Διαχείριση της περιφερικής ολιγοαρθρίτιδας στην Ψωριασική Νόσο

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Ιπποκράτειο Νοσοκομείο

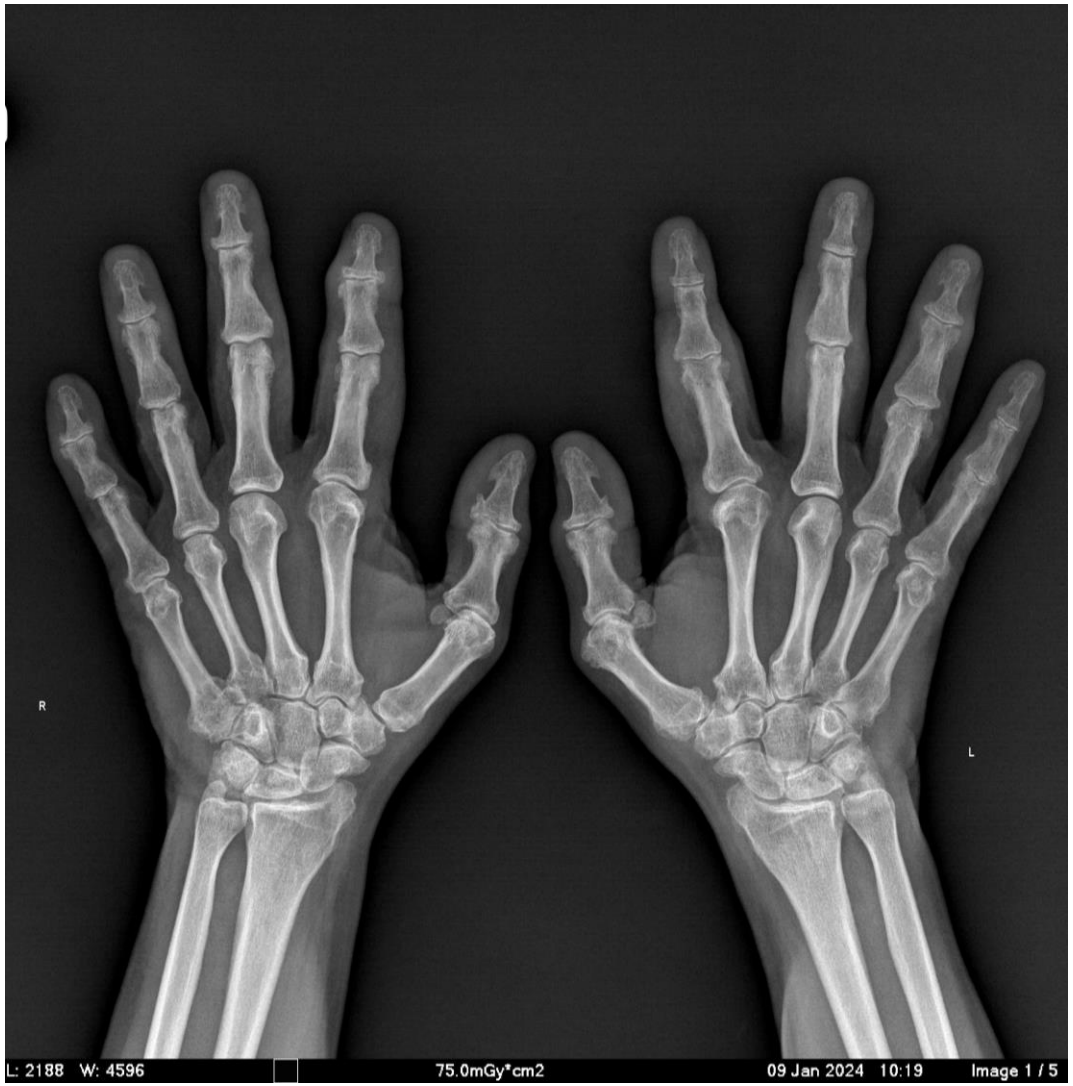
Σύγκρουση συμφερόντων

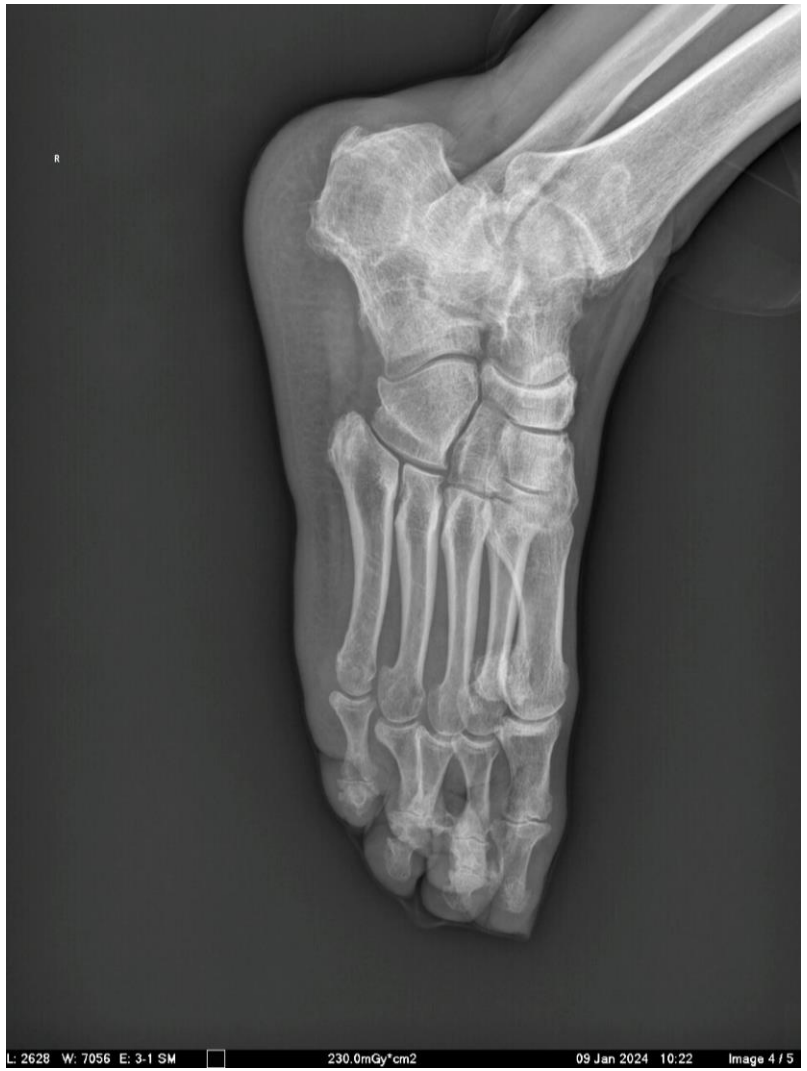
- Τιμητική αμοιβή από την εταιρία Amgen

Παρουσίαση περιστατικού 1

- Άνδρας 56 ετών, καπνιστής 20 p/y
- Ιστορικό ψωρίασης από 10 ετίας υπό τοπική αγωγή (κυρίως στο τριχωτό της κεφαλής)
- Αρθραλγίες από μηνών άνω και κάτω ακρών
- Χειρωνακτική εργασία, συχνή χρήση αναλγητικών
- Κλινικά:αρθρίτιδα 2^{ης} PIP άμφω, 2^{ης} DIP δεξιά, ενθεσίτιδα ΔΕ αχιλ. Τένοντα, BSA < 2 %

Παρουσίαση περιστατικού 1

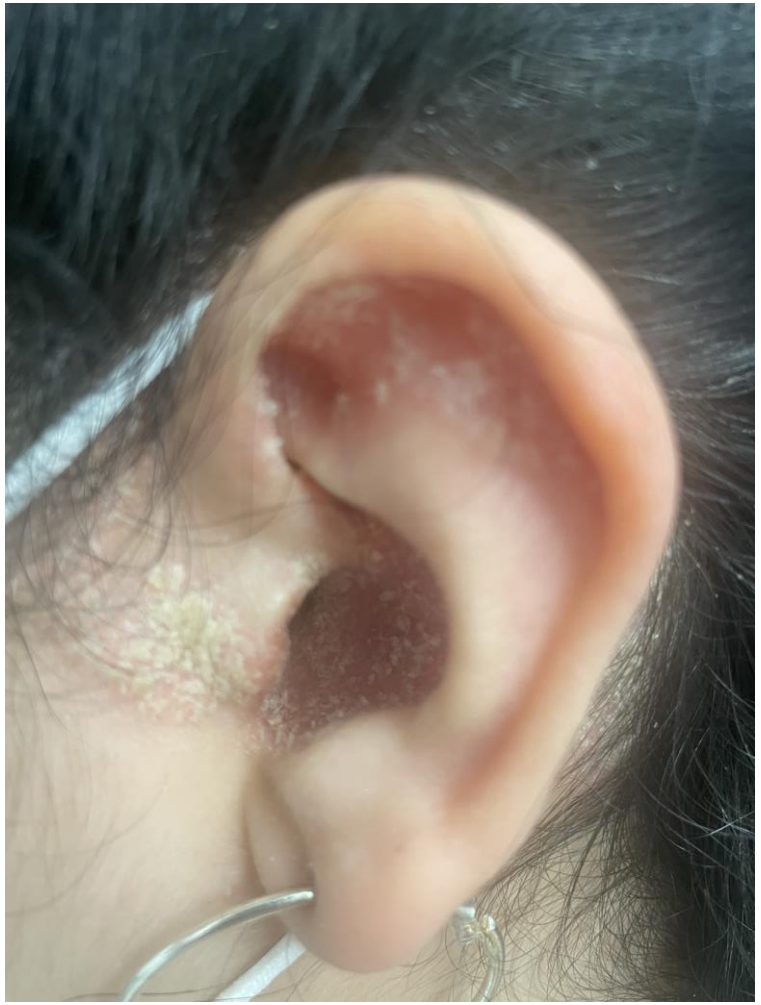


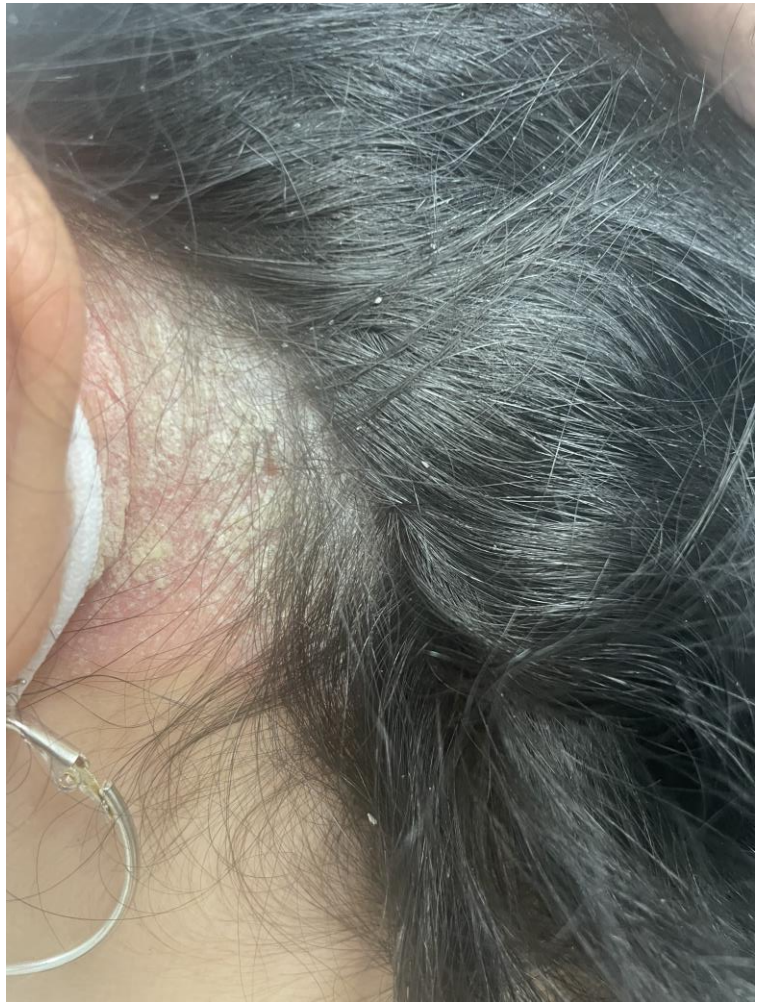


Παρουσίαση περιστατικού 2

- Γυναίκα 25 ετών
- Ψωρίαση από εφηβική ηλικία και διάγνωση ολιγοαρθρικής ψωριασικής αρθρίτιδας (γόνατα, ποδοκνημικές) από έτους
- Λήψη MTX 15mg/week με καλή ανταπόκριση από τις αρθρώσεις αλλά όχι από το δέρμα με επίμονες βλάβες στο τριχωτό της κεφαλής
- Αδυναμία τιτλοποίησης της δόσης λόγω ηπατοτοξικότητας

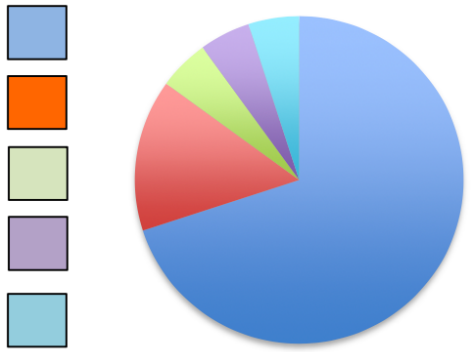
Παρουσίαση περιστατικού 2





Musculoskeletal manifestations

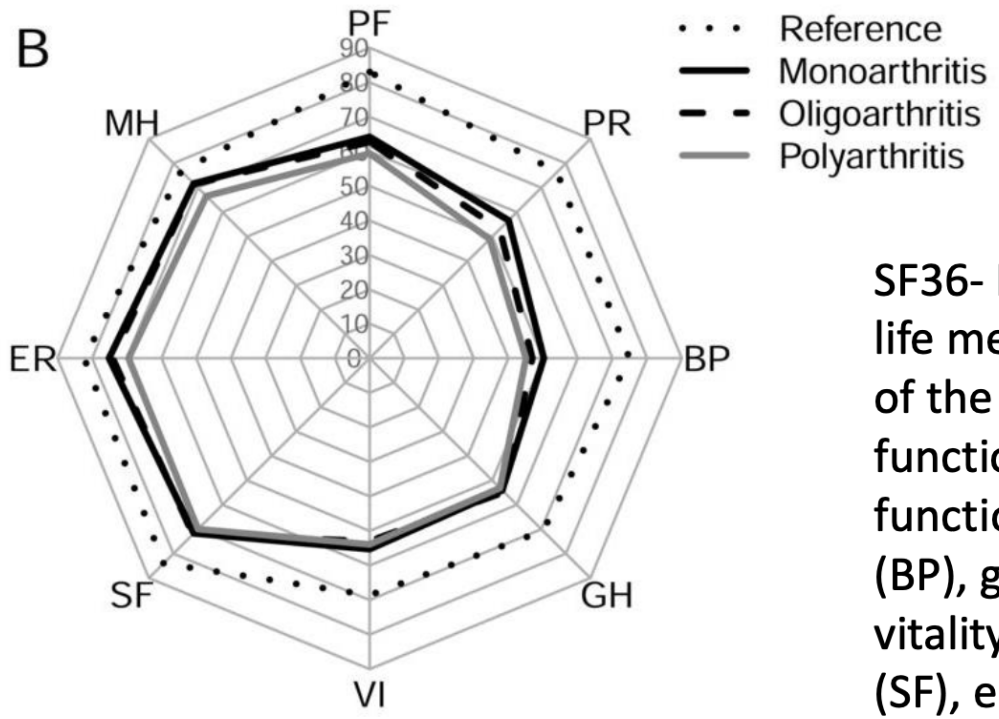
1. asymmetrical oligoarthritis (70%)
2. symmetrical polyarthritis (15%)
3. spondylitis (5%)
4. distal interphalangeal predominant (5%)
5. arthritis mutilans (5%)



	Category at Examination as Evaluated by Rheumatologist				
Category at Onset as Recalled by the Patient	Oligo-arthritis, n = 58	Poly-arthritis, n = 40	Inflammatory Back Pain, n = 9	Enthesitis, n =11	None** n = 13
Oligoarthritis, n = 86	39*	31	2	7	7
Polyarthritis, n = 31	15	8*	2	3	3
Inflammatory back pain, n = 7	3	1	3*	0	0
Enthesitis, n = 1	0	0	1	0*	0
Unknown†, n = 6	1	0	1	1	3

Moll JM and Wright V. Semin Arth Rheum. 1973;3(1):55-7; Serre H, et al. J Med Montpellier 4:3, 1969; Thorvardur JL et al. 2007; J Rheum 34:2082-8.

Oligo/mono-articular PsA is characterized by high disease burden

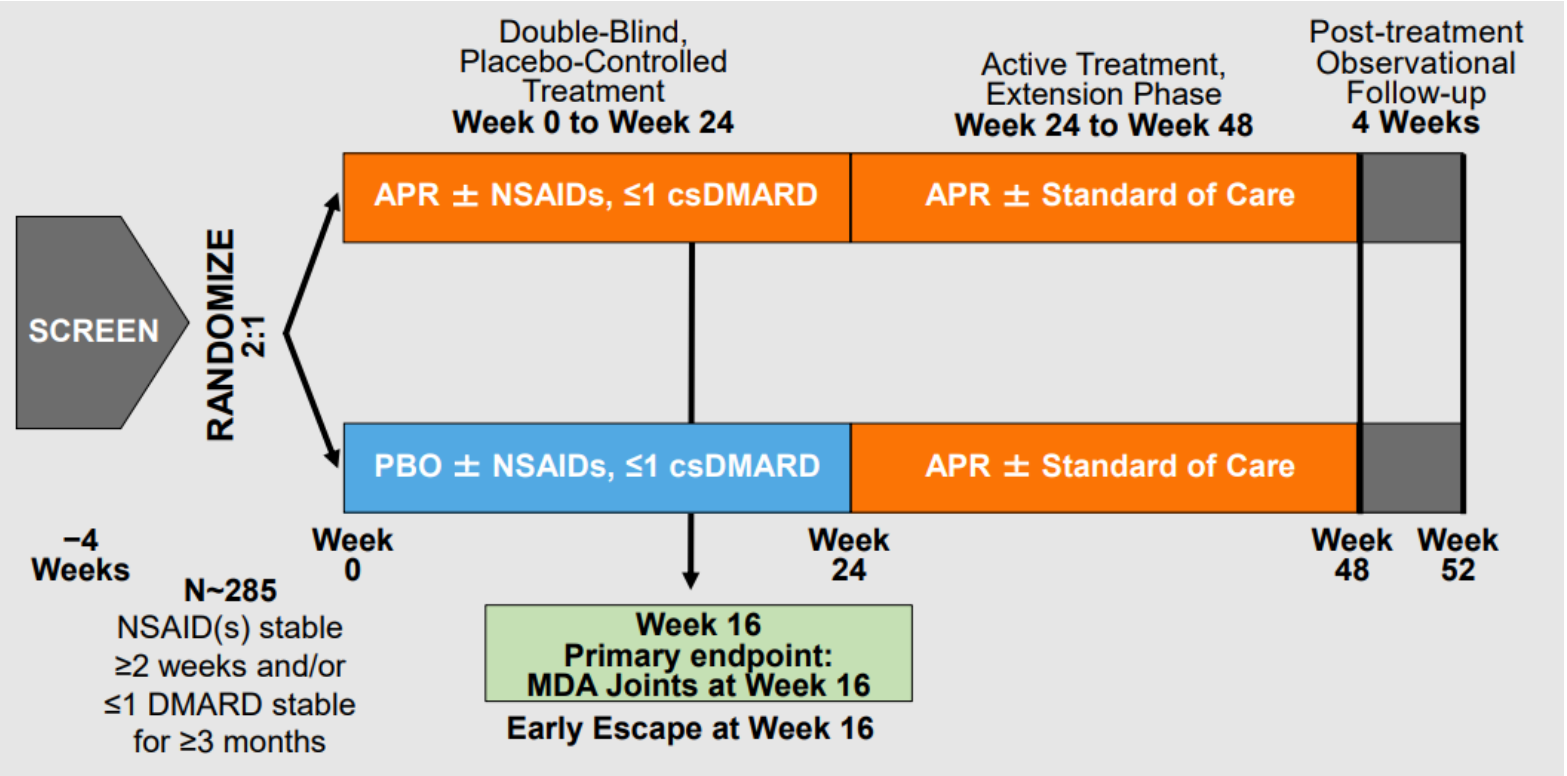


SF36- Health-related quality of life measured by these domains of the SF-36: physical functioning (PF), physical role functioning (PR), bodily pain (BP), general health (GH), vitality (VI), social functioning (SF), emotional role functioning (ER), and mental health (MH).

Wervers K et al., J Rheum 2018, 45 (11) 1526-1531

FOREMOST Study design[1]

- FOREMOST (NCT03747939) is a phase 4, multicenter, randomized, double-blind, PBO-controlled, parallel-group study



1. Mease P. et al Effect of Apremilast Treatment on the Domains of MDA-Joints in Patients With Early Oligoarticular Psoriatic Arthritis: 16-Week Results From FOREMOST. Poster presented at ACR 2023; San Diego California 1413

Baseline Characteristics[1]

	Placebo (n=105)	Apremilast (n=203)	Total (N=308)
Age, mean (SD), years	50.2 (13.0)	51.3 (12.3)	50.9 (12.5)
Women, n (%)	51 (48.6)	118 (58.1)	169 (54.9)
Race, white, n (%)	99 (94.3)	192 (94.6)	291 (94.5)
PsA duration, mean (SD), months	10.0 (10.6)	9.8 (10.0)	9.9 (10.2)
Median (Q1, Q3)	6.0 (3.6, 12.7)	6.1 (3.7, 11.2)	6.0 (3.7, 11.7)
SJC (0–66), mean (SD)	2.6 (0.7)	2.7 (0.7)	2.6 (0.7)
Median (Q1, Q3)	2.0 (2.0, 3.0)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)
SJC category, n (%)			
2	57 (54.3)	93 (45.8)	150 (48.7)
3	38 (36.2)	79 (38.9)	117 (38.0)
4	10 (9.5)	31 (15.3)	41 (13.3)
TJC (0–68), mean (SD)	3.2 (0.8)	3.2 (0.8)	3.2 (0.8)
Median (Q1, Q3)	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)
TJC category, n (%)			
2	23 (21.9)	41 (20.2)	64 (20.8)
3	38 (36.2)	77 (37.9)	115 (37.3)
4	44 (41.9)	85 (41.9)	129 (41.9)
Active joint involvement*, n (%)			
Small only	51 (48.6)	104 (51.2)	155 (50.3)
Large only	7 (6.7)	19 (9.4)	26 (8.4)
Small and large	47 (44.8)	80 (39.4)	127 (41.2)
PhGA (0–100 mm VAS), mean (SD)	43.2 (19.2)	42.2 (18.6)	42.6 (18.8)

1. Gossec L. et al Ann Rheum Dis 2024 20:ard-2024-225833. doi: 10.1136/ard-2024-225833. Online ahead of print.

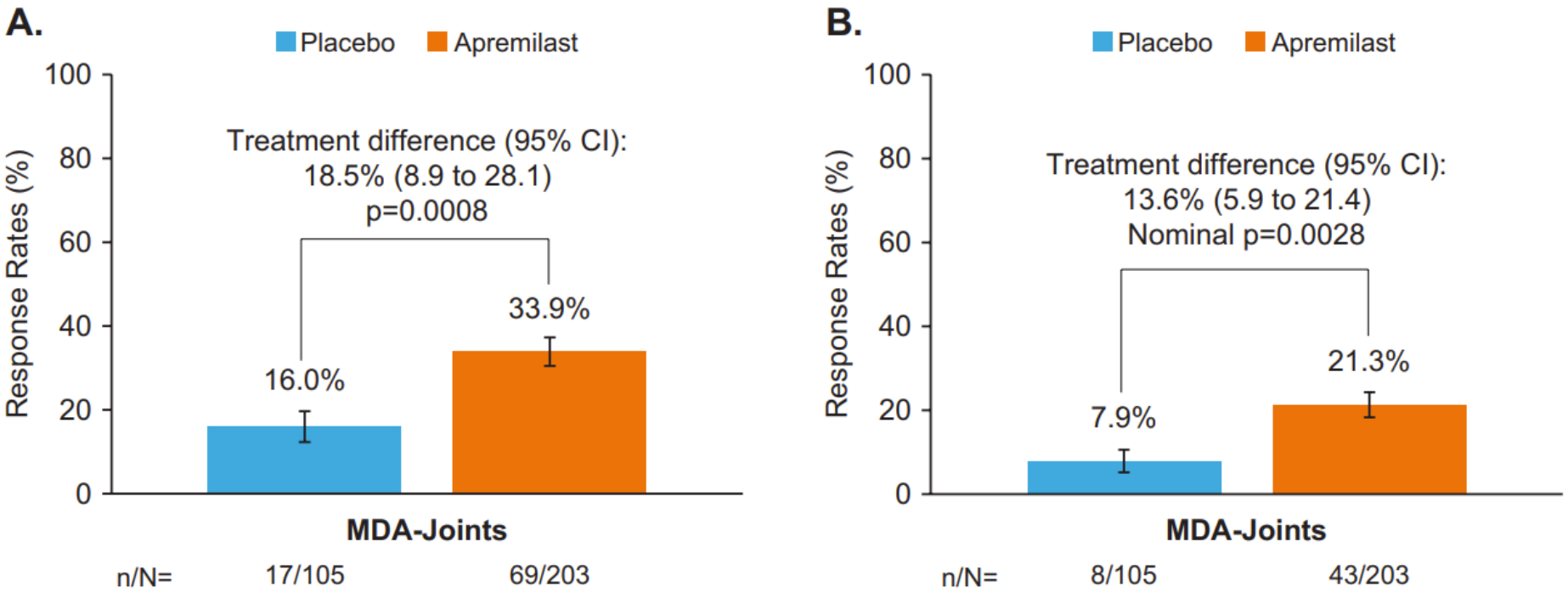
Baseline Characteristics continued[1]

PtGA (0–100 mm VAS), mean (SD)	50.5 (20.7)	51.6 (22.0)	51.3 (21.5)
Patient's assessment of pain (0–100 mm VAS), mean (SD)	51.1 (22.7)	52.3 (22.0)	51.9 (22.2)
cDAPSA (0–154), mean (SD)	15.9 (4.5)	16.3 (4.3)	16.2 (4.4)
PASDAS (0–10), mean (SD)	4.9 (1.0)	4.9 (1.1)	4.9 (1.1)
BSA, mean (SD), %	6.3 (10.9)	6.9 (12.3)	6.7 (11.8)
BSA>3%, n (%)	42 (40.0)	78 (38.4)	120 (39.0)
HAQ-DI (0–3), mean (SD)	1.1 (0.6)	1.0 (0.6)	1.0 (0.6)
LEI (0–6), mean (SD)†	2.6 (1.6)	2.4 (1.5)	2.5 (1.5)
LEI>0, n (%)	38 (36.2)	70 (34.5)	108 (35.1)
SPARCC Index (0–16), mean (SD)†	4.3 (3.9)	3.9 (3.5)	4.0 (3.6)
Physician's assessment of nail psoriasis (0–100 mm VAS), mean (SD)‡	28.9 (26.3)	30.8 (25.9)	30.2 (26.0)
PsAID-12 (0–10), mean (SD)	4.8 (2.2)	4.7 (2.0)	4.7 (2.1)
Prior csDMARD, n (%)	69 (65.7)	135 (66.5)	204 (66.2)
Concomitant csDMARD, n (%)	41 (39.0)	82 (40.4)	123 (39.9)
Methotrexate	34 (32.4)	73 (36.0)	107 (34.7)
Sulfasalazine	7 (6.7)	9 (4.4)	16 (5.2)

FAS.
*Active joints are defined as swollen and/or tender joints. Large joints included shoulder, elbow, hip, knee and ankle. The remaining joints were considered small.
†In patients with pre-existing enthesopathy.
‡In patients with baseline nail VAS>0.
BSA, body surface area; cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; csDMARD, conventional synthetic disease-modifying antirheumatic drug; FAS, full analysis set; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; PASDAS, Psoriatic Arthritis Disease Activity Score; PhGA, Physician's Global Assessment of disease activity; PsA, psoriatic arthritis; PsAID-12, Psoriatic Arthritis Impact of Disease 12-item; PtGA, Patient Global Assessment of disease activity; SJC, swollen joint count; SPARCC, Spondyloarthritis Research Consortium of Canada; TJC, tender joint count; VAS, Visual Analogue Scale.

1. Gossec L. et al Ann Rheum Dis 2024 20:ard-2024-225833. doi: 10.1136/ard-2024-225833. Online ahead of print.

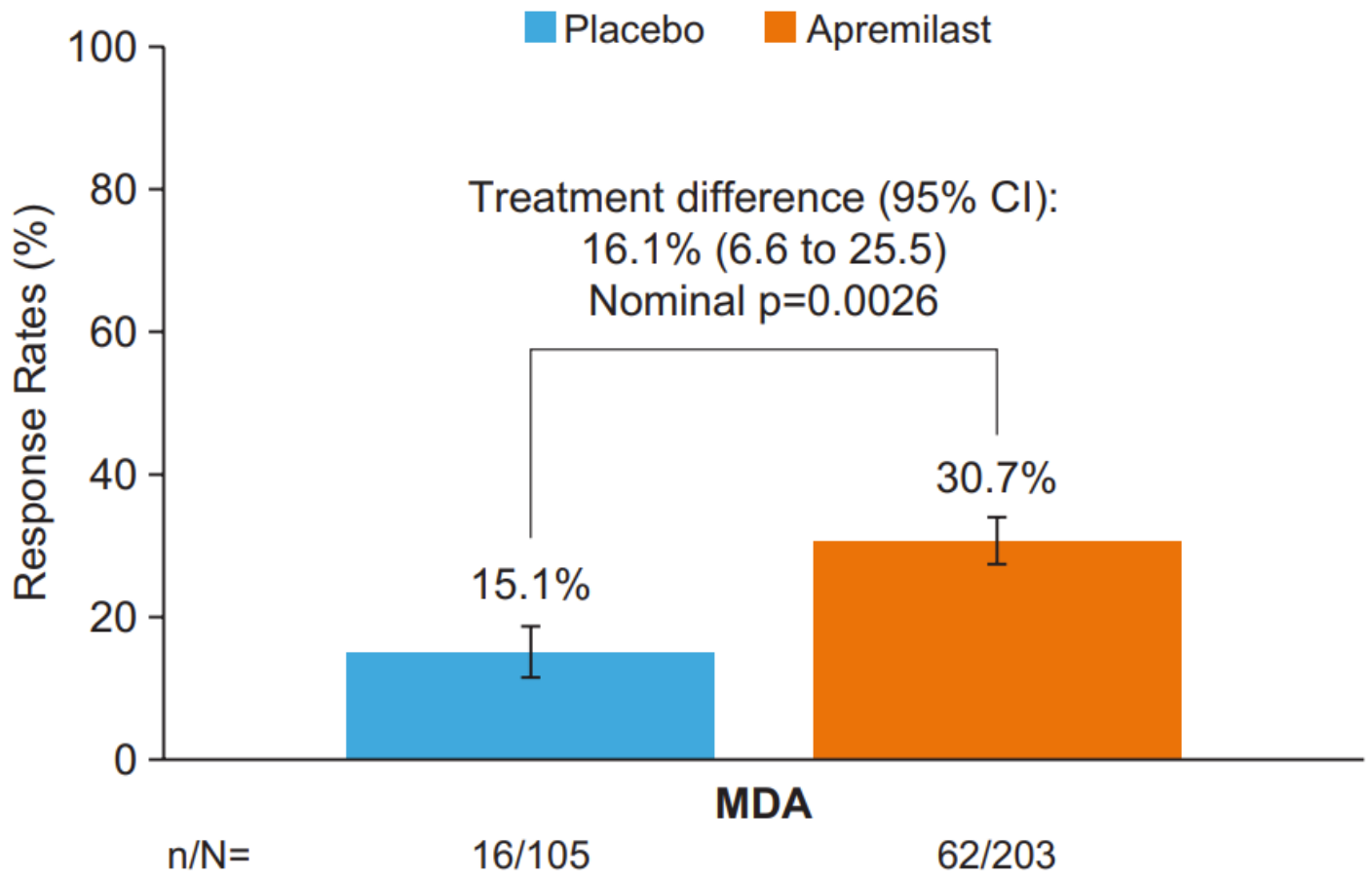
Primary Endpoint: MDA-Joints[1]



MDA-joints response at week 16. (A) Based on sentinel joints. (B) Based on all joints. FAS. Error bars represent SE. The number of responders was rounded based on the value given by multiple imputations. MDA-joints is a composite of TJC≤1 and SJC≤1 plus achievement of three of the following: BSA≤3%, patient pain VAS≤15, PtGA≤20, HAQ-DI≤0.5 and LEI≤1. BSA, body surface area; CI, confidence interval; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; PtGA, Patient Global Assessment of disease activity; SE, standard error; SJC, swollen joint count; TJC, tender joint count; VAS, Visual Analogue Scale

1. Gossec L. et al Ann Rheum Dis 2024 20:ard-2024-225833. doi: 10.1136/ard-2024-225833. Online ahead of print.

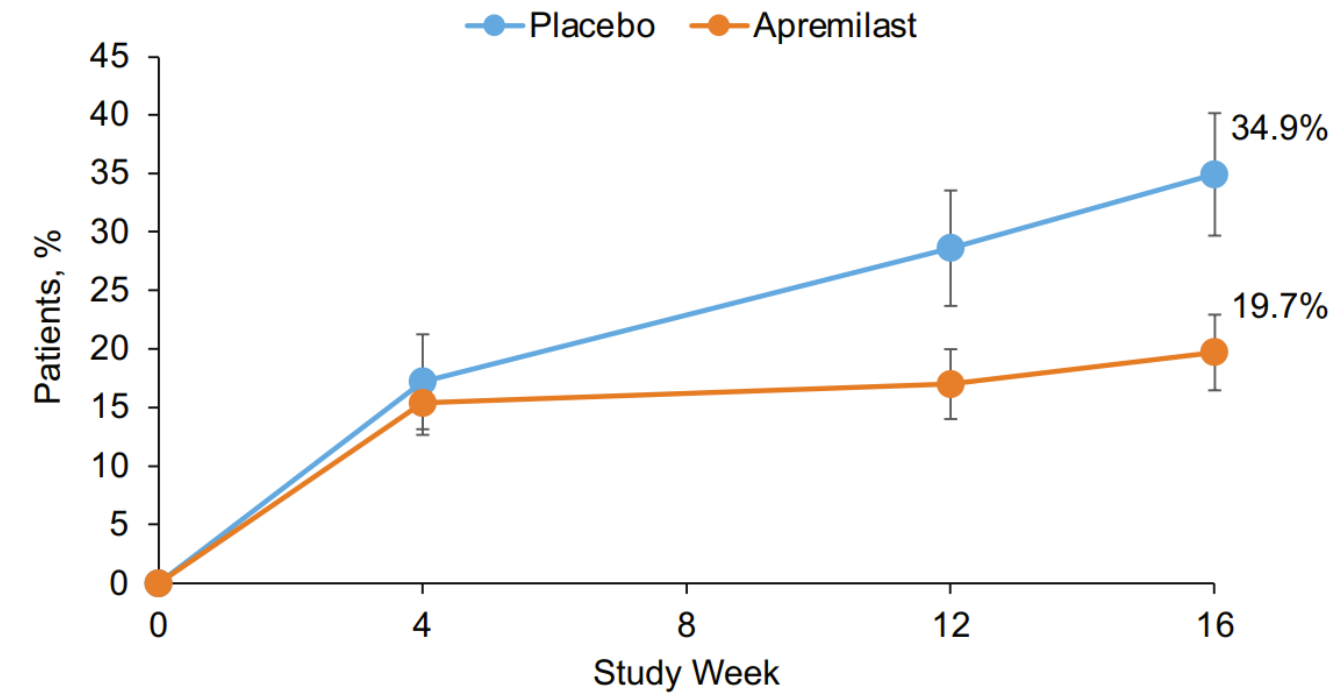
Proportion of patients achieving MDA at week 16[1]



Proportion of patients achieving MDA at week 16. FAS. Based on all joints. Error bars represent SE. CI, confidence interval; FAS, full analysis set; MDA, minimal disease activity; SE, standard error

1. Gossec L. et al Ann Rheum Dis 2024 20:ard-2024-225833. doi: 10.1136/ard-2024-225833. Online ahead of print.

Proportion of patients who progressed to active joint count >4 among patients with ≤4 active joints at baseline [1]



Placebo, n/N	15/87		24/84	29/83
Apremilast, n/N	27/175		27/159	30/152

Proportion of patients who progressed to active joint count >4 among patients with ≤4 active joints at baseline. FAS with ≤4 active joints at baseline. Error bars represent SE based on all joints. Data are as observed. FAS, full analysis set; SE, standard error

1. Gossec L. et al Ann Rheum Dis 2024 20:ard-2024-225833. doi: 10.1136/ard-2024-225833. Online ahead of print.

Outcomes at week 16 comparing apremilast and placebo[1]

	Sentinel* joints			All joints		
	Placebo (n=105)	Apremilast (n=203)	Difference (95% CI)	Placebo (n=105)	Apremilast (n=203)	Difference (95% CI)
cDAPSA REM/LDA, n (%)	54 (51.8)	143 (70.2)	18.6% (7.0 to 30.2) p=0.0017	40 (38.0)	122 (60.3)	22.5% (10.7 to 34.3) p=0.0004†
SJC≤1, n (%)	72 (69.0)	150 (74.0)	5.1 (–5.8 to 16.0) p=0.3539	43 (41.5)	117 (57.9)	16.4 (4.7 to 28.0) p=0.0068†
TJC≤1, n (%)	47 (44.4)	134 (66.2)	22.1 (10.4 to 33.7) p=0.0003†	17 (16.7)	77 (38.0)	21.4 (11.6 to 31.2) p=0.0002†
PtGA VAS≤20, n (%)	–	–	–	20 (19.1)	62 (30.4)	11.8% (1.7 to 22.0) p=0.0286†
Patient pain VAS≤15, n (%)	–	–	–	14 (13.1)	60 (29.4)	16.3% (6.9 to 25.8) p=0.0022†
PsAID-12, LS mean (SE) change from baseline	–	–	–	–0.4 (0.2)	–1.5 (0.2)	–1.0 (–1.5 to –0.6) p<0.0001†
PASDAS good/moderate response, n (%)	45 (42.7)	122 (59.9)	17.7% (5.7 to 29.7) p=0.0043†	42 (39.8)	120 (59.3)	20.0% (8.1 to 32.0) p=0.0014†

FAS. The number of responders was rounded based on the value given by multiple imputations. *Sentinel joints are defined as joints affected at baseline. †Nominal p value.

cDAPSA, Clinical Disease Activity in Psoriatic Arthritis; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; FAS, full analysis set; LDA, low disease activity; LS, least squares; MDA, minimal disease activity; PASDAS, PsA Disease Activity Score; PsAID-12, Psoriatic Arthritis Impact of Disease; PtGA, Patient Global

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Safety[1]

	PBO (n=104)	APR (n=204)
Any TEAE	49 (47.1)	121 (59.3)
Any drug-related TEAE	20 (19.2)	67 (32.8)
Any severe TEAE	4 (3.8)	8 (3.9)
Any serious TEAE	6 (5.8)	9 (4.4)
TEAEs leading to drug withdrawal	7 (6.7)	21 (10.3)
TEAEs leading to death	0 (0.0)	2 (1.0)*
TEAEs occurring in ≥5% of patients		
Diarrhea	11 (10.6)	47 (23.0)
Nausea	4 (3.8)	22 (10.8)
Headache	3 (2.9)	16 (7.8)

*Two deaths reported (sudden cardiac death and anoxic brain injury) in the APR group were not related to study drug as assessed by the investigator. Sudden cardiac death occurred in a 52-year-old male with a history of hypertension concomitantly receiving aspirin and methotrexate 78 days after the first dose of apremilast. Anoxic brain injury occurred in a 69-year old female with extensive medical history and concomitant medications due to post-surgical complications following a routine abdominal hymenorrhaphy. Safety analysis set. Data are n (%). Includes data through Week 16/Visit 5 for PBO-treated patients who escaped early and data up to Week 24 for all other patients. APR=apremilast 30 mg BID; PBO=placebo; TEAE=treatment-emergent adverse event

1. Gossec L. et al Ann Rheum Dis 2024 20:ard-2024-225833. doi: 10.1136/ard-2024-225833. Online ahead of print.

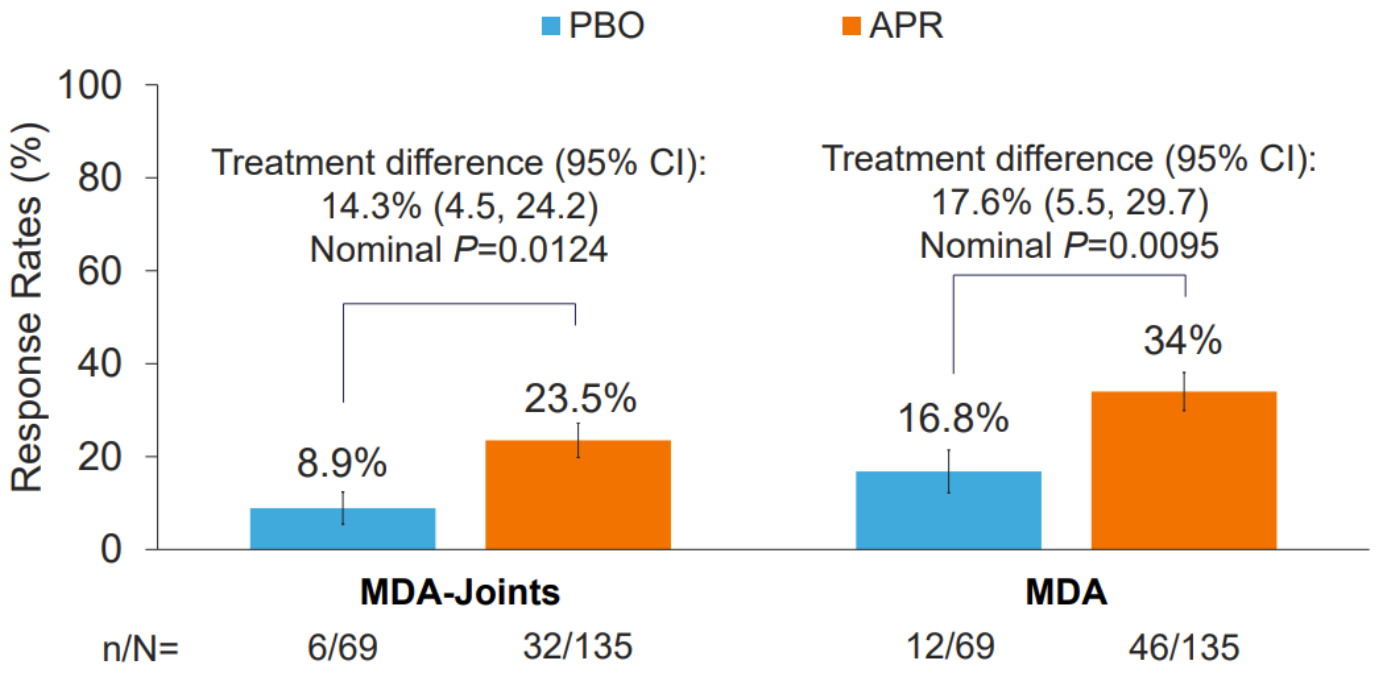
Baseline demographics of the csDMARD-exposed patients

	PBO (n=69)	APR (n=135)
Age, mean (SD), years	49.8 (12.9)	51.2 (12.7)
Women, n (%)	32 (46.4)	79 (58.5)
Men, n (%)	37 (53.6)	56 (41.5)
Race, White, n (%)	65 (94.2)	126 (93.3)
PsA duration, mean (SD), months	12.2 (12.1)	11.6 (10.4)
Prior use of csDMARDs, n (%)	28 (40.6)	54 (40.0)
SJC (0–66), mean (SD)	2.5 (0.6)	2.7 (0.7)
TJC (0–68), mean (SD)	3.1 (0.8)	3.2 (0.8)
BSA, mean (SD), %	4.2 (4.9)	6.4 (10.5)
Patient's Assessment of Pain (0-100 mm VAS), mean (SD)	50.9 (22.7)	51.0 (21.1)
HAQ-DI, mean (SD)	1.1 (0.7)	1.0 (0.6)
LEI*, mean (SD)	2.8 (1.7)	2.2 (1.5)
cDAPSA, mean (SD)	16.1 (4.5)	16.1 (4.2)
PASDAS, mean (SD)	4.9 (1.0)	4.9 (1.1)

*In patients with pre-existing enthesopathy.

1. Gossec L. et al Early Oligoarticular Psoriatic Arthritis Responds to Treatment With Apremilast: Week 16 Results From FOREMOST – a Phase 4 Randomized Controlled Trial. Poster Presented at: the 32nd EADV Congress; October 11-14, 2023; Berlin, Germany P2574.

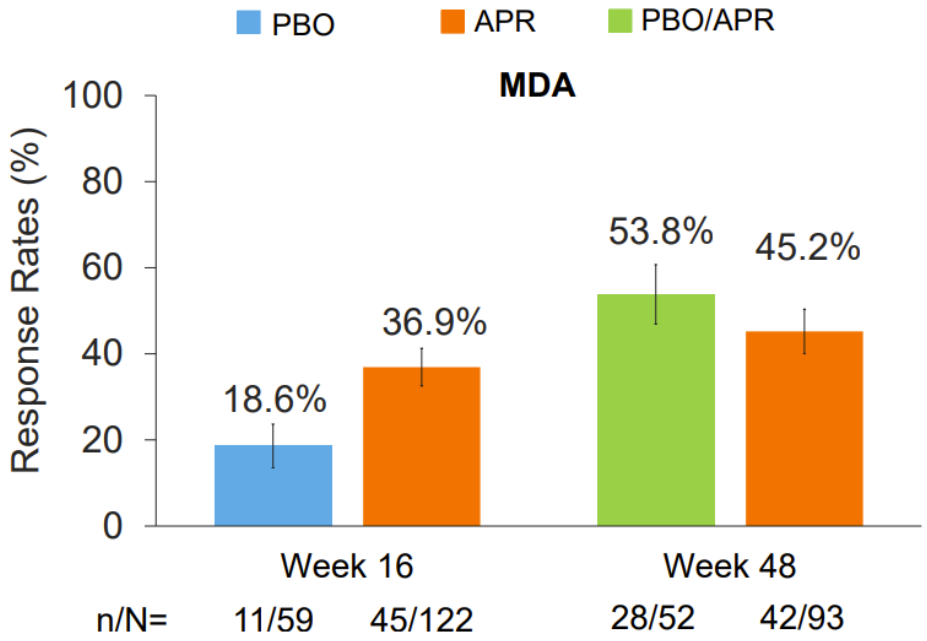
Achievement of MDA-Joints and MDA at Week 16 was consistently greater with apremilast vs placebo in csDMARD-experienced patients



Patients in the Full Analysis Set with prior csDMARD use; data based on all joints. Patients who discontinued the study prior to Week 16 due to adverse event or lack of efficacy imputed as non-responders; remaining missing values at Week 16 imputed using multiple imputation; number of responders rounded based on the value given by multiple imputation. Error bars represent standard error. P-value based on the CMH test, adjusting for prior/concomitant use of csDMARD and baseline glucocorticosteroid use, that is normalized via the Wilson-Hilferty transformation.

1. Gossec L. et al Apremilast Treatment in Early Oligoarticular Psoriatic Arthritis Improves Clinical and Patient-Reported Outcomes for up to 48 Weeks - Results from FOREMOST. Poster Presented at: EULAR; June 12-15, 2023; Vienna, Austria POS0976

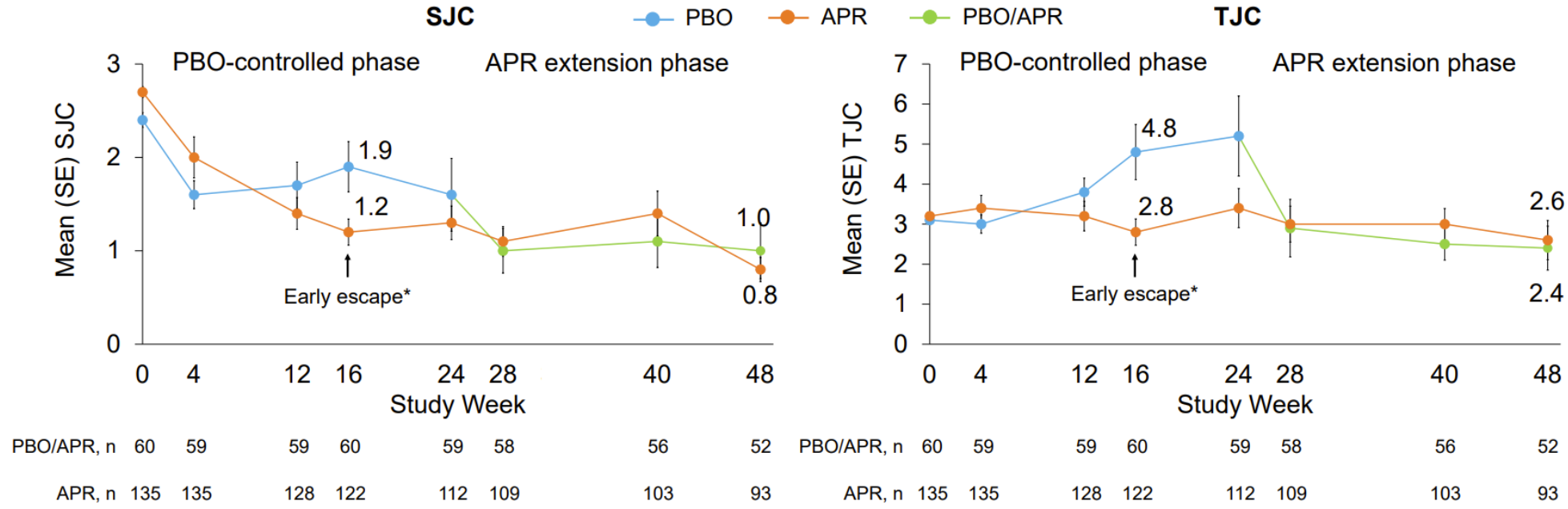
Rates of MDA achievement at Weeks 16 and 48 in csDMARD-experienced patients was consistent with the overall population



APR patients as randomized or transitioned with prior csDMARD use. Data as observed and based on all joints. Error bars represent standard error.

1. Gossec L. et al Apremilast Treatment in Early Oligoarticular Psoriatic Arthritis Improves Clinical and Patient-Reported Outcomes for up to 48 Weeks - Results from FOREMOST. Poster Presented at: EULAR; June 12-15, 2023; Vienna, Austria POS0976

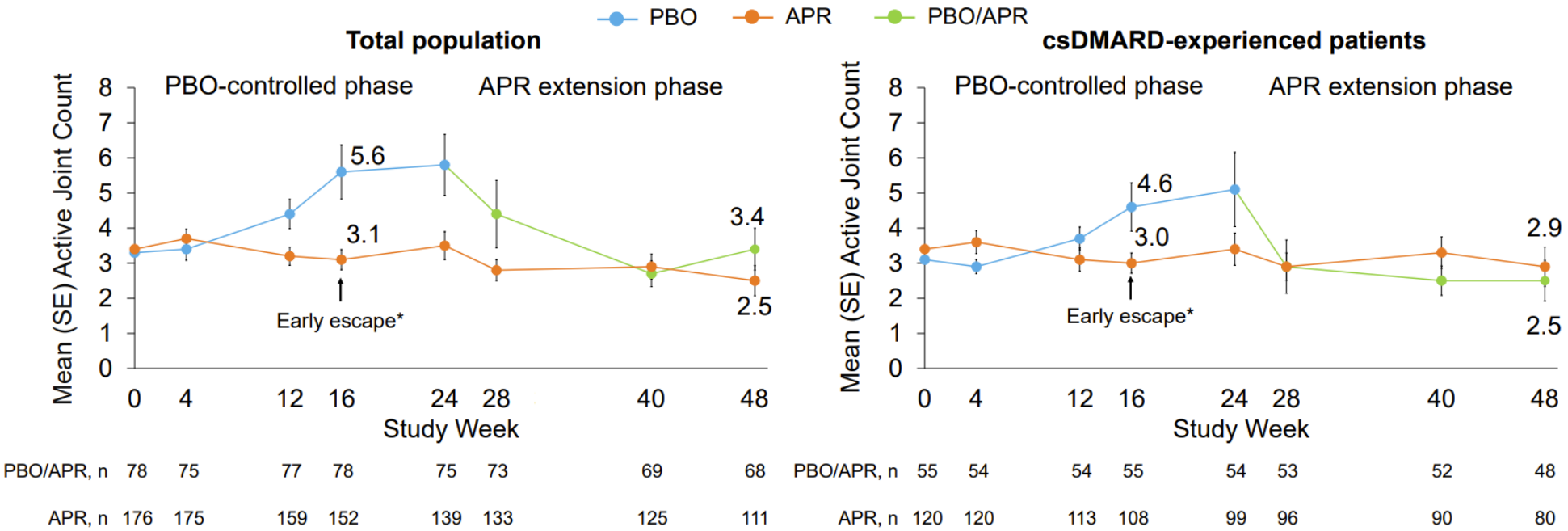
Improvements in SJC and TJC were consistently greater at Week 16 with APR than PBO in csDMARD-experienced patients and improvements continued through Week 48



APR patients as randomized or transitioned who had prior csDMARD use. Data as observed and based on all joints. *Patients who underwent early escape at Week 16 (PBO, n=19; APR, n=16) were analyzed at Week 24 per randomization

1. Gossec L. et al Apremilast Treatment in Early Oligoarticular Psoriatic Arthritis Improves Clinical and Patient-Reported Outcomes for up to 48 Weeks - Results from FOREMOST. Poster Presented at: EULAR; June 12-15, 2023; Vienna, Austria POS0976

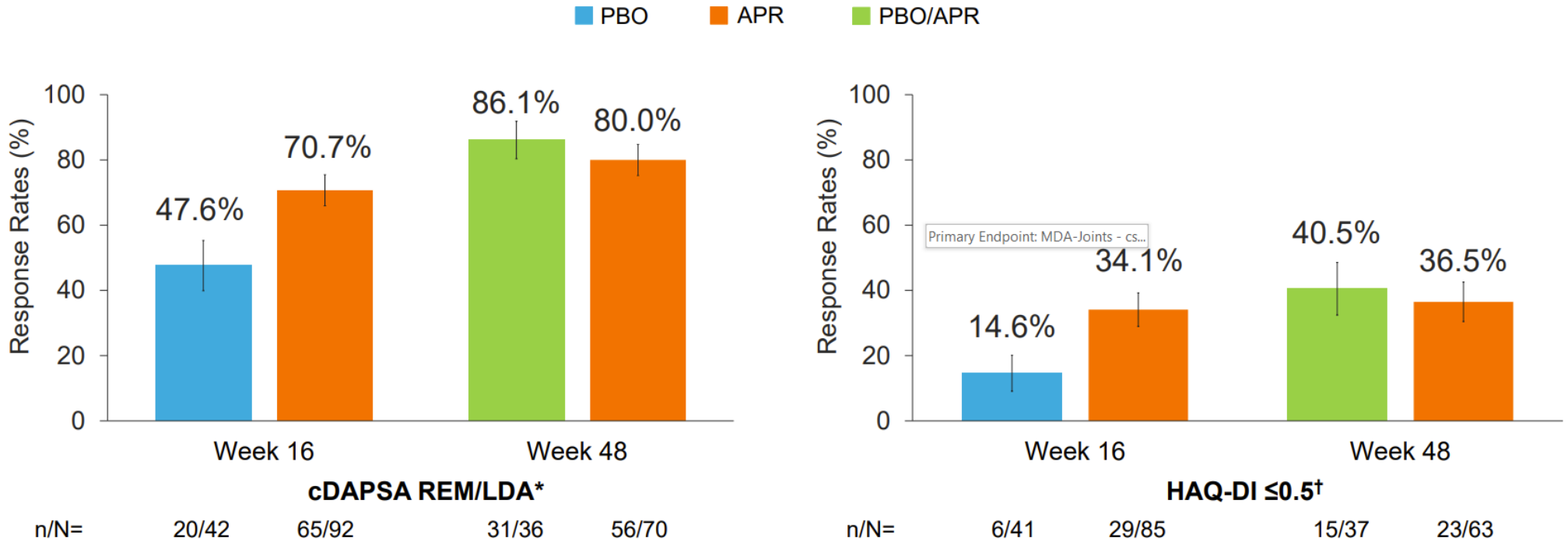
Mean total active joint count was lower with APR than PBO at Week 16 and did not increase through 48 weeks in both the total population and in csDMARD-experienced patients



APR patients as randomized or transitioned who had ≤4 active joints at baseline. Data as observed and based on all joints. Error bars represent standard error. *Patients who underwent early escape at Week 16 (Overall population: PBO, n=22; APR, n=18; csDMARD-experienced population: PBO: n=17; APR, n=14) were analyzed at Week 24 per randomization

1. Gossec L. et al Apremilast Treatment in Early Oligoarticular Psoriatic Arthritis Improves Clinical and Patient-Reported Outcomes for up to 48 Weeks - Results from FOREMOST. Poster Presented at: EULAR; June 12-15, 2023; Vienna, Austria POS0976

More patients achieved cDAPSA REM/LDA and HAQ-DI ≤0.5 with APR vs PBO at Week 16 in csDMARD-experienced patients and responses were maintained through Week 48



APR patients as randomized or transitioned who had prior DMARD use and *baseline cDPASA >13 (not in REM/LDA) or †baseline HAQ-DI >0.5. Data as observed and based on all joints. Error bars represent standard error.

1. Gossec L. et al Apremilast Treatment in Early Oligoarticular Psoriatic Arthritis Improves Clinical and Patient-Reported Outcomes for up to 48 Weeks - Results from FOREMOST. Poster Presented at: EULAR; June 12-15, 2023; Vienna, Austria POS0976

Conclusion[1]

- FOREMOST is the first global randomized controlled trial enrolling patients with early oligoarticular PsA
- In this study, better disease control was achieved by significantly more patients with apremilast, with twice the MDA-Joints response compared with placebo at 16 weeks
- Significantly greater improvements in additional measures of clinical disease activity and patient-reported outcomes also were seen with apremilast vs placebo
- A higher percentage of patients with baseline joint count ≤4 shifted to a joint count of >4 with placebo vs apremilast
- Findings from FOREMOST may inform treatment decisions regarding early introduction of apremilast in patients with early, oligoarticular PsA

1. Gossec L. et al Ann Rheum Dis 2024 20:ard-2024-225833. doi: 10.1136/ard-2024-225833. Online ahead of print.