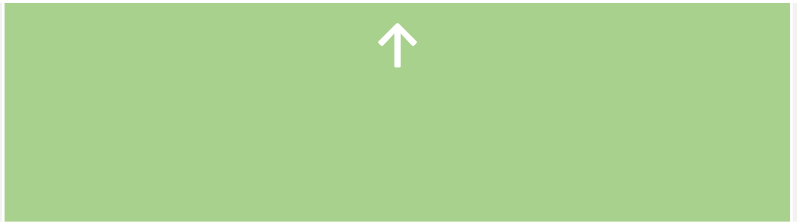
We suggest that **methotrexate**, **acitretin and apremilast** are considered as treatment in patients with psoriasis and advanced congestive heart failure.	↑	Strong consensus 100% agreement  EXPERT CONSENSUS

Nast A. et al., JEADV 2021, 35, 281-317, DOI: 10.1111/jdv.16926

Viral hepatitis: How should patients who test positive be managed?

We suggest, based on the common practice within the guideline group, **acitretin, apremilast, fumarates, MTX, ustekinumab and the anti-IL 17 and anti-IL 23 antibodies** as preferred systemic treatment options for patients that have a positive anti-HBc with a neg. HBsAG/HBV-DNA test.		Strong consensus 100% agreement EXPERT CONSENSUS

Tuberculosis: How to manage psoriasis in patients with positive tuberculosis test results?

We suggest **acitretin, apremilast or fumarates** or a treatment from the **anti-IL 17 and anti-IL 23 group** for patients with latent TB that require a systemic antisporiatic treatment.		Strong consensus 100% agreement EXPERT CONSENSUS

Nast A. et al., JEADV 2021, 35, 281-317, DOI: 10.1111/jdv.16926

DOI: 10.1111/jdv.16926 JEADV

GUIDELINES

EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris – Part 2: specific clinical and comorbid situations

Cancer: How should psoriasis patients with a history of malignancies be managed?

We suggest **apremilast** can be used in psoriasis patients with a previous history of cancer despite the lack of long-term experience based on pathophysiological considerations on a case-by-case basis including discussion with cancer specialist.	↑	Strong consensus 100% agreement EXPERT CONSENSUS

Nast A. et al., JEADV 2021, 35, 281-317, DOI: 10.1111/jdv.16926

Actas Dermosifiliogr. 2020;111(2):115–134

ORIGINAL ARTICLE

The Use of Apremilast in Psoriasis: A Delphi Study☆

J.M. Carrascosa,[a,*] I. Belinchón,[b] R. Rivera,[c] M. Ara,[d] M. Bustinduy,[e] P. Herranz[f]

Following a review of the literature, a panel of dermatologists with expertise in the management of psoriasis considered 5 scenarios in which the evidence supporting the use of apremilast to treat moderate psoriasis is insufficient or controversial. These scenarios were then assessed using a Delphi questionnaire.

Results: Consensus was reached on 96 (67%) of the 143 items (positive in 85 and negative in 11). The therapeutic goal for apremilast should be based on 4 outcomes: clinical response, symptoms, quality of life, and patient satisfaction. The scenario in which the use of apremilast was considered to have the greatest possibility of success was in patients with stable moderate psoriasis. Most of the clinicians considered apremilast to be an appropriate treatment when conventional therapies fail or are contraindicated, preferably before the prescription of biologic therapy. Consensus was reached that apremilast is an appropriate treatment for psoriasis in difficult locations, such as the scalp or the palms and soles. It was also agreed that apremilast requires less prescreening and monitoring than other conventional and biologic systemic therapies.

Conclusions: Apremilast could be a treatment option for patients with a different profile to that of clinical trial participants. The limitations of this proposal are the absence of consensus on

Actas Dermosifiliogr. 2020;111(2):115–134

The Use of Apremilast in Psoriasis: A Delphi Study☆

J.M. Carrascosa,[a,*] I. Belinchón,[b] R. Rivera,[c] M. Ara,[d] M. Bustinduy,[e] P. Herranz[f]

ical practice. The panel agreed that it was appropriate to maintain apremilast up to 24 weeks in patients with a partial response at week 16 (< 50% reduction in PASI or absolute PASI score > 5), as long as they were satisfied with the treatment and had not experienced significant impairment in quality of life (Dermatology Life Quality Index [DLQI] score < 1). It was even considered justifiable to maintain apremilast beyond week 24 in patients who had not achieved PASI-75 if they were satisfied with their treatment.

Actas Dermosifiliogr. 2020;111(2):115–134

The Use of Apremilast in Psoriasis: A Delphi Study☆

J.M. Carrascosa,[a,*] I. Belinchón,[b] R. Rivera,[c] M. Ara,[d] M. Bustinduy,[e] P. Herranz[f]

Apremilast was considered to be an appropriate treatment for patients with moderate psoriasis when conventional systemic treatments fail or are contraindicated and for patients who are not yet candidates for biologic therapy or who do not respond to or have a contraindication to biologic agents. The following factors were identified as having the greatest influence on the decision to prescribe apremilast: *i*) moderate skin involvement, *ii*) clinical stability, *iii*) associated symptoms, *iv*) presence of palmoplantar psoriasis, *v*) presence of comorbidities, *vi*) polymedication, *vii*) young patients expected to need treatment for a long time, and *viii*) patients with injection phobia. By contrast, apremilast was not considered appropriate for patients with extensive, unstable psoriasis or for patients requiring rapid clearance.

Effectiveness of Apremilast in Special Locations

The expert panel agreed in the first round that apremilast was an appropriate treatment for patients with psoriasis affecting special locations, such as the nails, the scalp, and the palms and soles (Table 3).

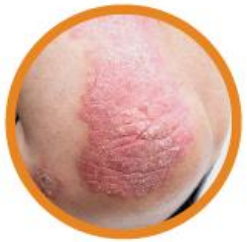
Effectiveness of Apremilast in Patients Wit
Concomitant Psoriasis and Psoriatic Arthrit

Positive consensus was reached for 3 (42.9%) of t
(2 in the first round and 1 in the second) on t
psoriasis in patients with concomitant psoriasis
atic arthritis. It was agreed that it was appropriate to use apremilast before biologic therapy in patients with moderate to severe psoriasis and concomitant psoriatic arthritis who have peripheral disease with moderate inflammatory activity (few joints affected) or dactylitis (Table 4).

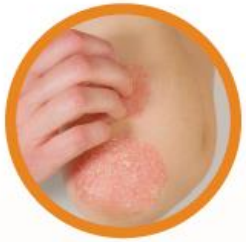
first round and 1 in the second. It was agreed that apremilast offered advantages over other conventional systemic treatments and biologic therapies in terms of its impact on comorbidities in patients with recurrent, chronic, or active infections, a recent history of cancer (< 5 years), active cancer, other immunosuppressive states, or metabolic disorders. The panel also agreed that apremilast was safer than biologic agents for patients with congestive heart disease or demyelinating disorders. By contrast, apremilast was not

Ποιος είναι ο κατάλληλος ασθενής για την επιτυχία της θεραπείας με απρεμιλάστη

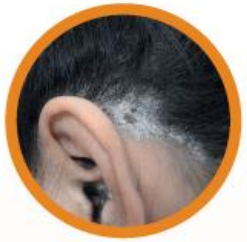
Περιορισμένη δερματική προσβολή, κλινικά σταθερή ψωρίαση[1*]



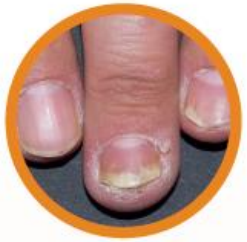
Συμμετοχή ορατών, ή ενοχλητικών περιοχών[1]



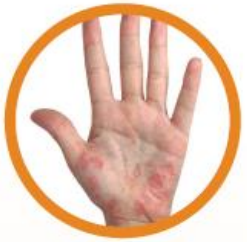
Κνησμός



Προσβολή τριχωτού κεφαλής



Προσβολή ονύχων



Προσβολή παλαμών/ πελμάτων

Προσβολή γεννητικής περιοχής

Συννοσηρότητες[1,2]

Ψωριασική αρθρίτιδα[1,2]

Επαναλαμβανόμενες ή χρόνιες λοιμώξεις[1]

Πρόσφατο ιστορικό καρκίνου (<5 έτη) ή ενεργός καρκίνος[1,2]

Μεταβολικό σύνδρομο[1]

Συμφορητική καρδιακή ανεπάρκεια[1,2]

- Λανθάνουσα φυματίωση[1,2]
- Ήπια-μέτρια νεφρική ανεπάρκεια[1,2]
- Χρόνια φλεγμονώδη νόσο του εντέρου, (ελκώδης κολίτιδα)[2]
- Απομυελυνωτική νόσος
- Πολυφαρμακία[1,2]

Νέοι ασθενείς που προβλέπεται ότι θα λαμβάνουν θεραπεία για πολλά χρόνια[1]