Η τρέχουσα εμπειρία με την αναστολή της IL-23.

Παρουσίαση ενδιαφέρουσας κλινικής περίπτωσης

Κωνσταντίνα Ζουπίδου

Ρευματολόγος, Επιμελήτρια Β΄ΕΣΥ, Δ΄ Παν. Παθολογική Κλινική, Π.Γ.Ν. «Αττικό»

Jennifer Jacobs_Stowaway

Ερέτρια 16-06-2022

Σύγκρουση συμφερόντων

Παρούσα παρουσίαση :Τιμητική αμοιβή από JANSSEN

Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις την τελευταία διετία:

AEnorasis

Κλινική Περίπτωση

Διάγνωση Ψωρίασης

2008, 15 ετών

Διάγνωση Ψωριασικής Αρθρίτιδας

2014, 22 ετών

AGE: 30 ετών

SEX: άνδρας

OCCUPATION:
Ιδιωτικός υπάλληλος

Medical history

- Δυσλιπιδαιμία (υπό στατίνη)
- Κατάθλιψη (υπό SNRI)
- BMI 41.5 (120kg , 170cm)

Lifestyle

- Αλκοόλ (-)
- Κάπνισμα (-)

Κλινική Περίπτωση : Πορεία νόσου

Medical history

MTX → Ηπατοτοξικότητα

CyA → Αρτηριακή Υπέρταση

antiTNF cycling / 9 μήνες :

- Adalimumab
- Golimumab
- Infliximab

Medical history

Ustekinumab 45mg →μερική ανταπόκριση

Ustekinumab 90mg ,30 μήνες →μερική ανταπόκριση

Secukinumab , 18 μήνες → μερική ανταπόκριση

Κλινική Περίπτωση : Πορεία νόσου

MTX (2014) → CyA → antiTNF cycling (2015) → UST 45mg → UST 90mg → SEC (2021)

Ιανουάριος 2021

PsA characteristics

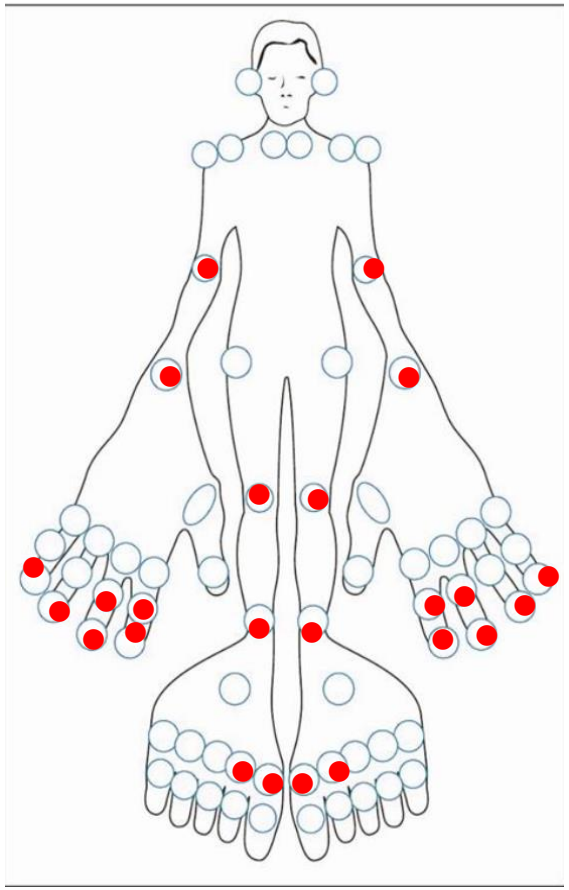
- Συμμετρική πολυαρθρίτιδα
- **DAPSA 55,54**

Patient characteristics

- Κακή ποιότητα ζωής
- κατάθλιψη

PsO characteristics

- Ψωριάση κατά πλάκας τριχωτό κεφαλής ,κορμό , άνω και κάτω άκρα
- **BSA 28%**
- **PASI 14**
- ονυχοδυστροφία



Κλινική Περίπτωση : Πορεία νόσου

Διάγνωση Ψωρίασης — 2008, 15 ετών

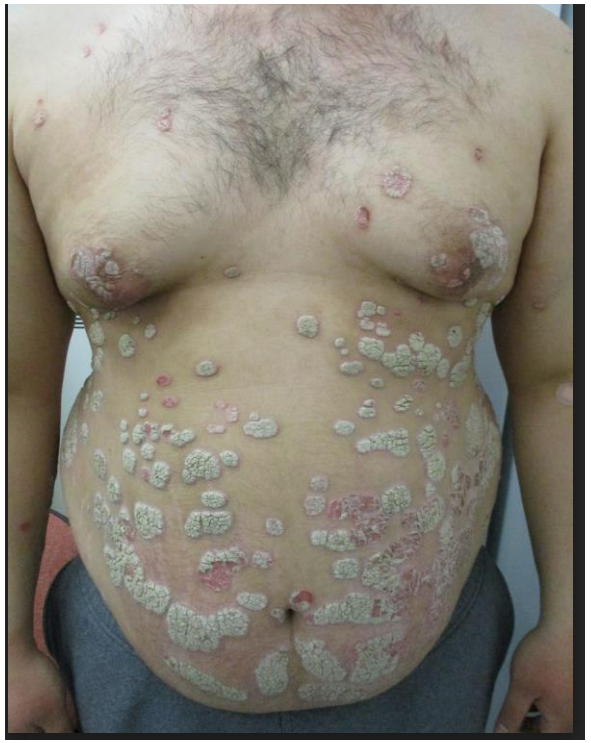
Διάγνωση Ψωριασικής Αρθρίτιδας — 2014, 22 ετών

Persistent PSO and PsA

GUS 100mg W0,W4,q8w — Ιανουάριος 2021 , 29 ετών

Ιανουάριος 2021

BSA %	28 %
PASI	14
DAPSA 55,54	TJC = 22 SJC = 12 PtGA (0-10) = 10 PGA (0-10) = 8 CRP = 35,4 mg/L



έναρξη GUS

GUS 100 mg Week 0, Week 4, q8w

Κλινική Περίπτωση : Πορεία νόσου

Διάγνωση Ψωρίασης — 2008, 15 ετών

Διάγνωση Ψωριασικής Αρθρίτιδας — 2014, 22 ετών

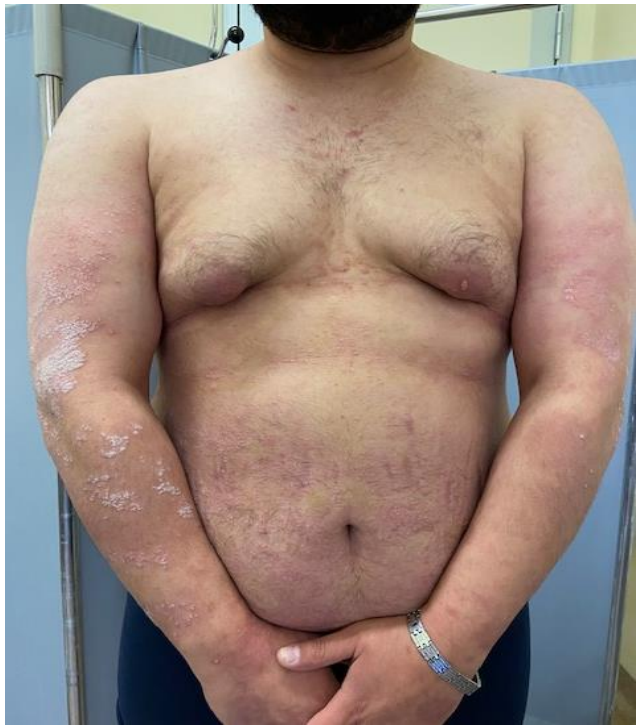
Persistent PSO and PsA

GUS 100mg W0,W4,q8w — Ιανουάριος 2021 , 29 ετών

GUS — 2022

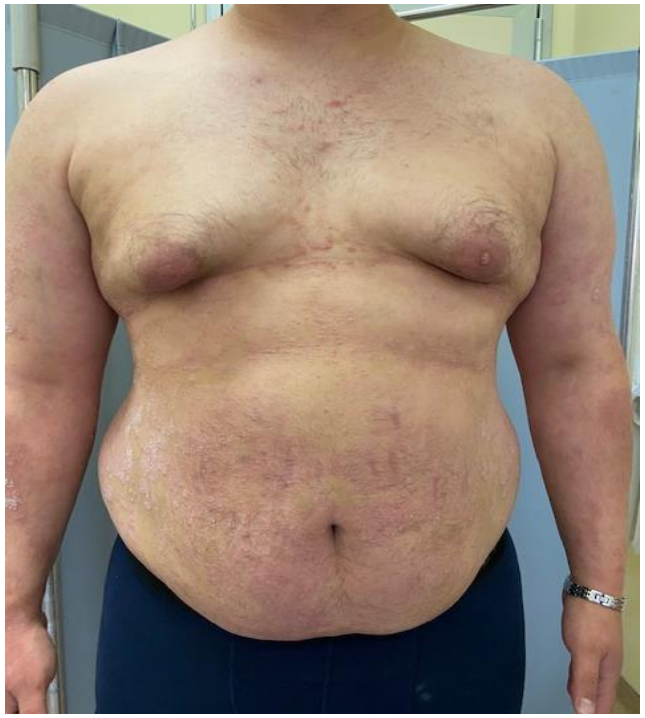
6 μήνες μετά ...

DAPSA	16
PASI	7



18 μήνες μετά ...

DAPSA	6
PASI	2



Κλινική Περίπτωση : Πορεία νόσου

Διάγνωση Ψωρίασης — 2008, 15 ετών

Διάγνωση Ψωριασικής Αρθρίτιδας — 2014, 22 ετών

Persistent PSO and PsA

GUS 100mg W0,W4,q8w — Ιανουάριος 2021 , 29 ετών

GUS — 2022

Σήμερα …

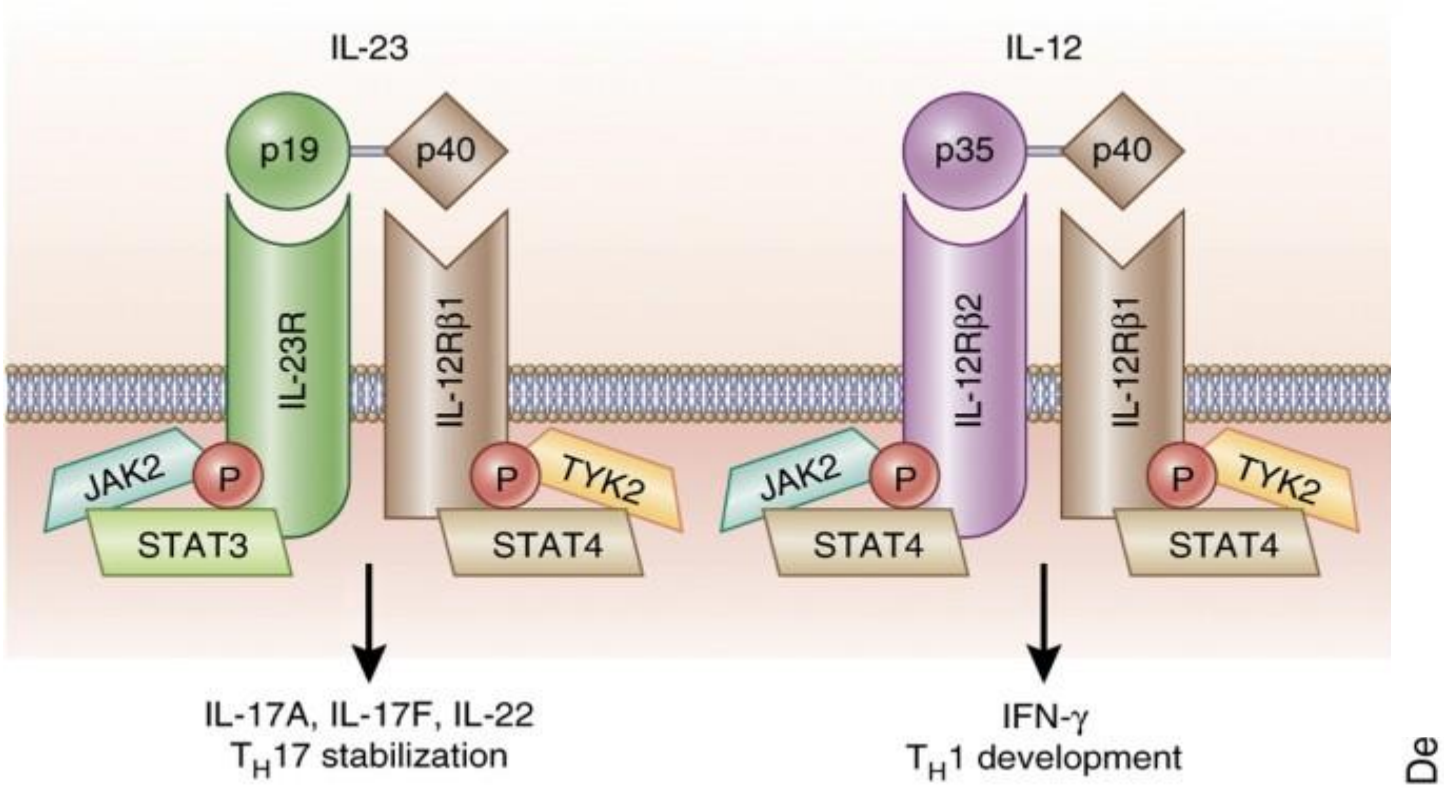
Remission: σε αρθρώσεις, δέρμα και στην ψωριασική ονυχία

Βελτίωση ποιότητας ζωής

- Διακοπή αγωγής με SNRI
- Άσκηση και βελτίωση του BMI
- Κλιμάκωση θεραπείας με στατίνη

Χωρίς σημάνσεις ασφάλειας

Guselkumab is a fully human IgG1λ monoclonal antibody against the p19 subunit of the IL-23 cytokine



IL-12 and IL-23 cytokines: from discovery to targeted therapies for immune-mediated inflammatory diseases
•Michele W L Teng et al. *Nature Medicine* **volume 21**, pages719–729 (2015)

Phase 3 Clinical Development of Guselkumab in PsA

Trial	Phase 3	Study Population
DISCOVER 1	bio-naïve and TNF-experienced study	Patients are Bio-naive or TNF-experienced**. TNF-experienced** patients received ≤2 prior anti-TNFα agents, accounting for **approximately 30% of the overall study population.**
DISCOVER 2	bio-naïve study	**All patients are bio-naïve** and have had an inadequate response to standard therapies (e.g. DMARDS, apremilast and NSAIDs)
COSMOS	TNF irresponders study	**All patients are TNF-experienced**. Bio-experienced patients received previous treatment with either 1 or 2 anti-TNF alpha agents.

70% patients = Naïve to bDMARDs

30% = TNF experienced

100% patients = Naïve to bDMARDs

100% patients = TNF experienved

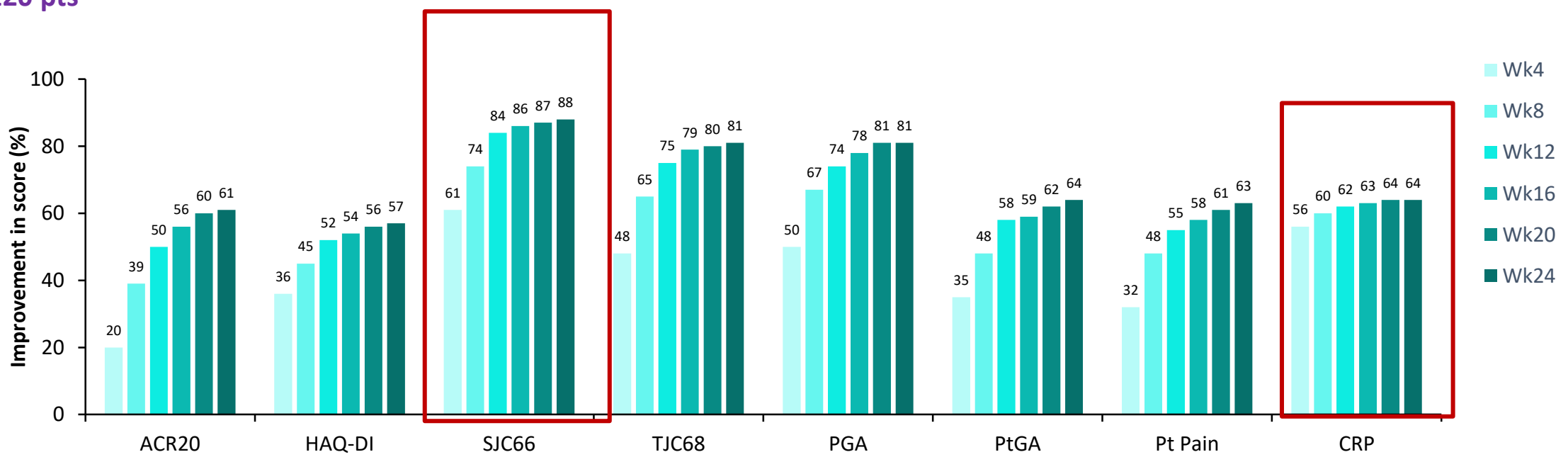
Αποτελεσματικότητα σε όλες τις παραμέτρους του ACR 20 από την 1η χορήγηση

- **48–61% of pts** had ≥20% improvement in **TJC68/SJC66/PGA at Wk 4**;
- **45–48% of pts** had ≥20% improvement in **HAQDI, PtGA, and Pt Pain by Wk 8**

- By Wk 24, ≥20% improvement was reported for SJC66/TJC68/PGA (>80% of pts), PtGA, CRP, Pt Pain (**63–64% of pts**), and HAQ-DI (**57% of pts**)

Effects of GUS on Individual Components of ACR Response

N=1120 pts



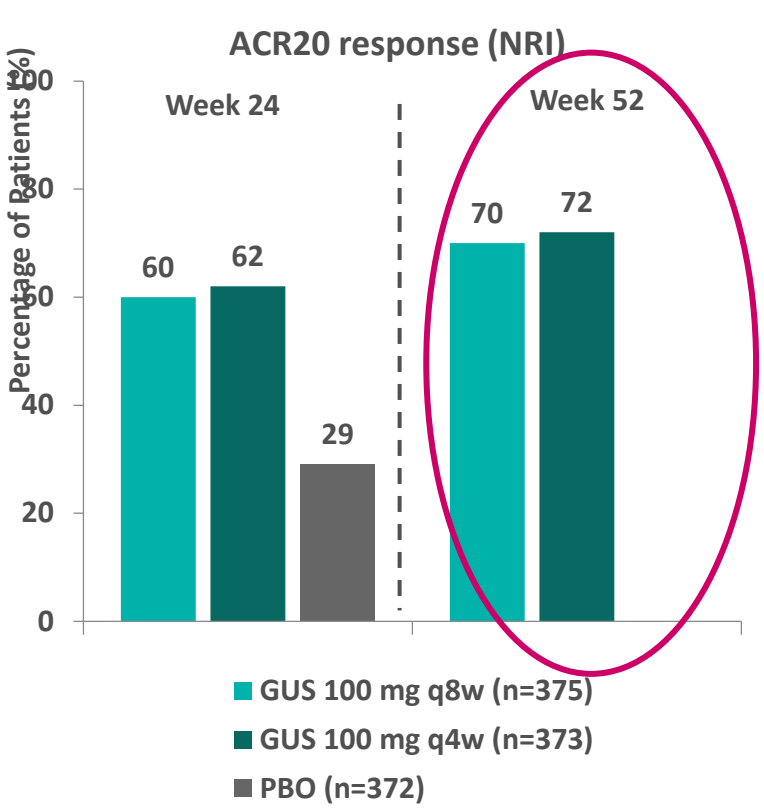
- Pts were randomized to GUS 100 mg Q4W (N=373); GUS 100 mg at Wk 0, Wk 4, then Q8W (N=375); or matching PBO (N=372)
- For each ACR component, ≥20% improvement from BL was assessed over time through Wk 24 for the combined (Q4W+Q8W) GUS groups

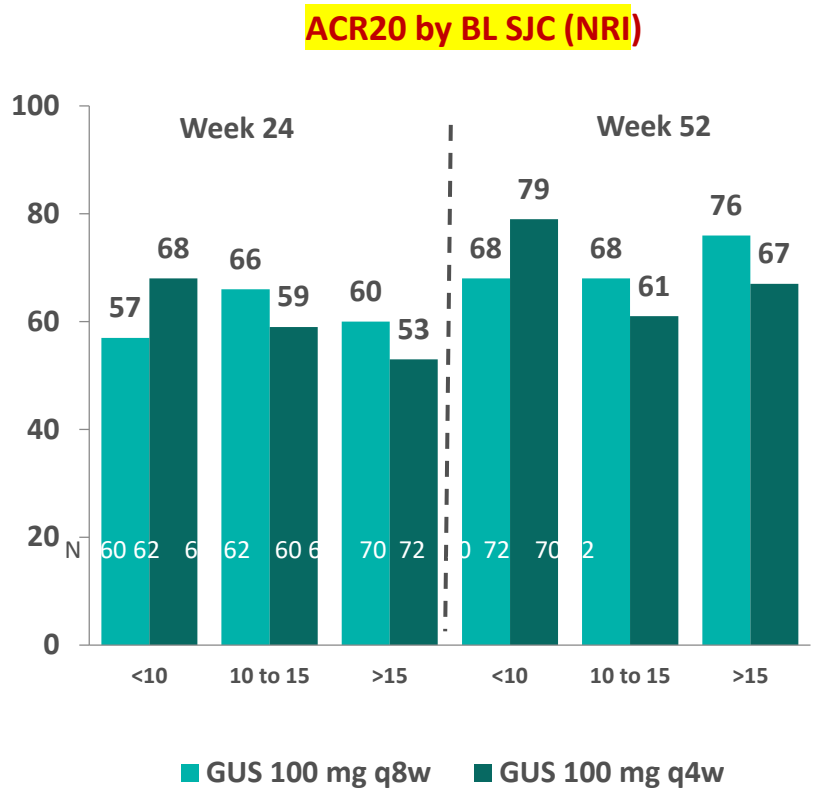
Nash et al. EULAR 2021 AB0525

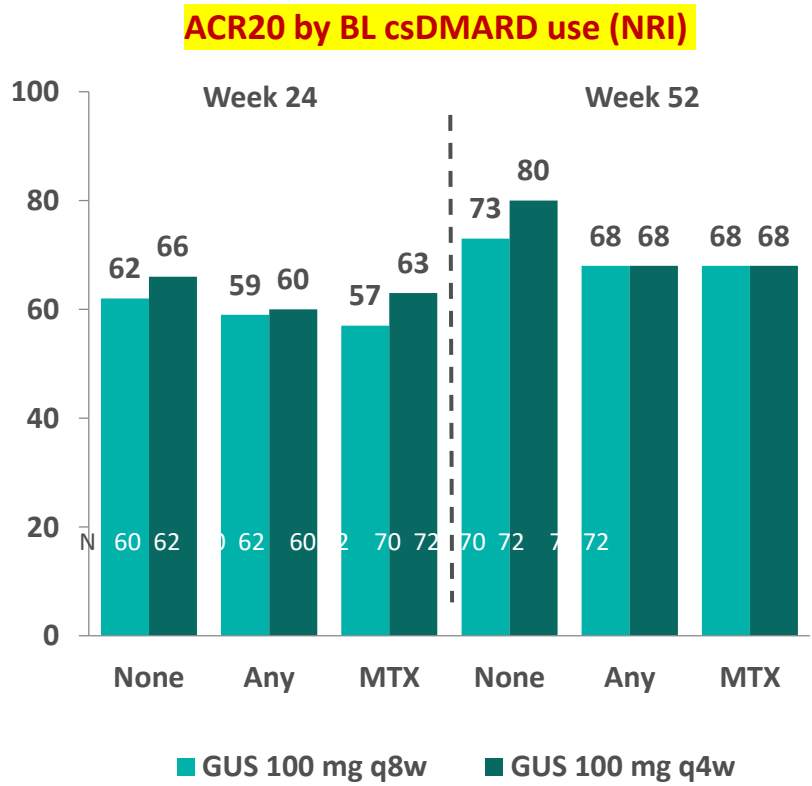
Αποτελεσματικότητα κατά ACR ανεξάρτητα από τα baseline χαρακτηριστικά

Pooled data from DISCOVER 1 and DISCOVER 2 (**N=1120**)
Mean SJC=11, mean TJC=21, 68% used csDMARDs

ACR20 through Week 52 by baseline characteristics



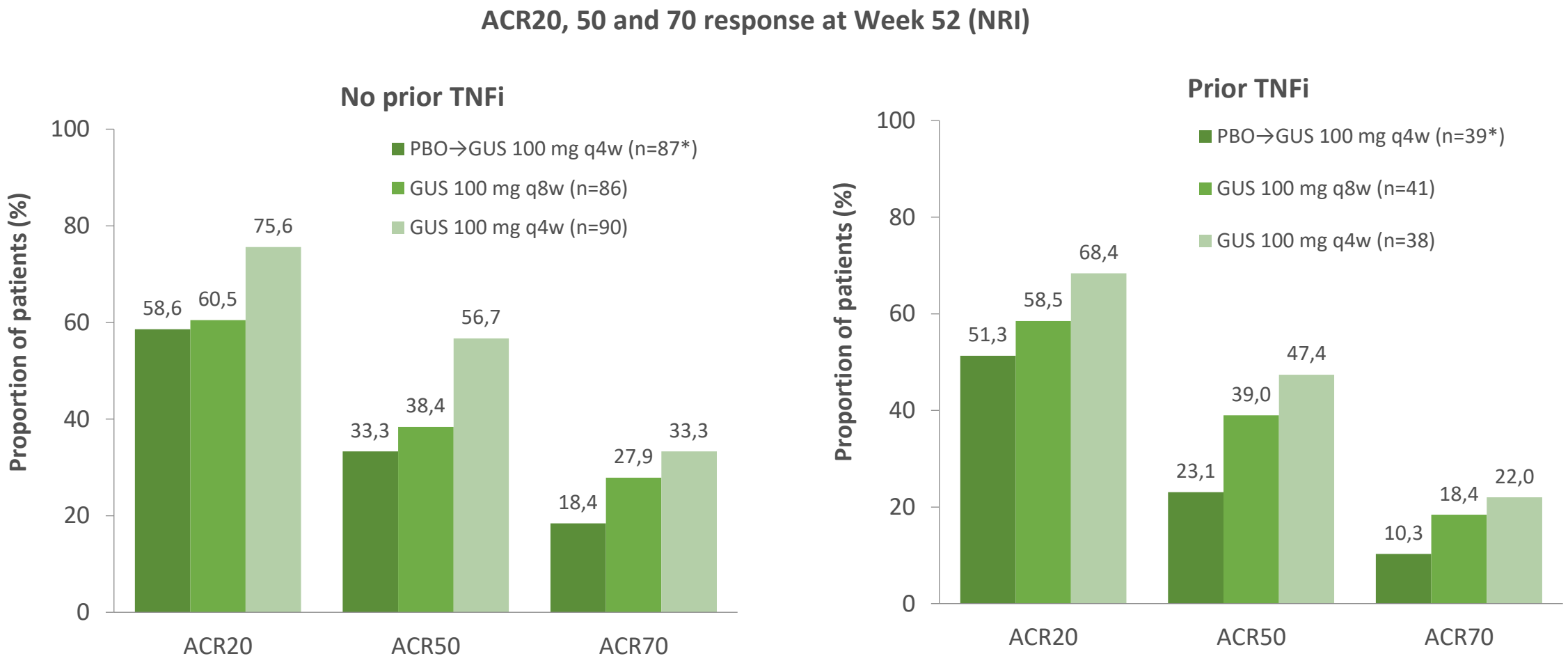




ACR, American College of Rheumatology; BL, baseline; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; MTX, methotrexate; PBO, placebo; q4w, every 4 weeks; q8w, every 8 weeks; SJC, swollen joint count; TJC, tender joint count.

Ritchlin CT, *et al*. *RMD Open* 2022;8:e002195. doi:10.1136/rmdopen-2022-002195

Αποτελεσματικότητα κατά ACR ανεξάρτητα από την προηγούμενη θεραπεία με anti-TNFi

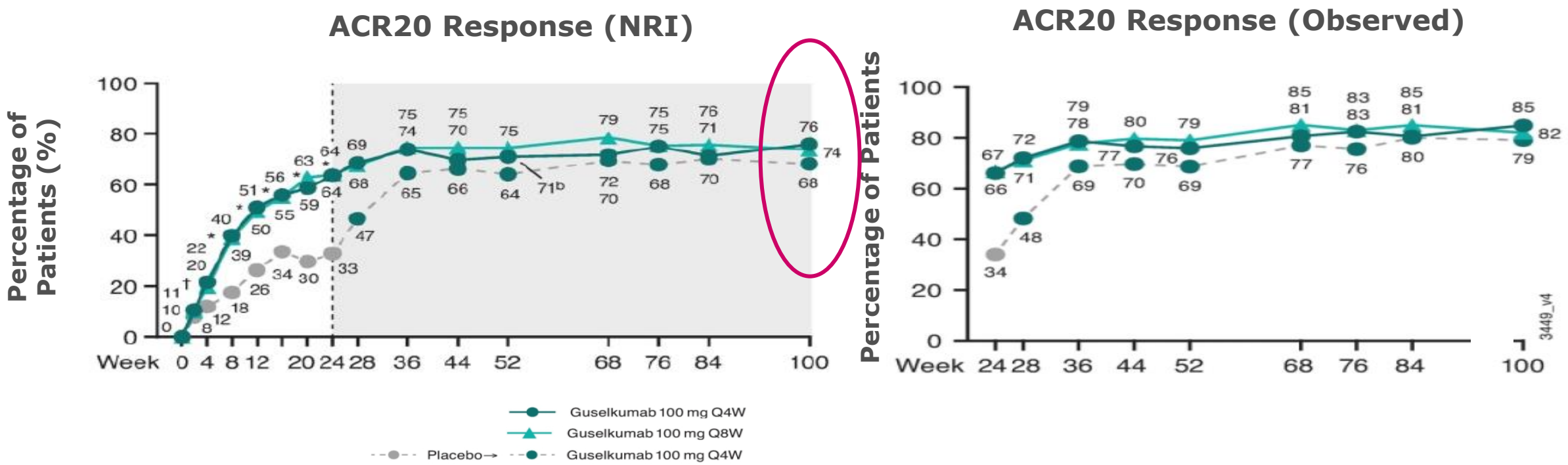


*Among the 39 TNFi-experienced and 87 TNF-naïve patients randomised to receive PBO followed by GUS q4w, 7 and 5, respectively, received PBO only and 32 and 82, respectively, started GUS q4w at Week 24 (post-Week 24 response assessments).
ACR, American College of Rheumatology; GUS, guselkumab; PBO, placebo; q4w, every four weeks; q8w, every eight weeks ; TNFi, tumour necrosis factor inhibitor.

Ritchlin CT, *et al*. *RMD Open* 2021;7:e001457. doi:10.1136/rmdopen-2020-001457

Διατήρηση θεραπευτικού αποτελέσματος στα 2έτη

88% of randomized and treated patients completed study treatment



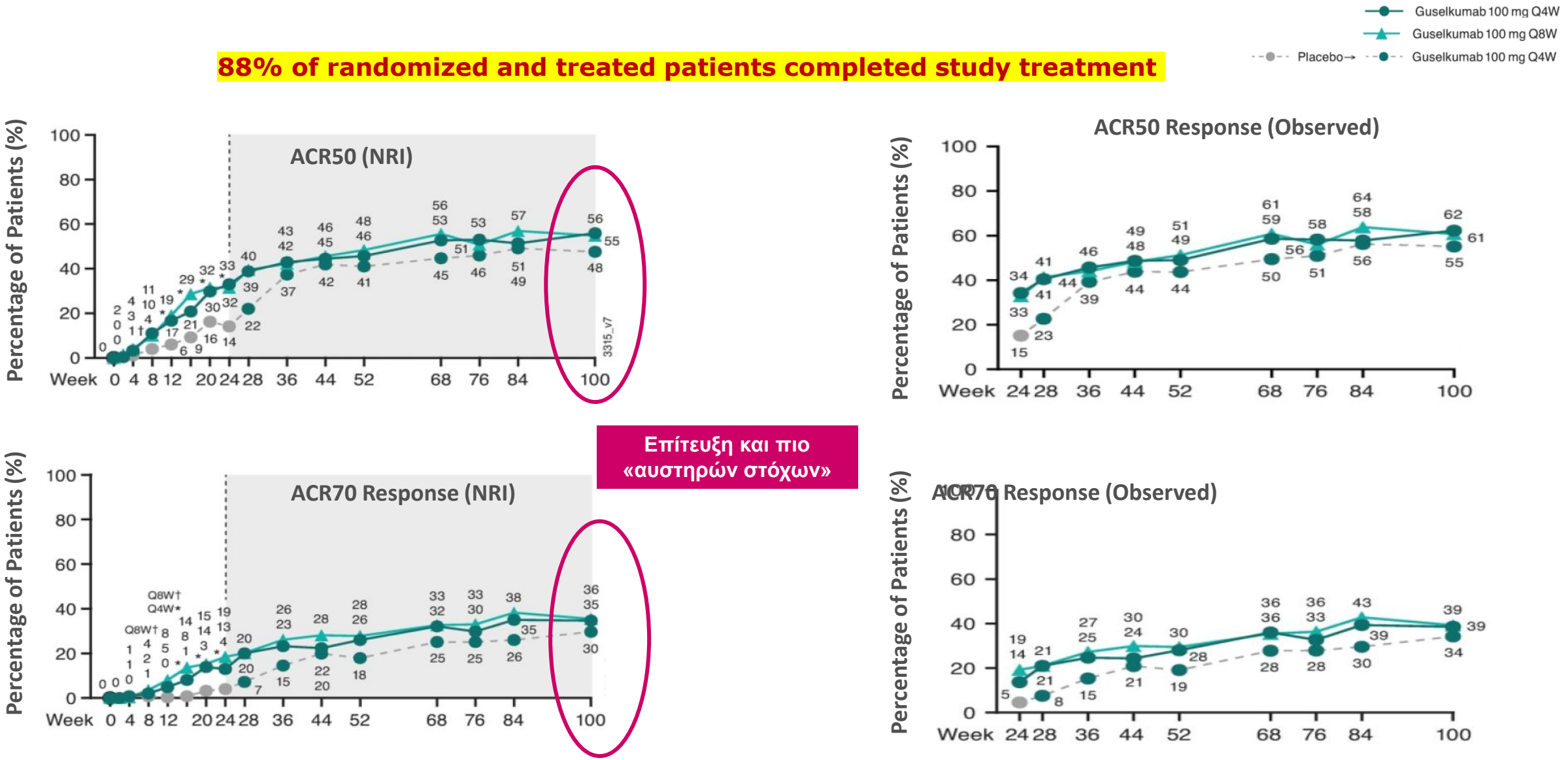
*p≤0.001; †p<0.05
ACR20: at least 20% improvement in American College of Rheumatology response criteria; GUS: guselkumab;
NRI: non-responder imputation; PBO: placebo. NRI=non-responder imputation. Response rates among randomized pts with applicable treatment failure rules and missing data considered non-responders

McInnes et al. Arthritis Rheumatol 2021; e-pub 01NOV; doi:10.1002/art.42010;

DISCOVER 2

Διατήρηση θεραπευτικού αποτελέσματος στα δυο έτη

88% of randomized and treated patients completed study treatment



Επίτευξη και πιο «αυστηρών στόχων»

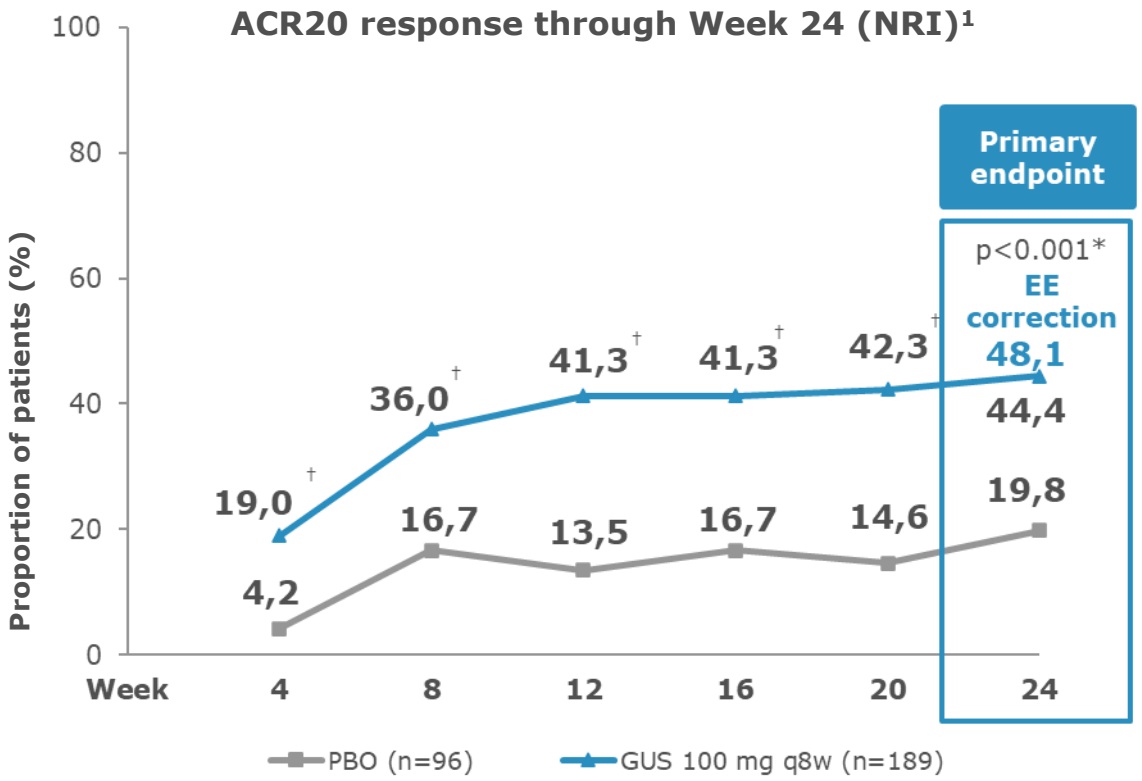
*p≤0.001; †p<0.05

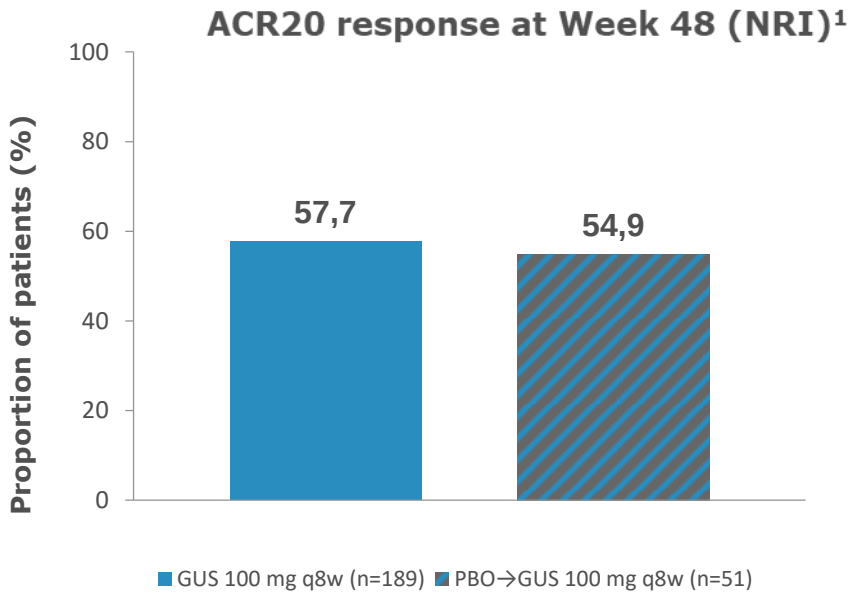
ACR50/70: at least 50/70% improvement in American College of Rheumatology response criteria; GUS; guselkumab; NRI: non-responder imputation; PBO: placebo.

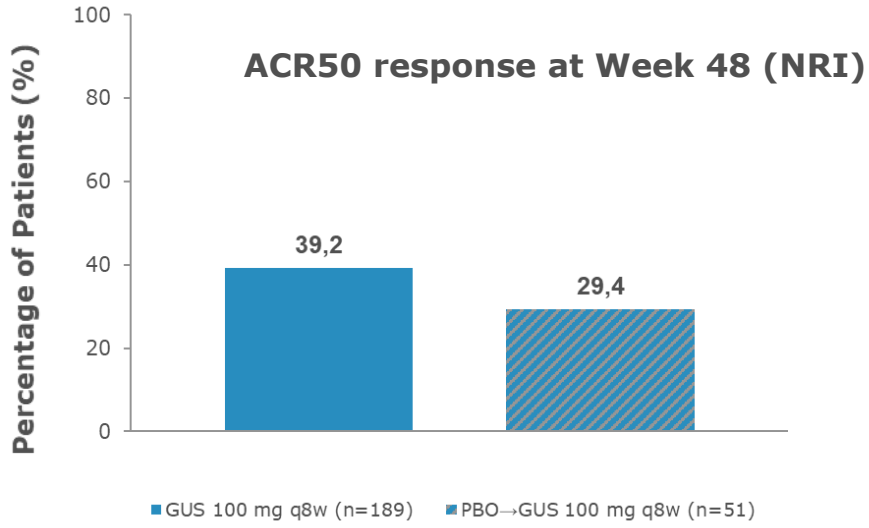
McInnes et al. Arthritis Rheumatol 2021; e-pub 01NOV; doi:10.1002/art.42010;

Αποτελεσματικότητα σε ασθενείς που έχουν αποτύχει σε έναν ή δυο anti-TNFs

88% completed study agent through Week 44







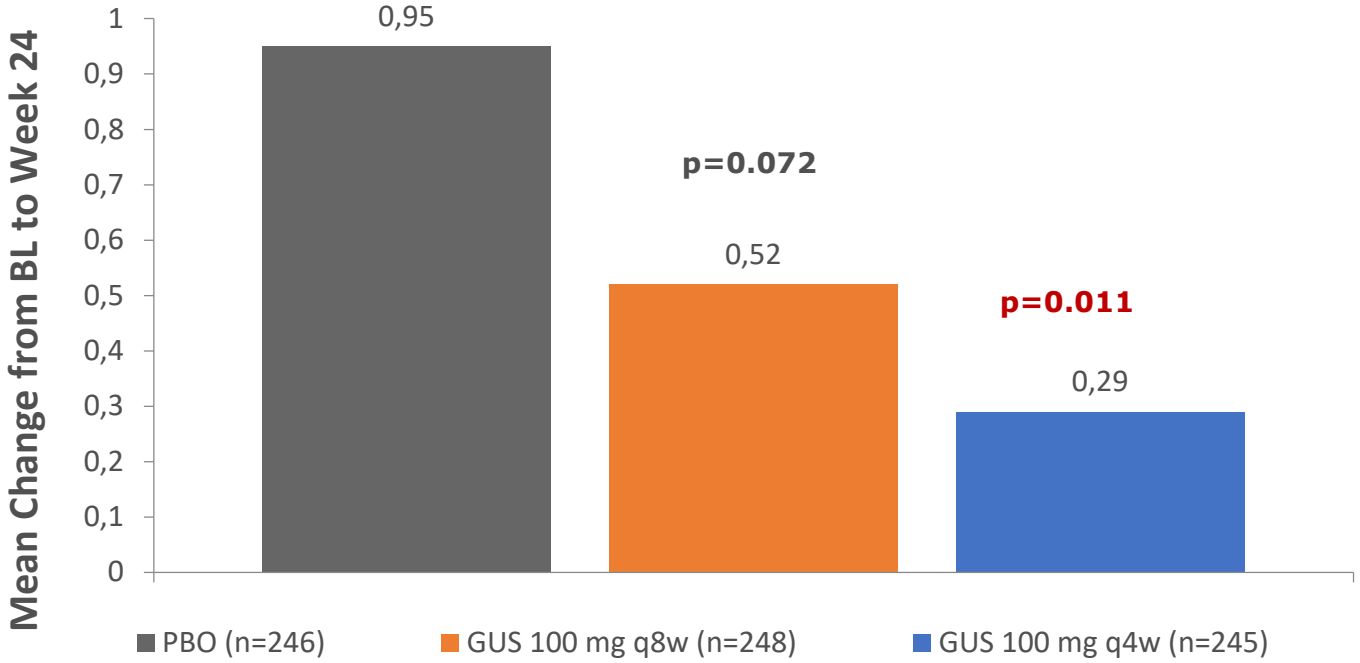
*p<0.001 adjusted for multiplicity testing; †p<0.001 nominal (not adjusted for multiplicity testing); ‡Efficacy results for the PBO→GUS group at Week 48 include patients who did not enter EE and crossed over to GUS at Week 24 (those who entered EE at W16 were considered non-responders at subsequent timepoints). ACR, American College of Rheumatology; EE, early escape; GUS, GUSELKUMAB; NRI, non-responder imputation; PBO, placebo; q8w, every 8 weeks.

Coates LC, et al. Ann Rheum Dis 2021;**0**:1–11. doi:10.1136/annrheumdis-2021-220991

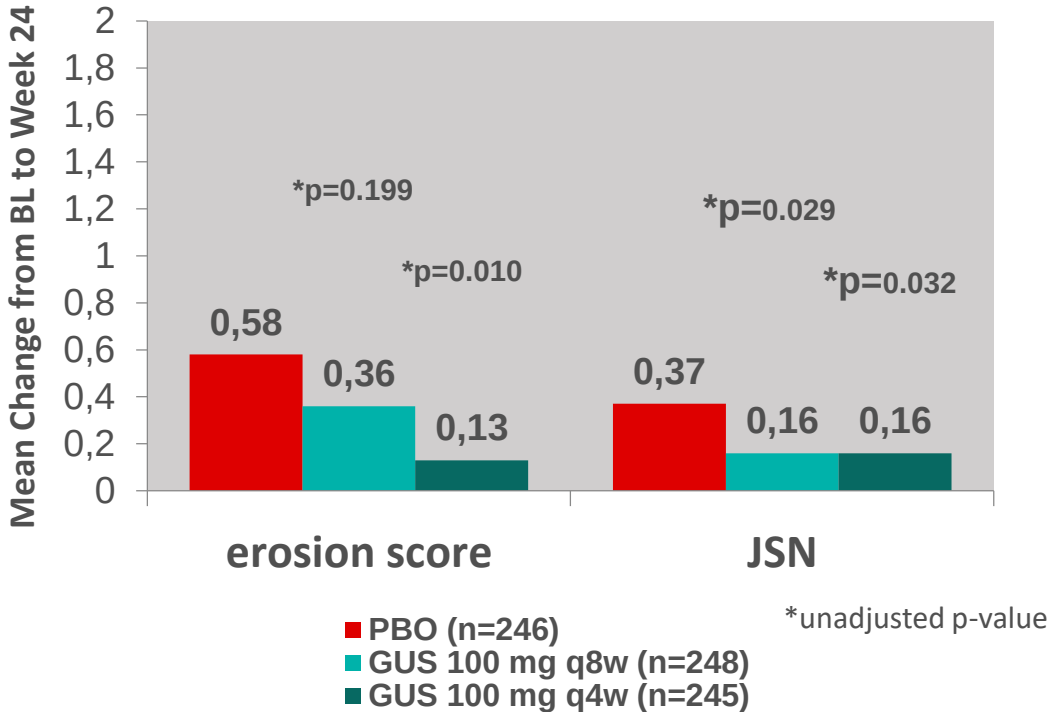
DISCOVER 2

Μειωμένη ακτινολογική «εξέλιξη» στους ασθενείς υπό Guselkumab σε σχέση με το εικονικό φάρμακο την 24 εβδομάδα

LS Mean Change in modified vdHSS from BL to Week 24



LS Mean Change in Erosions and Joint Space Narrowing from BL to Week 24 (FAS



*unadjusted p-value

P values shown are for each dose vs. PBO dose.

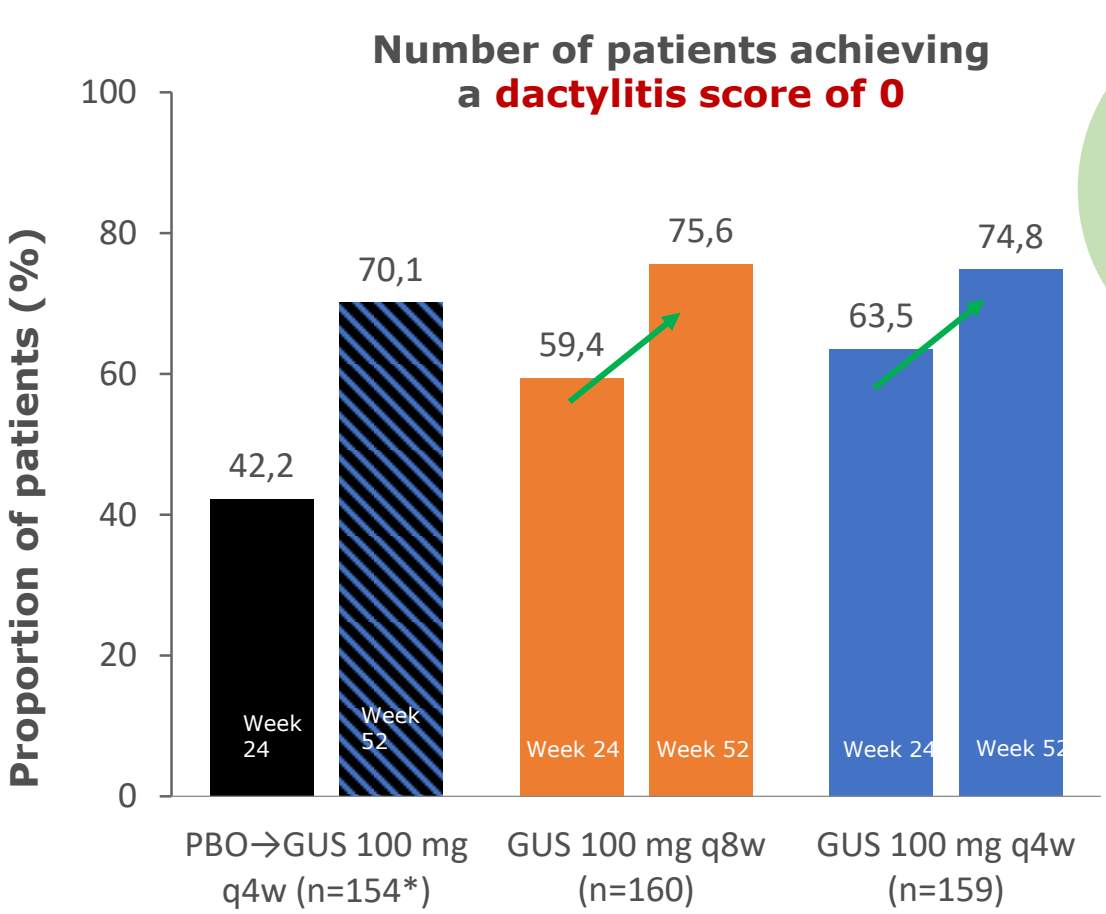
BL, baseline; GUS, guselkumab; PBO, placebo; q4w, every four weeks; q8w, every eight weeks; vdHSS, van der Heijde Sharp Score.

No progression = mean change ≤ 0,5

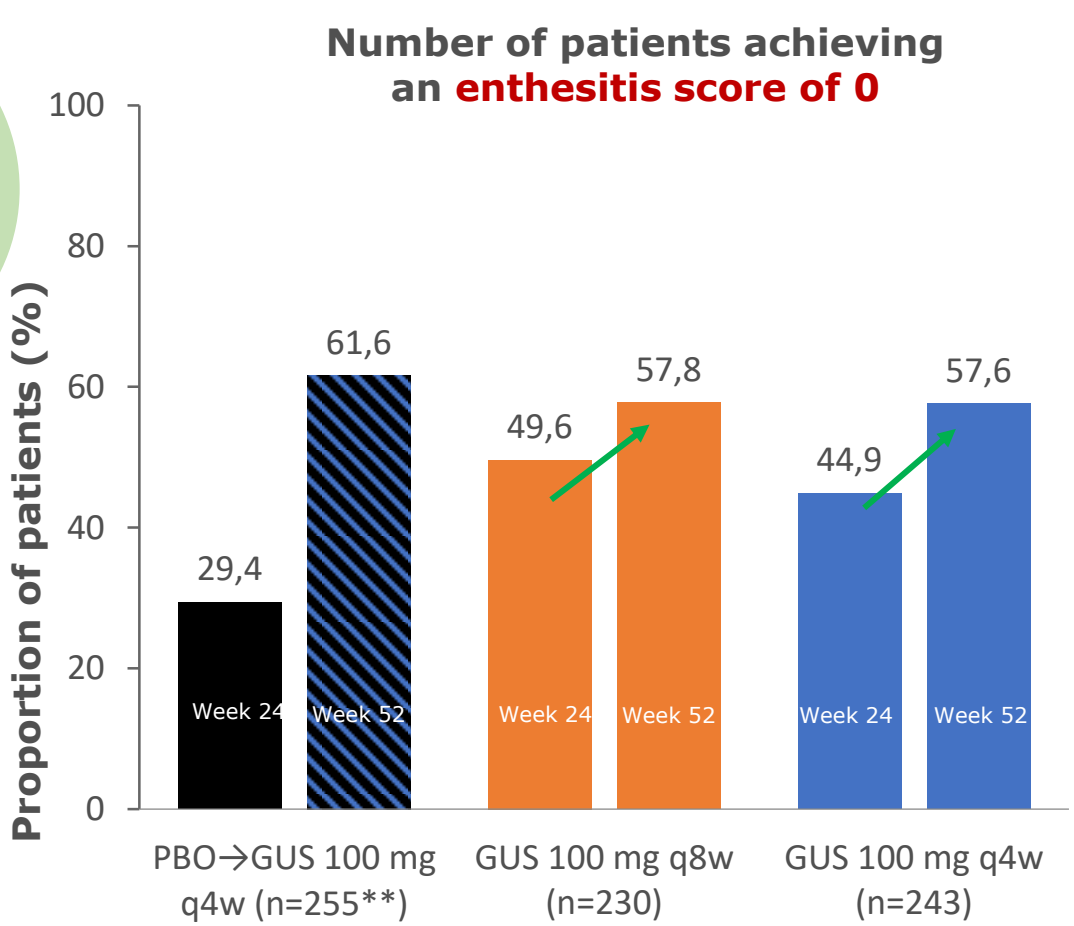
Mease P, et al. *Lancet* 2020;395:1126–1136. Supplement to: Mease et al. Guselkumab in biologic naïve patients with active psoriatic arthritis (DISCOVER-2): a double-blind,randomised, placebo-controlled phase 3 trial. *Lancet* 2020; published online March 13. http://dx.doi.org/10.1016/S0140-6736(20)30263-4.

Αποδρομή Ενθεσίτιδας και Δακτυλίτιδας

Resolution of dactylitis and enthesitis at Week 24 and Week 52



Μεγαλύτερη βελτίωση με την πάροδο του χρόνου

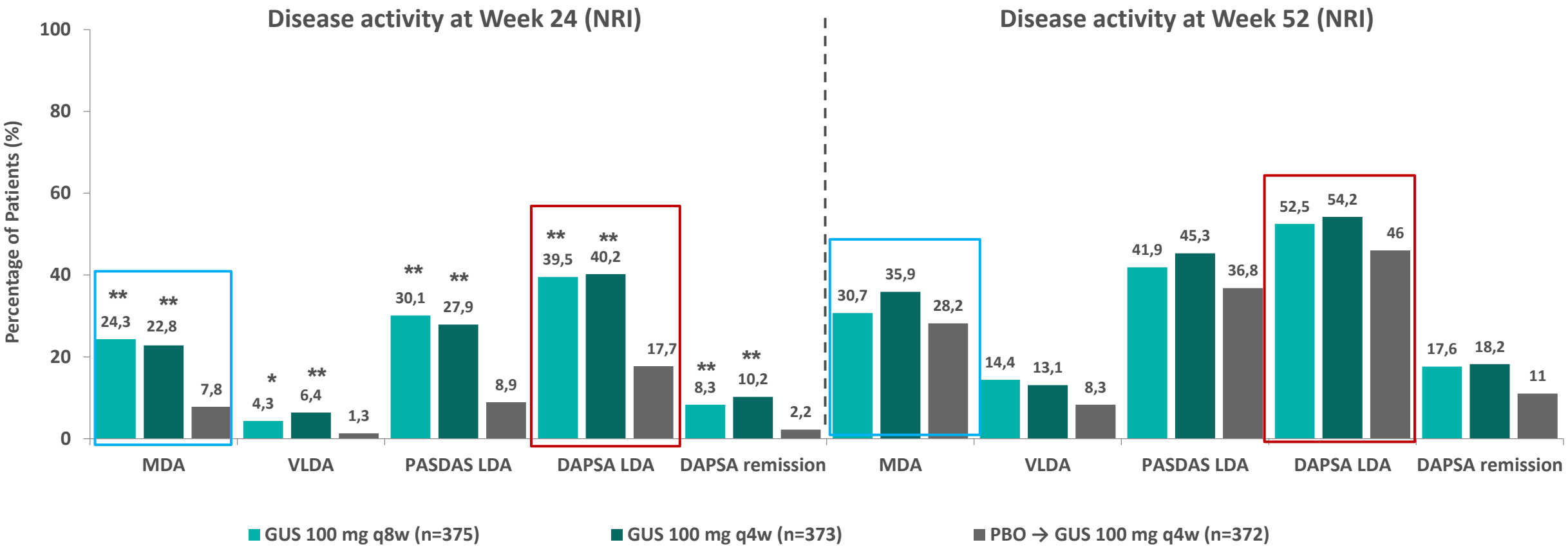


*142 patients crossed over from PBO to GUS q4w at Week 24 and 12 received PBO only before study agent discontinued; **243 patients crossed over to GUS q4w at Week 24 and 12 received PBO only before study agent discontinued.
GUS, guselkumab; PBO, placebo; q4w, every four weeks; q8w, every eight weeks.

1. McInnes IB, et al. Presented at the EULAR e-Congress, June 2020. Poster 0402 2..Rheumatology 2021;60:5337–5350doi:10.1093/rheumatology/keab285

From **1120 pts** in Discover 1 and 2 ,728 (**65%**) had **enthesitis** and 473 (**42%**) had **dactylitis** in BL

Διατήρηση αποτελέσματος σε πιο «απαιτητικούς» θεραπευτικούς στόχους



*p<0.05; **p<0.001; Unadjusted (nominal) p-values are not controlled for multiplicity and are descriptive/supportive only. Further information on PASDAS and DAPSA cut-off values can be found in the slide notes.

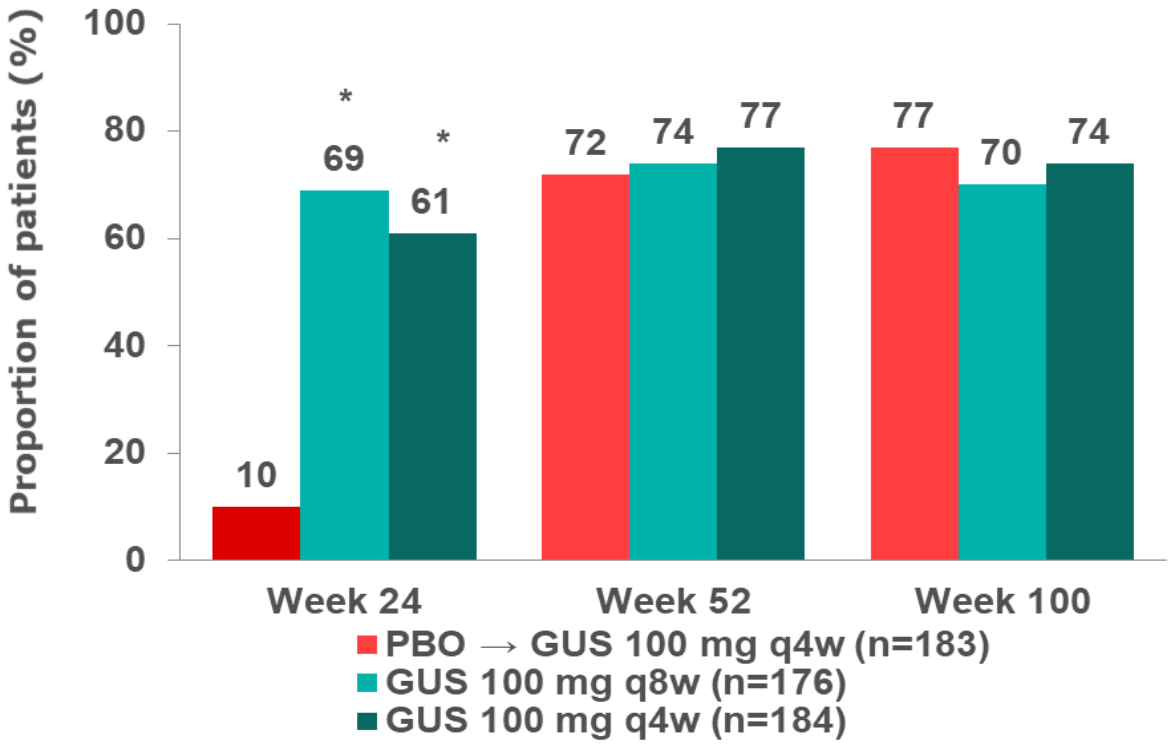
GUS, guselkumab; DAPSA, Disease Activity Index for Psoriatic Arthritis; LDA, low disease activity; MDA, Minimal Disease Activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; q4w, every 4 weeks; q8w, every 8 weeks; VLDA, Very Low disease Activity.

Coates et al. EULAR 2021 POS1024.

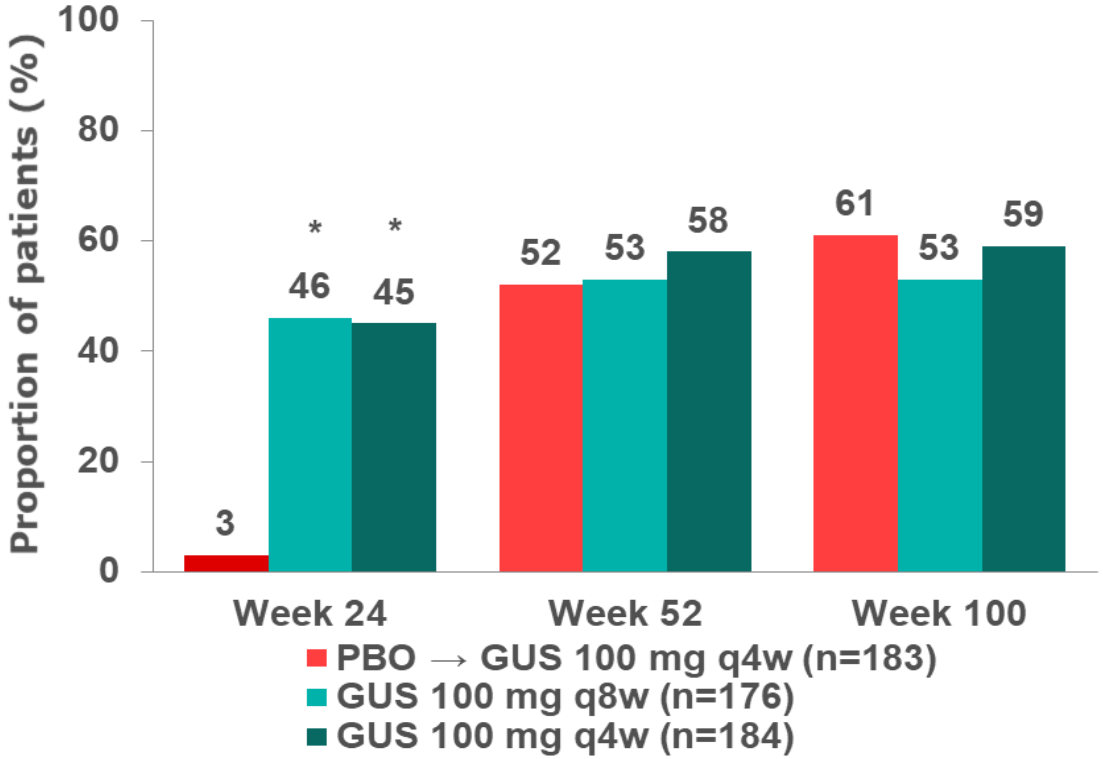
Αποτελεσματικότητα στο δέρμα σε ασθενείς με BSA ≥ 3% and IGA ≥ 2 (NRI)

88% completed study agent through Week 100

PASI 90 Responses through Week 100 (NRI)



PASI 100 Responses through Week 100 (NRI)



*unadjusted p-value p<0.0001

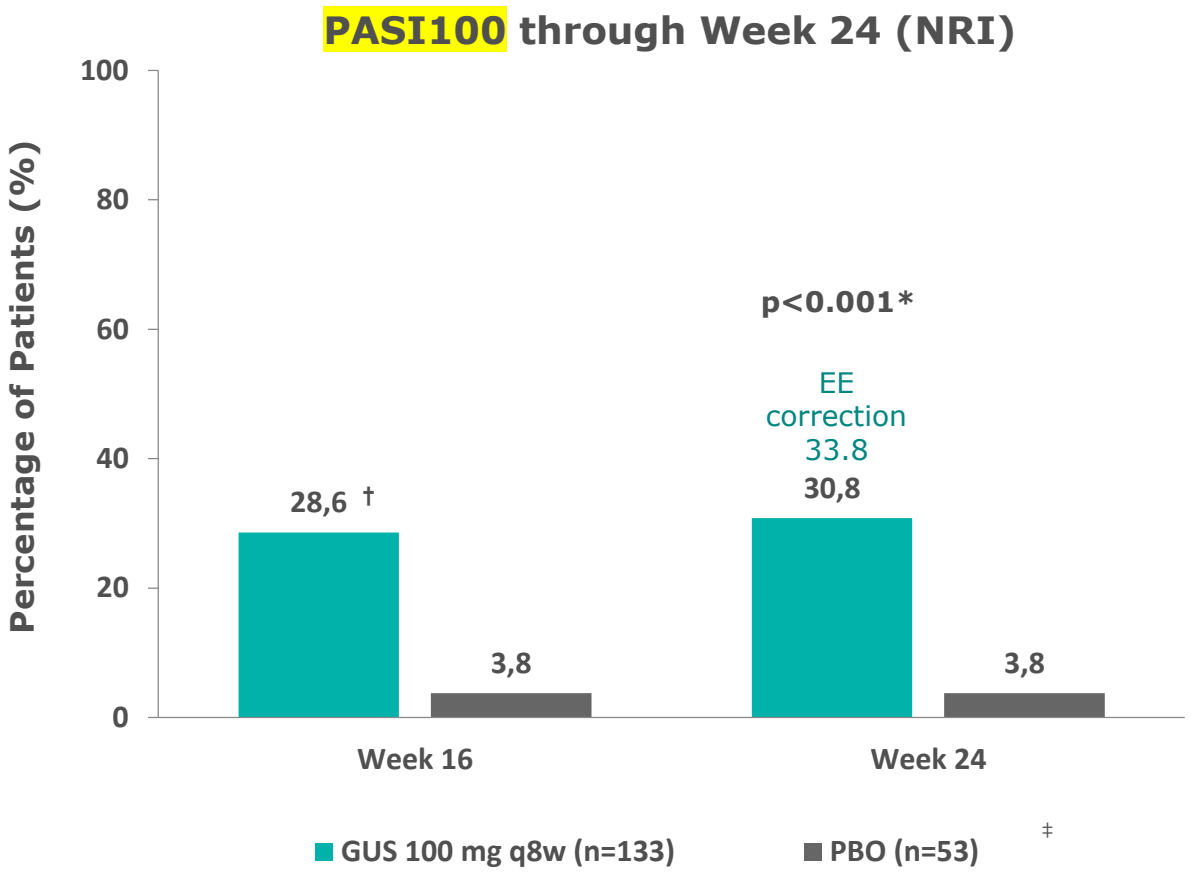
BSA, body surface area; GUS, guselkumab; IGA, Investigator Global Assessment; PASI, Psoriatic Area and Severity Index; PBO, placebo; q4w, every 4 weeks; q8w, every 8 weeks

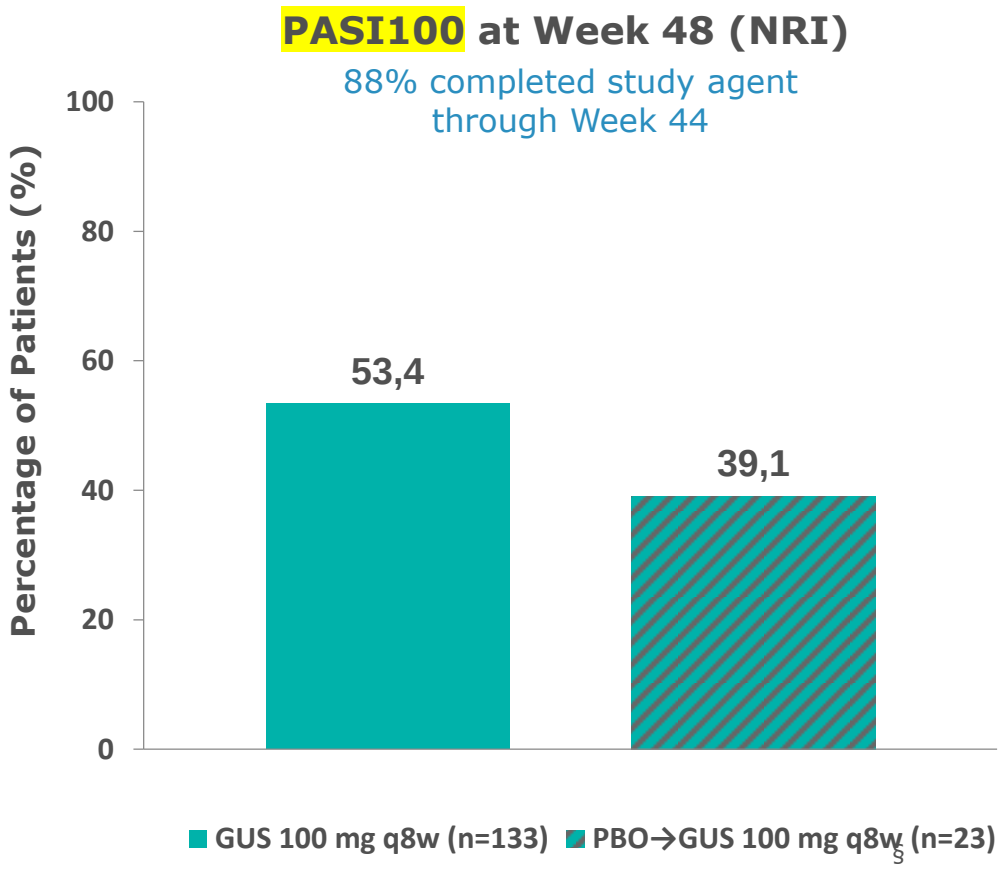
Mease et al. Lancet 2020;395:1126-36

McInnes et al. Arthritis & Rheumatology Vol. 73, No. 4, April 2021, pp 604–616 DOI 10.1002/art.41553

McInnes et al. Arthritis Rheumatol 2021; e-pub 01NOV; doi:10.1002/art.42010.

Πλήρης κάθαρση δέρματος σε TNF IR ασθενείς με BSA ≥ 3% and IGA ≥ 2 (NRI)





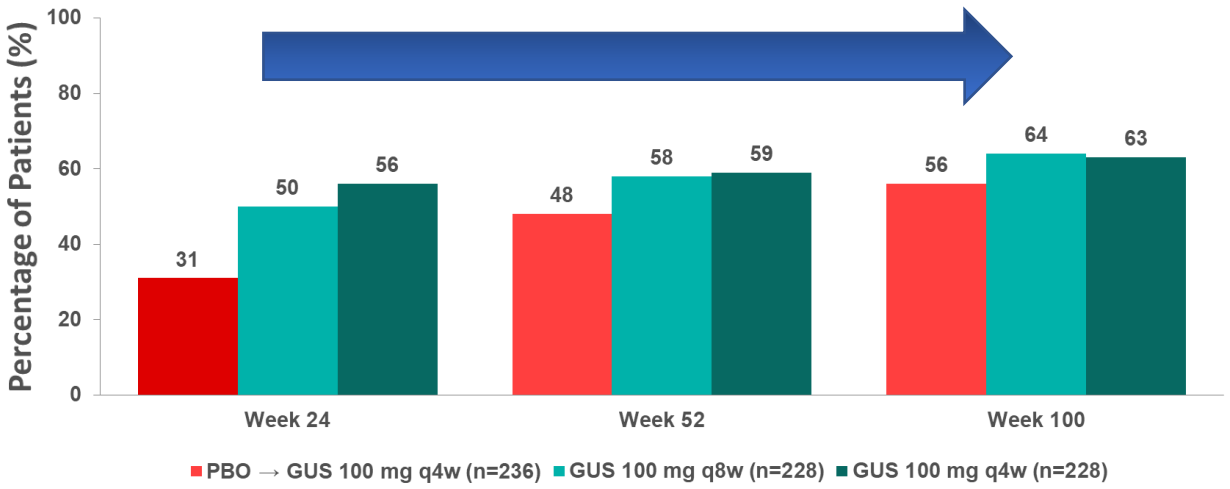
*p<0.001 adjusted for multiplicity testing; †p<0.001 nominal (not adjusted for multiplicity testing); ‡In patients with significant skin disease at baseline; §Efficacy results for the PBO→GUS group at W48 include pts who did not enter EE and crossed over to GUS at W24 (those who entered EE at W16 were considered nonresponders at subsequent timepoints).
EE, early escape; GUS, guselkumab; NRI, non-responder imputation; PASI, Psoriasis Area and Severity Index; PBO, placebo; q8w, every 8 weeks.

Coates LC, et al. Ann Rheum Dis 2021;**0**:1–11. doi:10.1136/annrheumdis-2021-220991

Βελτίωση του λειτουργικού επιπέδου των ασθενών και διατήρηση σε βάθος χρόνου

HAQ-DI ≥0.35 through Week 100 (NRI)

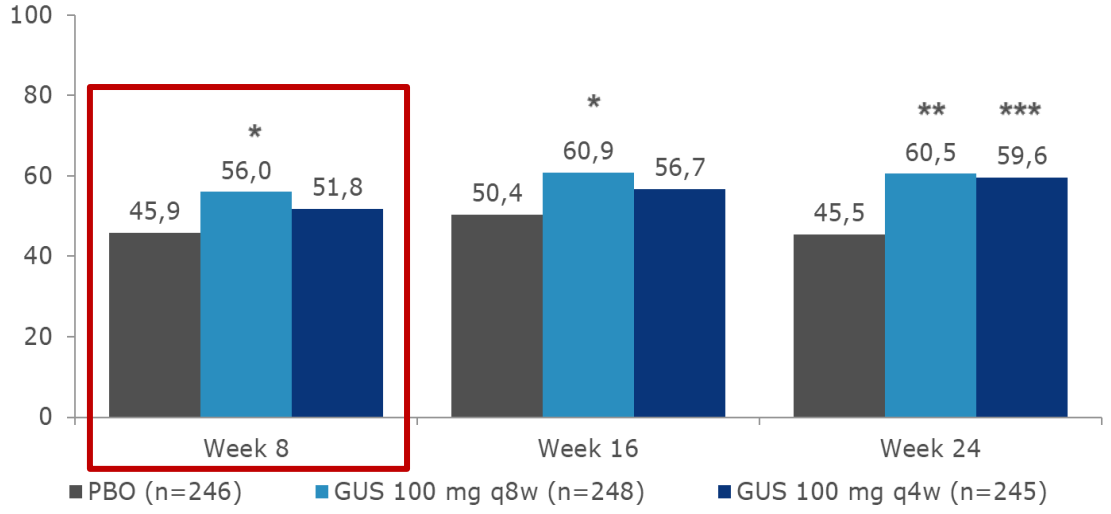
88% completed study agent through Week 100



McInnes et al. Arthritis Rheumatol 2021; e-pub 01NOV; doi:10.1002/art.42010;

Βελτίωση στο αίσθημα κόπωσης από την 8η εβδομάδα

Patients achieving clinically meaningful improvement (≥ 4 point change) in FACIT-Fatigue score at Week 8, 16 and 24



*P vs. placebo<0.05; **P vs. placebo<0.001; ***P vs. placebo<0.01.

Rahman et al. Arthritis Research & Therapy (2021) 23:190https://doi.org/10.1186/s13075-021-02554-3

Adverse Events of Interest

Time period	Week 0-24				1 Year[a]			
Treatment group	**PBO[b]**	**GUS 100 mg q8w**	**GUS 100 mg q4w**	**GUS all[c]**	**PBO → GUS 100 mg q4w[d]**	**GUS 100 mg q8w**	**GUS 100 mg q4w**	**GUS all[c]**
Patients, N	372	375	373	748	352	375	373	1100
Death, %	0.5	0	0	0	0	0	0	0
Malignancy, %	0.3	0.5	0	0.3	0.3	0.5	0	0.3
MACE, %	0.3	0	0.3	0.1	0	0	0.3	0.1
Opportunistic infections, %	0	0	0	0	0	0	0	0
Tuberculosis, %	0	0	0	0	0	0	0	0
IBD, %	0.3	0	0	0	0	0	0	0
Injection-site reaction, %	0.3	1.3	1.1	1.2	1.1	1.6	2.4	1.7
Anti-GUS antibody positive*, %	NA	1.6 (n=373)	2.4 (n=371)	2.0 (n=744)	4.0 (n=350)	4.8 (n=373)	4.6 (n=371)	4.5 (n=1094)

*Presence of antibodies to GUS in serum samples of GUS-treated patients was assessed using a validated immunoassay method; [a]Through Week 60 for DISCOVER 1 and Week 52 for DISCOVER 2. [b]For pts who switched from PBO to GUS, only data prior to first GUS administration were included in this group; [c]Combined GUS q8w and q4w treatment groups (incl. pts who crossed over from PBO for 1-year results). [d]For pts who switched from PBO to GUS, only data on and after the first GUS administration were included in this group. GUS: Guselkumab; IBD: Inflammatory bowel disease; N: Number of patients; MACE: Major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke); PBO: Placebo; q8w/q4w: Every eight/four weeks

Rahman et al. J Rheumatol 2021; epub 01MAY doi: 10.3899/jrheum.201532

Δεδομένα ασφάλειας σε βάθος 2ετίας (PsA) και 5ετίας (PsO)

Μακροχρόνιο ευνοικό προφίλ ασφάλειας σε ασθενείς με ενεργό Ψωριασική Αρθρίτιδα και μέτρια-σοβαρή Ψωρίαση
χωρίς επισημάνσεις ή προειδοποιήσεις

	Pooled Psoriasis through 5 Years			Pooled PsA through 2 Years				
	GUS 100 mg q8w (N=1221)[b]	ADA→GUS 100 mg q8w (N=500)[c]	GUS Combined (N=1721)	GUS Combined (N=1229)	GUS 100 mg q8w (N=475)	PBO→GUS 100 mg q4w (N=352)[a]	PBO→GUS 100 mg q8w (N=29)[a]	GUS Combined (N=1229)
Total Patient-years (PY)	5254	1912	7166	645	748	461	17	1871
Mean PY	4.3	3.8	4.2	1.7	1.6	1.3	0.6	1.5
Events/100 PY[d]								
Overall serious AE (SAE)	5.18	4.55	5.01	4.65	6.42	5.86	0.00	5.61
Gastrointestinal-related SAE	0.44	0.42	0.43	0.46	0.27	0.00	0.00	0.27
Opportunistic infections	0.00	0.00	0.00	0.00	0.27	0.22	0.00	0.16
Candida infections	0.49	0.52	0.50	0.31	0.00	0.00	0.00	0.11
Non-pathogen specific fungal infections, suspicious for candida	0.11	0.16	0.13	0.00	0.27	0.00	0.00	0.11
Uveitis/Iridocyclitis	0.00	0.00	0.00	0.00	0.13	0.00	0.00	0.05

a.For pts in PBO who change d treatment to GUS due to cross –over or inadvertently, only data on and after 1st administration of GUS were included in this group. Data prior to the 1st administration of GUS were not included in this group; b.PBO crossover pts were included in the GUS column after crossover to GUS; c.Events which occurred prior to GUS administration (ADA events) were excluded from the analyses. Only include patients who were randomized to ADA at Week 0 and croosed over to GUS at or after Week 52 for VOYAGE 1 & Week 28 for VOYAGE 2; d.Events are counted only once. *More details on events in notes.* ADA: adalimumab; GUS: guselkumab; PBO: placebo.

Mease et al. ACR 2021 #1804 [poster].

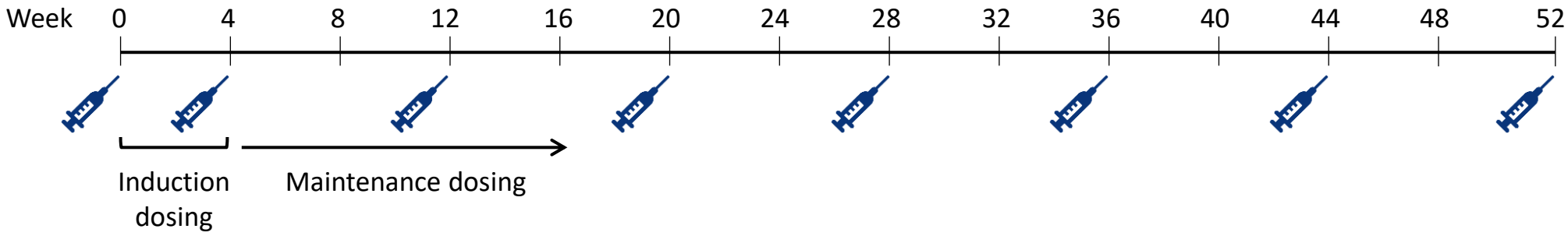
Το Guselkumab …

- Επιτυγχάνει σημαντική βελτίωση στην περιφερική αρθρίτιδα, ενθεσίτιδα, δακτυλίτιδα και ψωρίαση
- Βελτιώνει σημαντικά την ποιότητα ζωής των ασθενών (λειτουργικό επίπεδο , κόπωση)
- Η αποτελεσματικότητά του είναι ανεξάρτητη από τη συγχορήγηση csDMARDs ή την προηγούμενη χρήση antiTNFs
- Η αποτελεσματικότητά του είναι ανεξάρτητη από τα baseline χαρακτηριστικά των ασθενών
- Το θεραπευτικό αποτέλεσμα διατηρείται σε βάθος χρόνου
- Ευνοικό προφίλ ασφάλειας σε βάθος 5ετίας στις μελέτες της Ψωρίασης και 2ετίας στις μελέτες της Ψωριασικής Αρθρίτιδας

Δοσολογικό σχήμα του Guselkumab στην Ψωριασική Αρθρίτιδα

The recommended dose of Guselkumab is **100 mg** by **s.c**. injection at **Weeks 0 and 4, followed by a maintenance dose q8w**

Injections in the first year of treatment



For patients at high risk for joint damage according to clinical judgement, a dose of 100 mg q4w may be considered

Consideration should be given to discontinuing treatment in patients who have shown no response after 24 weeks of treatment

PsA, psoriatic arthritis; q4w, every 4 weeks; q8w, every 8 weeks; s.c., subcutaneous. Tremfya (guselkumab) Summary of Product Characteristics, 2022.