Ο ασθενής στο επίκεντρο

Παρουσίαση κλινικών περιστατικών

Πελαγία Κατσιμπρή,
Ρευματολόγος,Επιμελήτρια Α΄,
Μονάδα Ρευματολογίας και Κλινικής Ανοσολογίας
Δ’ Πανεπιστημιακή Παθολογική Κλινική,
ΠΓΝ «Αττικόν», Αθήνα

Melinda, *Tree of Life*

Conflict of Interest

Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις την τελευταία διετία:

UCB .,Janssen, Genesis pharma, Novartis, Abbvie, Hospital Line, Actelion Pharmaceuticals

Προβλέπεται τιμητική αμοιβή από την εταιρεία Janssen για τη συμμετοχή μου στη παρούσα εκδήλωση.

CASE REPORT 1

Άνδρας 28 ετών,

ιδιωτικός υπάλληλος

- α/α : Ψωρίαση από 14 ετών (2007)
- Ψωριασική Αρθρίτιδα από 20 ετών (2013)

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Comorbidities

- Δυσλιπιδαιμία
- Κατάθλιψη
- BMI 45 (ΣΒ:130kg, Υ:1,7m)

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Comorbidities

- Δυσλιπιδαιμία
- Κατάθλιψη
- BMI 45 (ΣΒ:130kg, Υ:1,7m)

Drug history:

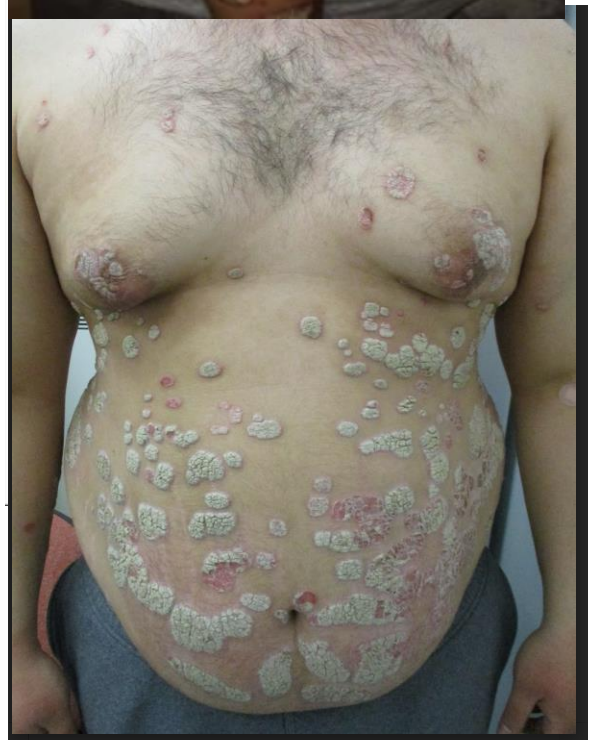
- MTX (διακοπή λόγω ηπατοτοξικότητας)
- CyA (διακοπή λόγω αρτηριακής υπέρτασης)
- anti- TNF (< 6 μήνες/ each – 1ο failure) : **Etanercept/Adalimumab/ Infliximab**
- **Ustekinumab 45mg** - 1ο failure (2014)
- **Secukinumab** - 14 months, partial response (2017)
- **Ustekinumab 90 mg** - 16 months, partial response.
- **Brodalumab** 22 month

24/11/20
έναρξη
Guselkumab

- Συμμετρική πολυαρθρίτιδα, ονυχοδυστροφία
- Δέρμα : κατά πλάκας , τριχωτό κεφαλής και σταγονοειδής.
  BSA 30%, PASI 14,4

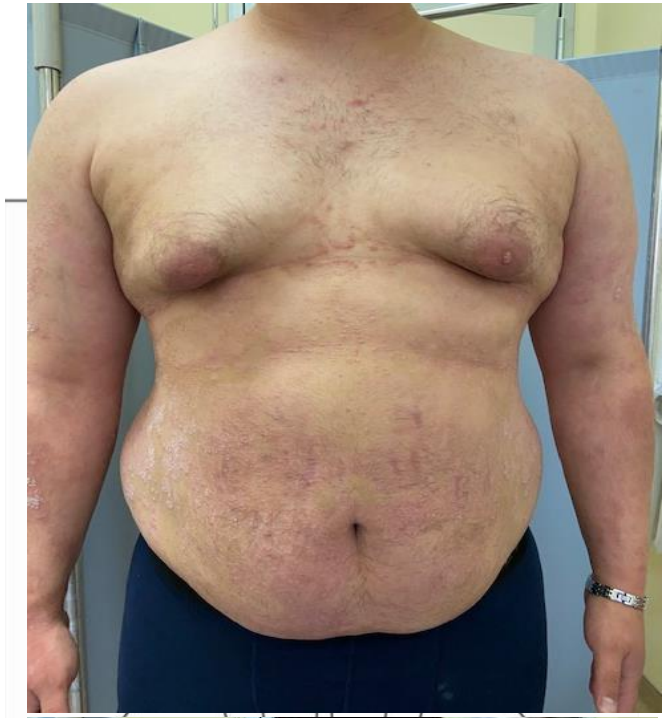
DAPSA
έναρξής
63,25

- No. ευαίσθητων αρθρώσεων = 20
- No. διογκωμένων αρθρώσεων= 20
- Γνώμη ασθενούς (0-10) = 10
- Γνώμη ιατρού (0-10) = 10
- CRP (mg/L). = 32,5



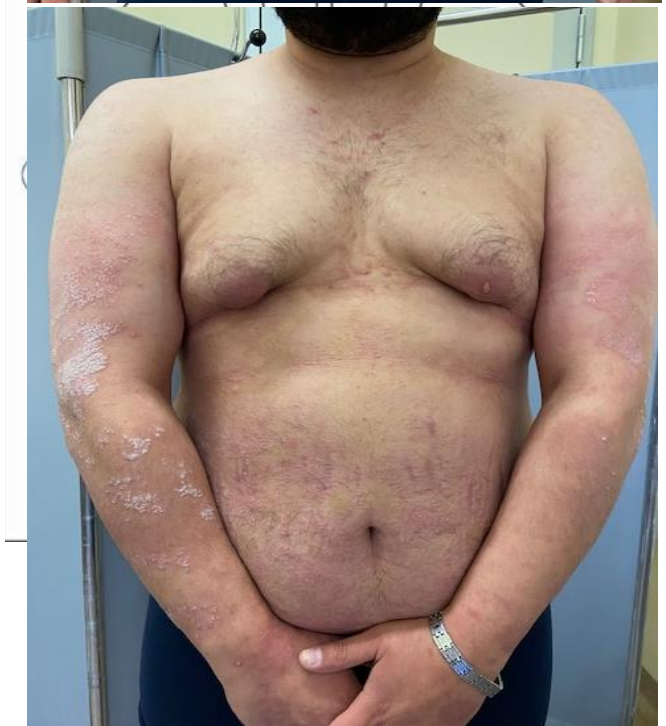
Υπό Guselkumab

- Μετά 5 μήνες θεραπεία, βελτίωση κατά 50% στο δέρμα…



Στους 5 μήνες DAPSA 63,25→**15**

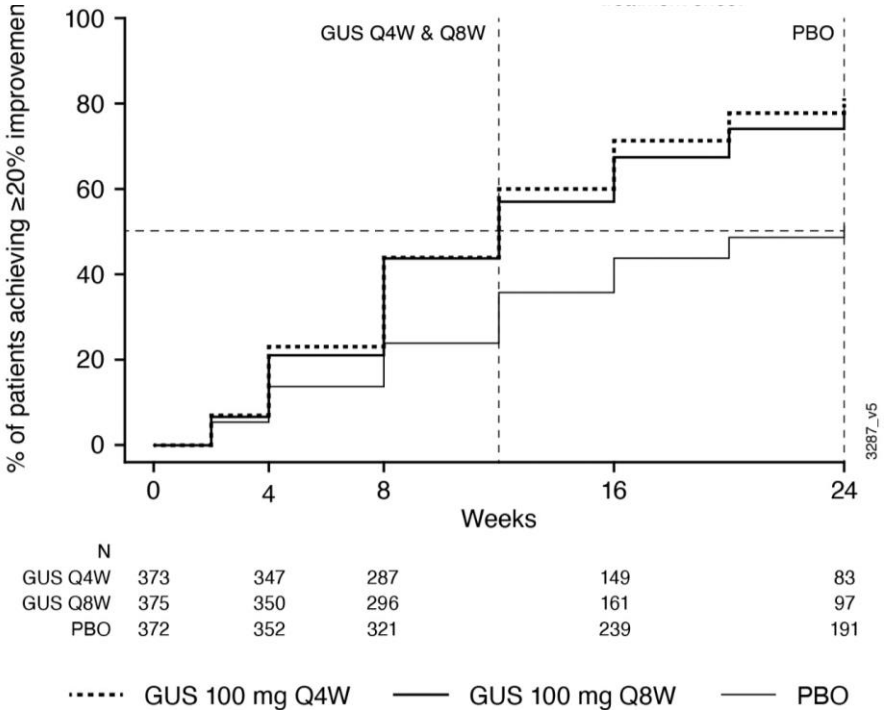
- No. ευαίσθητων αρθρώσεων = 2
- No. διογκωμένων αρθρώσεων= 2
- Γνώμη ασθενούς (0-10). = 5
- Γνώμη ιατρού (0-10). = 5
- CRP (mg/L). = 10



Guselkumab shows rapid onset of effect on components of ACR response criteria

- Pooled data from DISCOVER 1 and DISCOVER 2 (N=1120)
- For each ACR component, achievement of ≥20% improvement from BL was assessed over time through Week 24 for the combined GUS (q4w and q8w) groups

Median Time to ACR20 Response



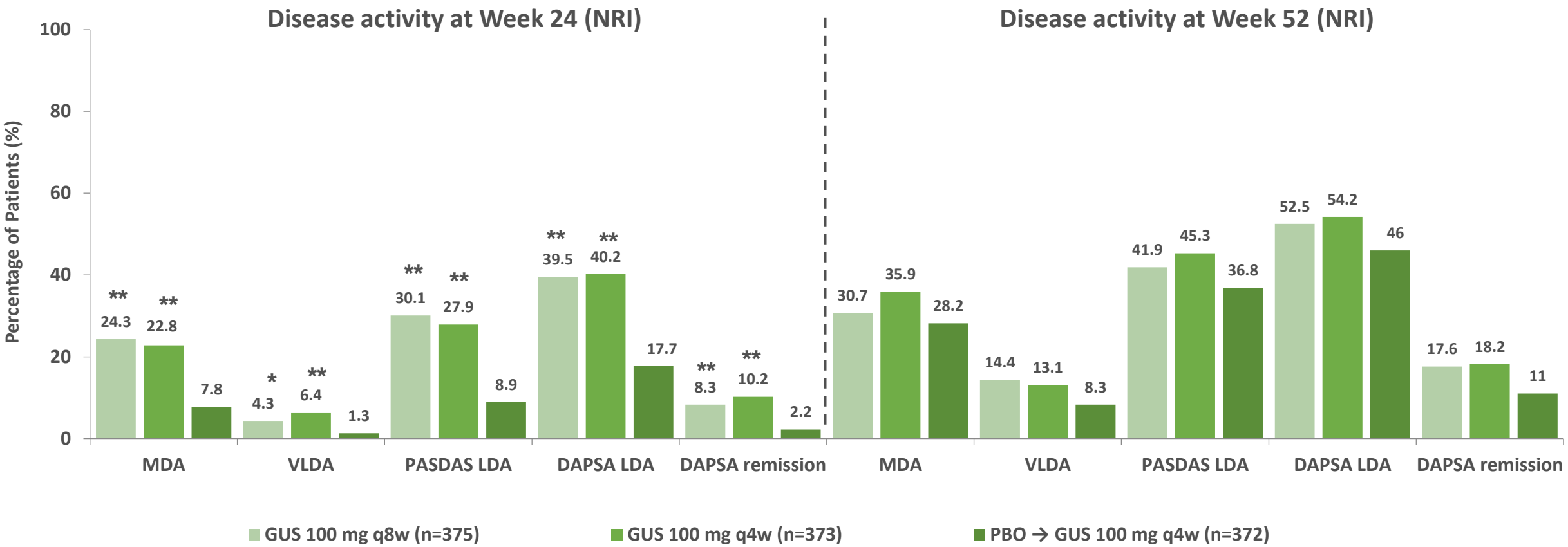
Proportion of patients with ≥20% improvement from BL through Week 24

≥20% improvement from BL, %	Week					
	4	8	12	16	20	24
ACR20	20	39	50	56	60	61
HAQ-DI	36	45	52	54	56	57
SJC66	61	74	84	86	87	88
TJC68	48	65	75	79	80	81
PGA	50	67	74	78	81	81
PtGA	35	48	58	59	62	64
Pt pain	32	48	55	58	61	63
CRP	56	60	62	63	64	64

GUS demonstrated ACR20 improvements with separation from PBO in ACR components as early as Wk 4 (consistent with ↓ inflammation by GUS and prior serological studies). At early study time points, both pts and physicians were able to discern improvements in S/S of arthritis that rapidly followed ↓ in systemic inflammation (CRP). The predominant drivers of ACR20 response rates at Wk 24 in GUS pts were SJC66/TJC68/PGA

Abbreviation definitions in slide notes. Nash et al. EULAR 2021 AB0525.

Guselkumab provides sustained domain-specific and comprehensive efficacy through Week 52

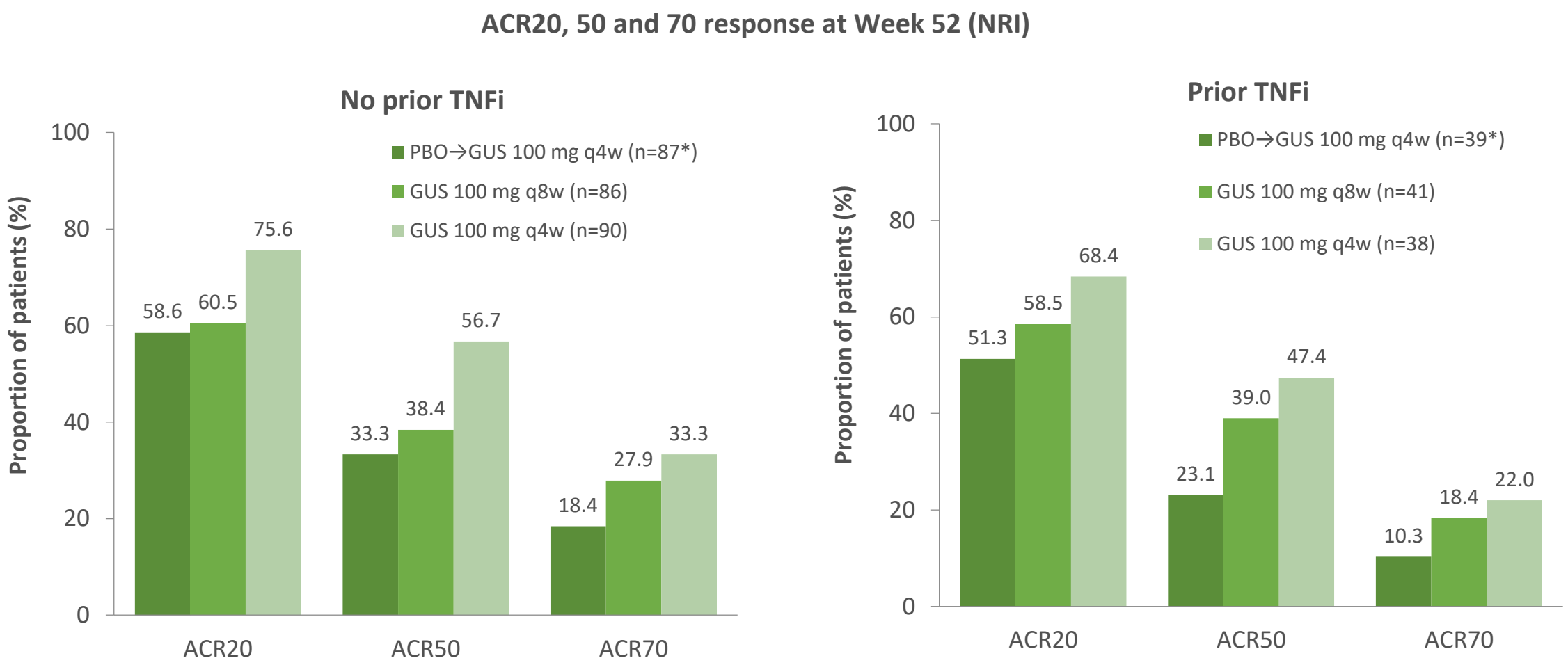


*p<0.05; **p<0.001; Unadjusted (nominal) p-values are not controlled for multiplicity and are descriptive/supportive only. Further information on PASDAS and DAPSA cut-off values can be found in the slide notes.

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.

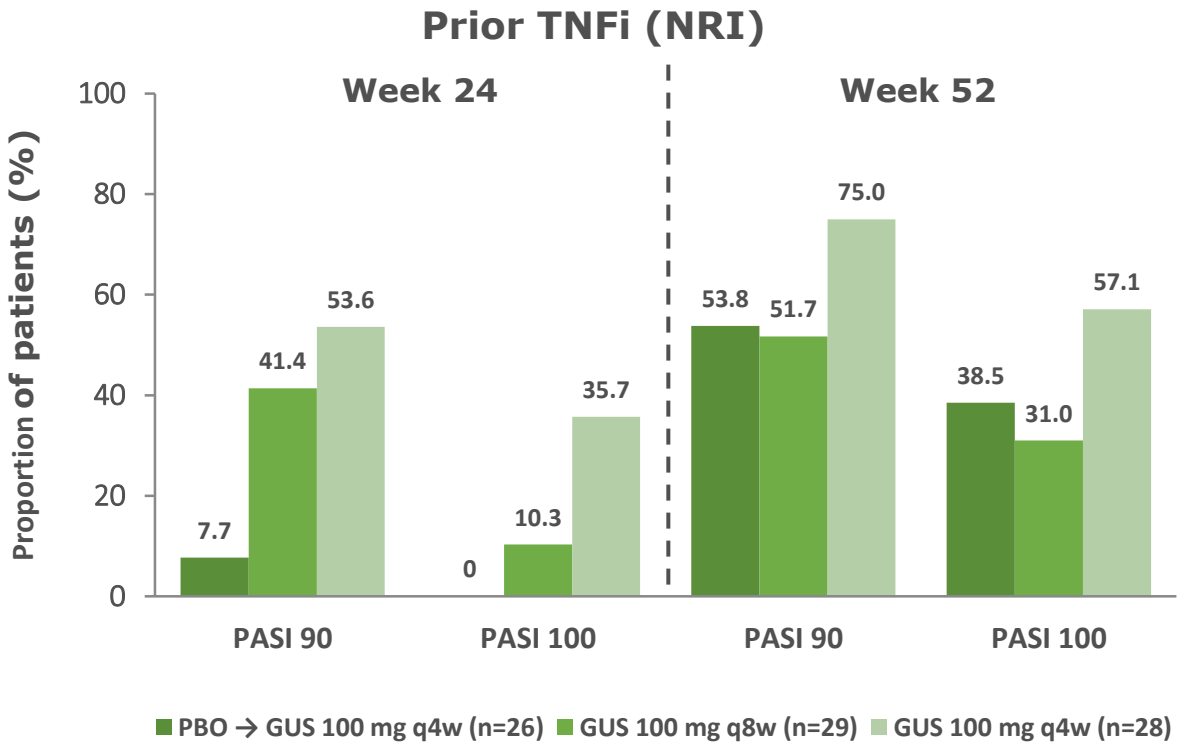
ACR responses at Week 52 by prior TNFi exposure[1]

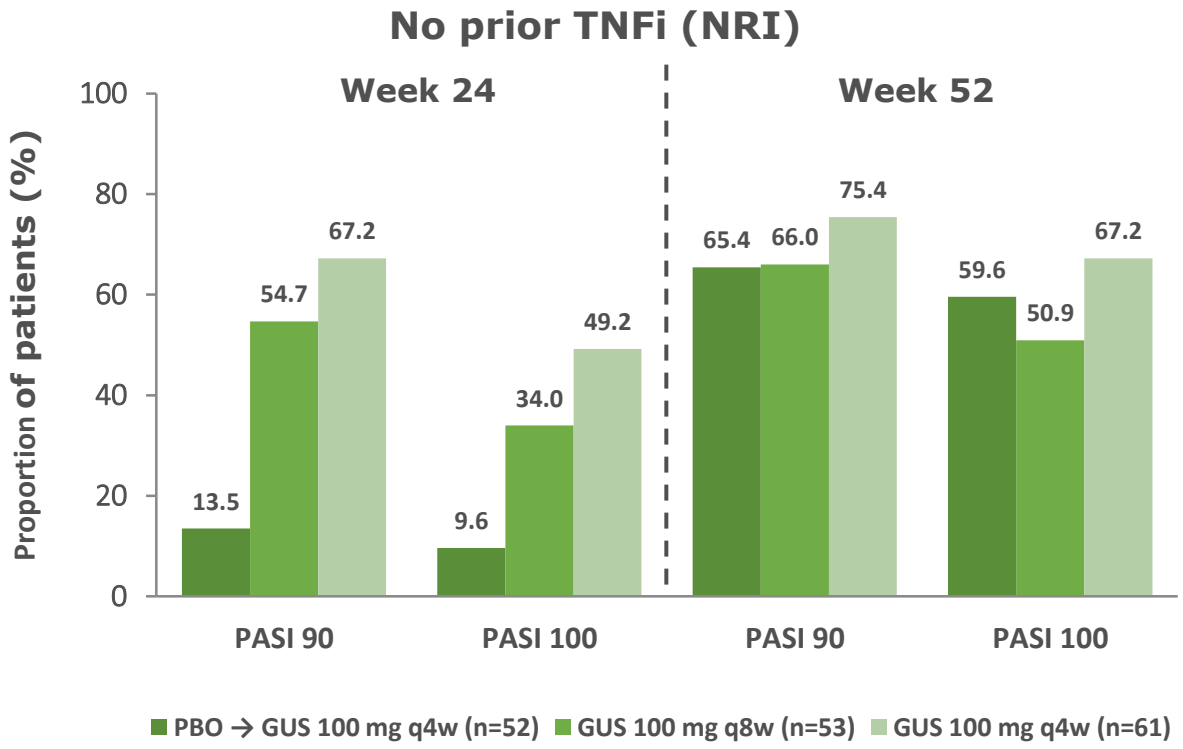


*Among the 39 TNFi-experienced and 87 TNF-naïve patients randomised to receive PBO followed by GUS q4w, 7 and 5, respectively, received PBO only and 32 and 82, respectively, started GUS q4w at Week 24 (post-Week 24 response assessments).
ACR, American College of Rheumatology; GUS, guselkumab; PBO, placebo;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

1. Ritchlin CT, et al. Presented at the EULAR e-Congress, June 2020. Poster 0397.

PASI responses at Weeks 24 and 52 by prior TNFi exposure

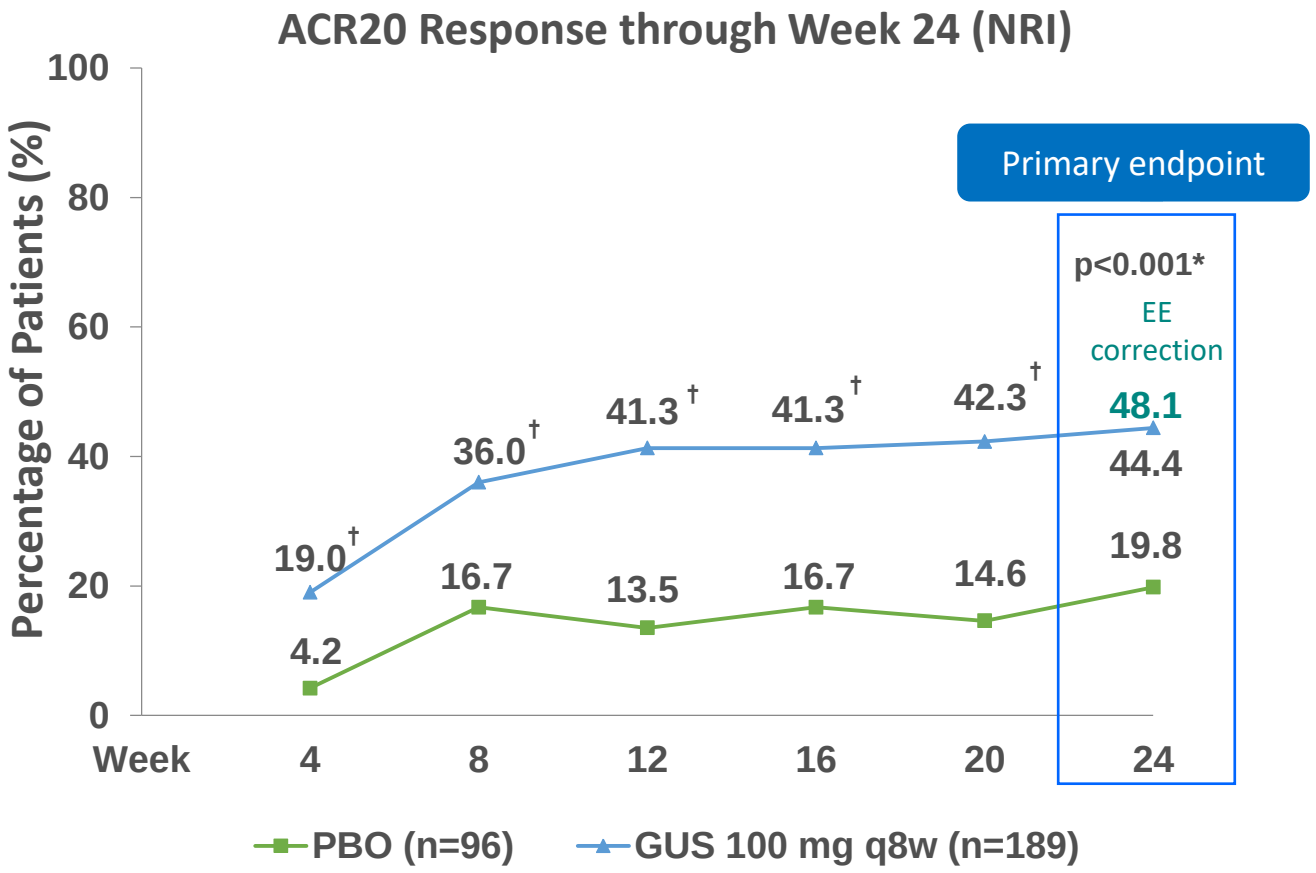


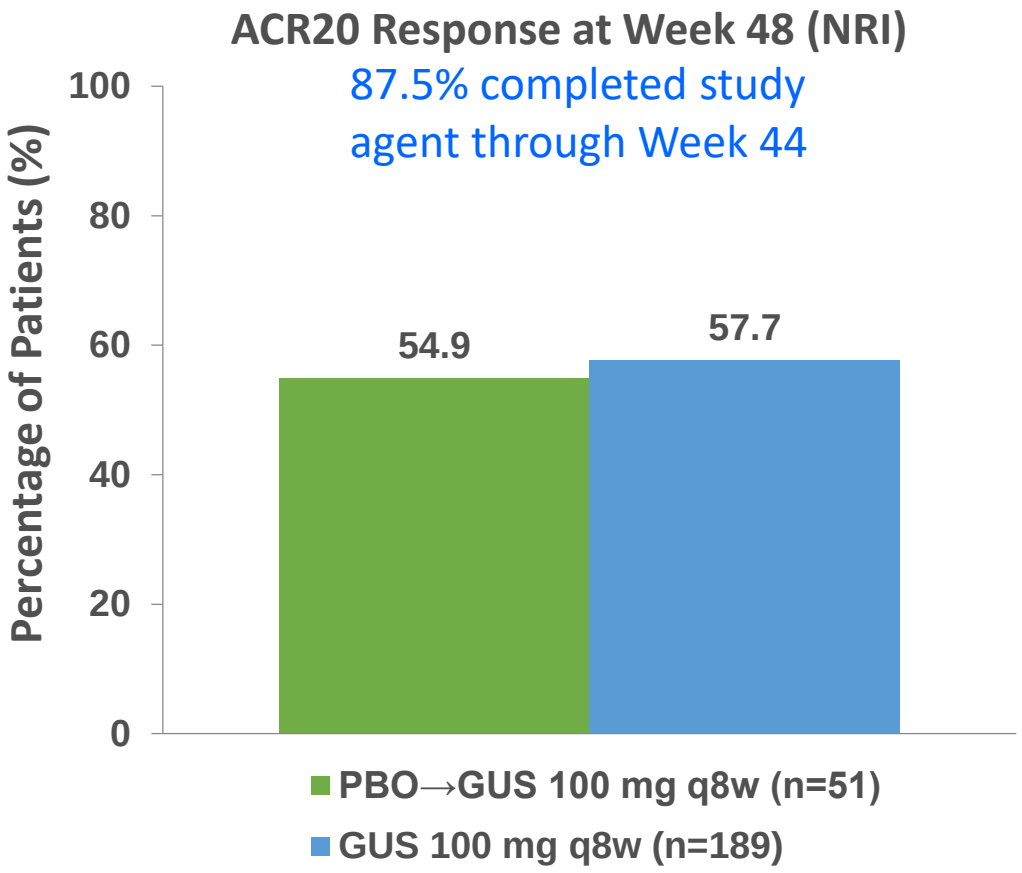


GUS, guselkumab; PASI, Psoriasis Area and Severity Index; PBO, placebo; PsA, psoriatic arthritis; q4w, every 4 weeks; q8w, every 8 weeks; TNFi, tumour necrosis factor inhibitor.

Ritchlin C, et al. ACR Convergence 2020, November 5-9. Poster 0888.

ACR20 Responses through 1 Year



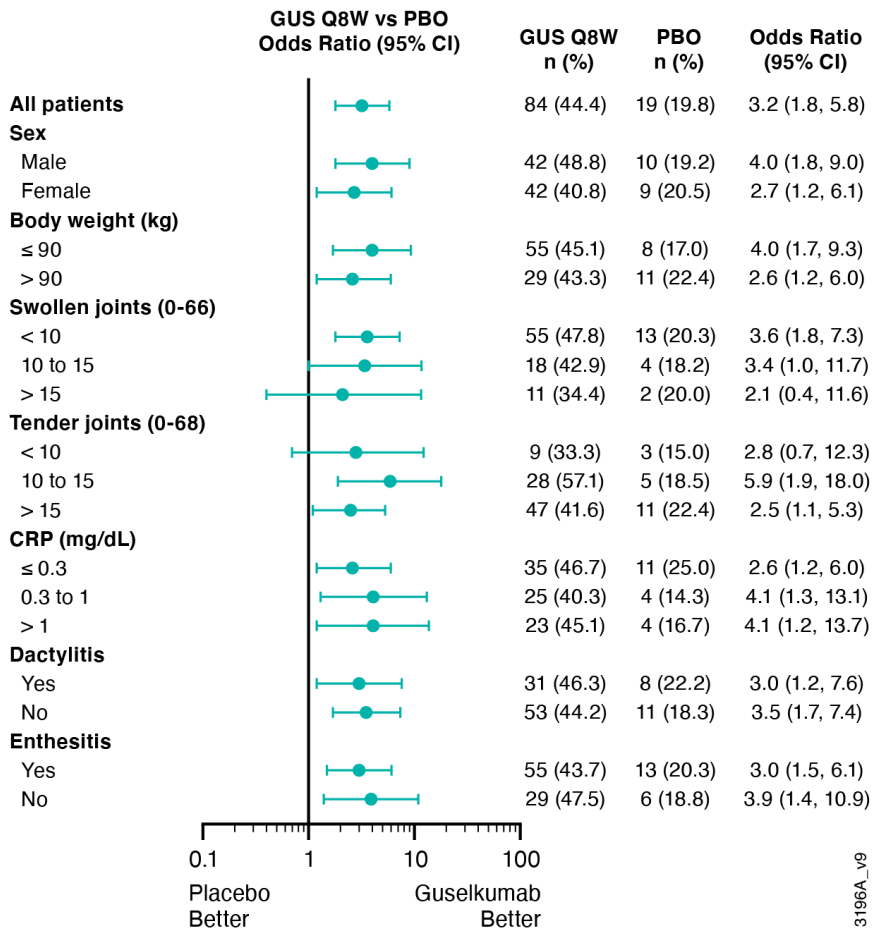


*p<0.001 adjusted for multiplicity testing; †p<0.001 nominal (not adjusted for multiplicity testing; GUS: Guselkumab

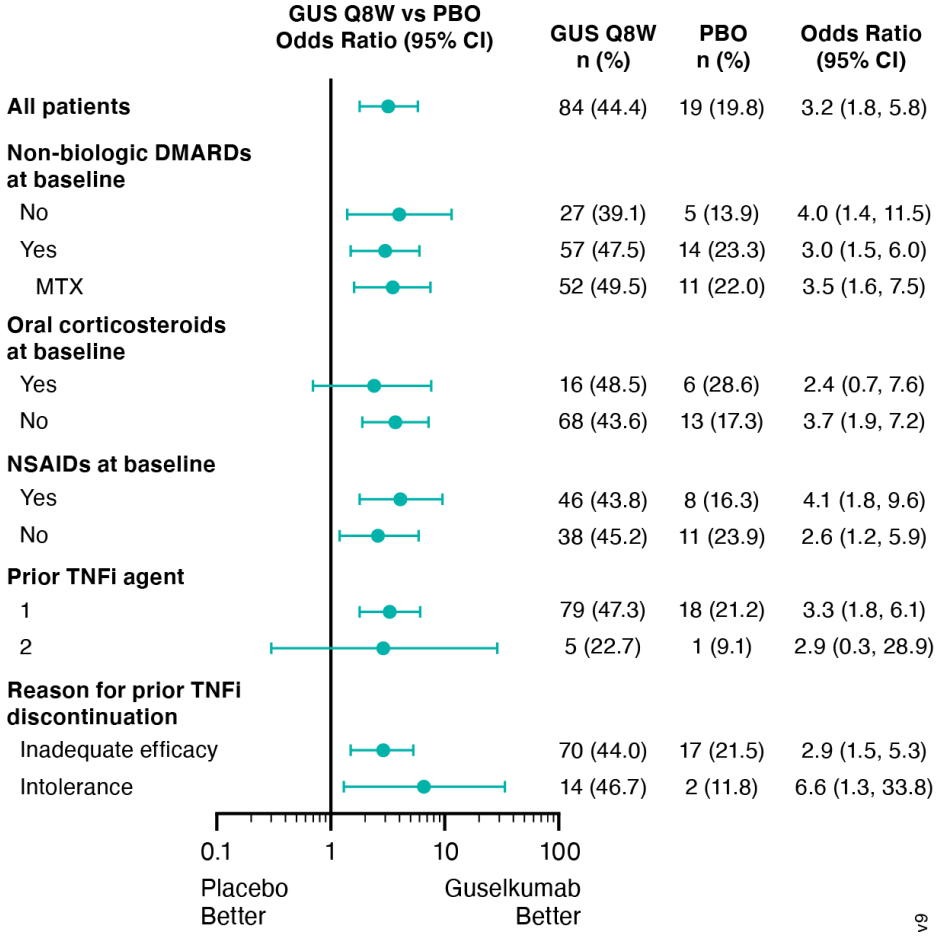
Coates et al. EULAR 2021 #OP0230.

ACR20 response at Week 24 (NRI)

By baseline patient and disease characteristics

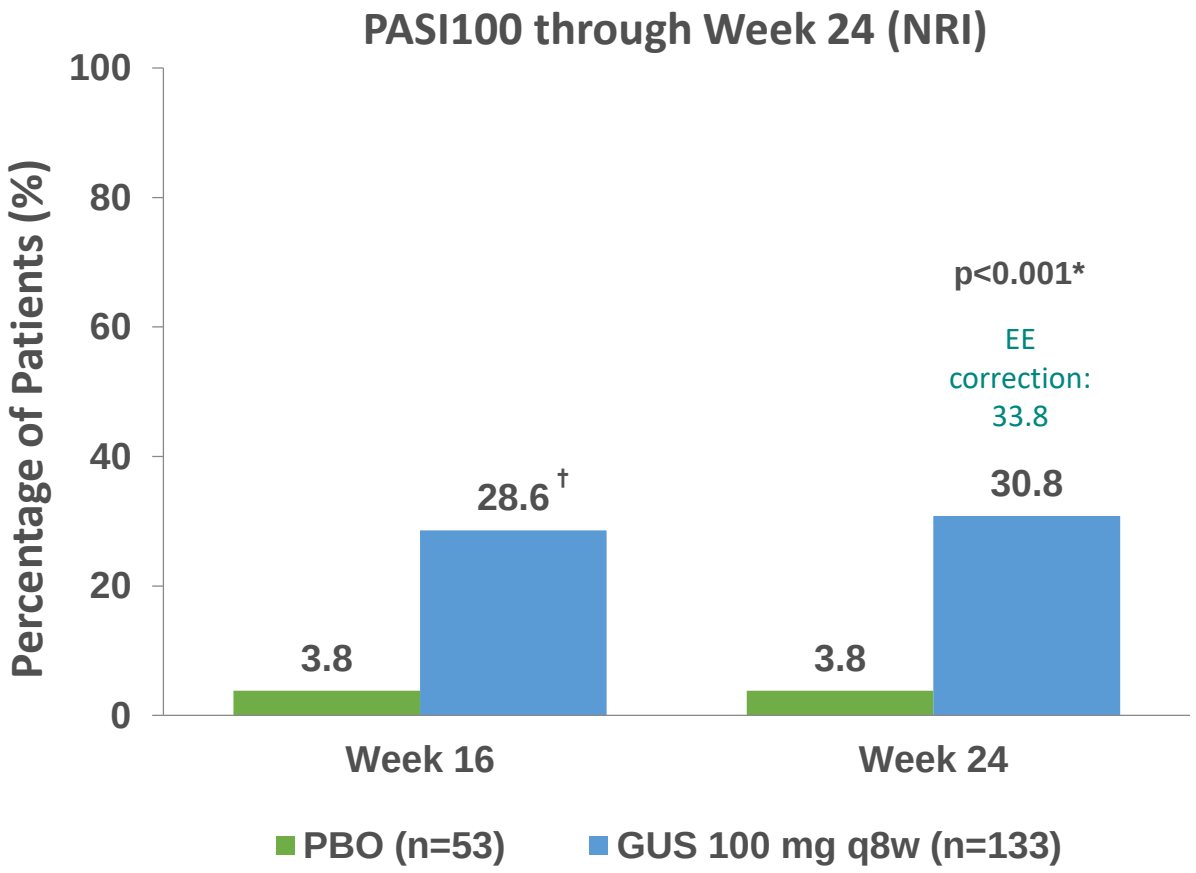


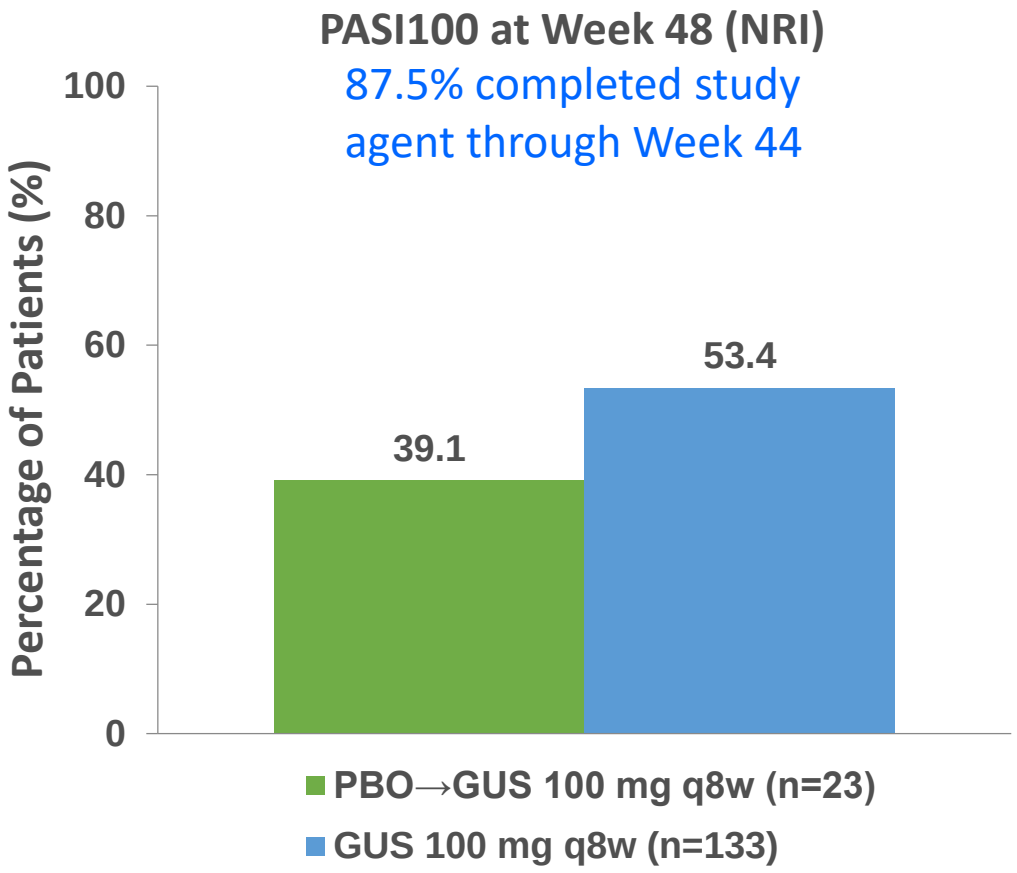
By prior and concomitant medication



ACR, American College of Rheumatology; CRP, C-reactive protein; DMARD, disease-modifying antirheumatic drug; GUS, guselkumab; MTX, methotrexate; NRI, non-responder imputation; NSAID, nonsteroidal anti-inflammatory drug; PBO, placebo; q8w, every 8 weeks; TNFi, tumour necrosis factor inhibitor. Coates LC, et al. Presented at EULAR 2021. OP0230.

Skin Responses through 1 Year





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Coates et al. EULAR 2021 #OP0230.

Γυναίκα 45 ετών

καπνίστρια,

BMI 35
(ΣΒ: 90kg, Υ: 1,6m)

Ψωρίαση από 27 ετών

Γυναίκα 45 ετών

καπνίστρια,

BMI 35
(ΣΒ: 90kg, Υ: 1,6m)

Ψωρίαση από 27 ετών

***Drug history*:**

CyA - 1ο failure

Efalizumab

Adalimumab - 1ο failure

Etanercept → 2ο failure → Inflam. back pain ,Polyarthritis, Enthesitis.

PsARC 50, BASDAI 7,5

Etanercept + MTX

PsARC 57,Enthesitis Achilles left, Nail involvement →

Secukinumab

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Ψωρίαση από 27 ετών

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PsARC 50, BASDAI 7,5

Etanercept + MTX

PsARC 57,Enthesitis Achilles left, Nail involvement →

Secukinumab

Secukinumab
→ 18 months well , lost F/UP

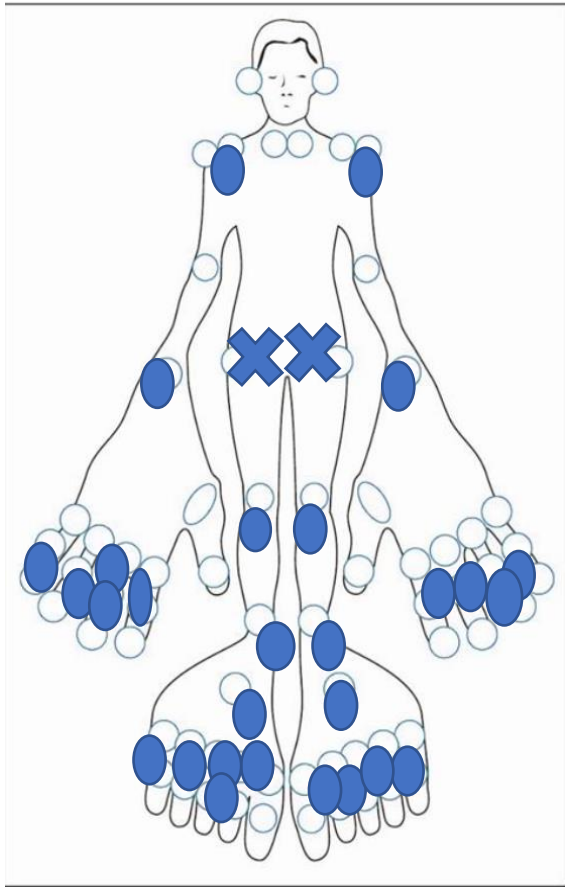
Relapse : T12, S 8, VAS p 8/10, enthesitis achilles

→ **+MTX 15mg/wk**
Treatment failure,
→ **certolizumab**
treatment failure
→ **golimumab**
treatment failure

έναρξη Guselkumab
(0,4,12 and every 8 wks)

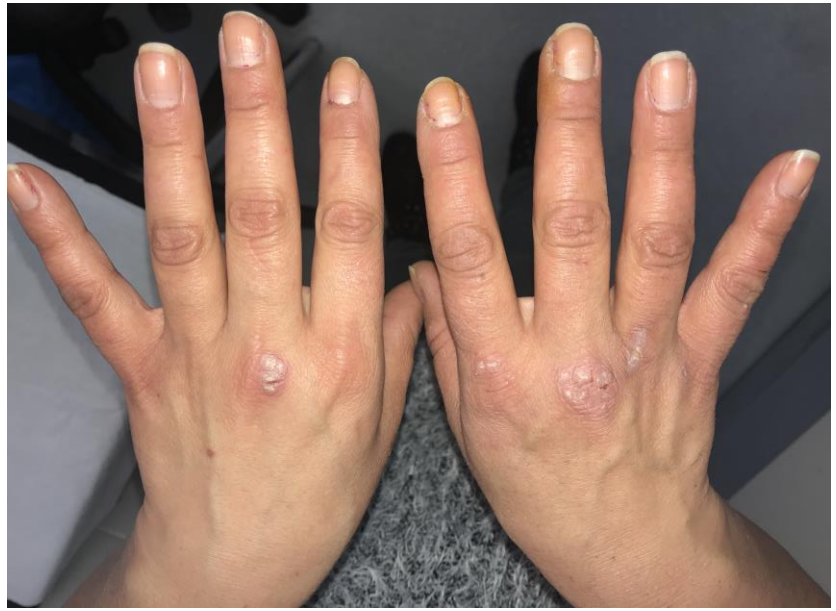
- Wk 0 : έξαρση πολυαρθρίτιδας, έξαρση δέρματος με Ψωρίαση κορμού, άκρων, τριχωτού κεφαλής και ανάστροφη. Φλεγμονώδη οσφυαλγία και αχίλλειο ενθεσίτιδα.

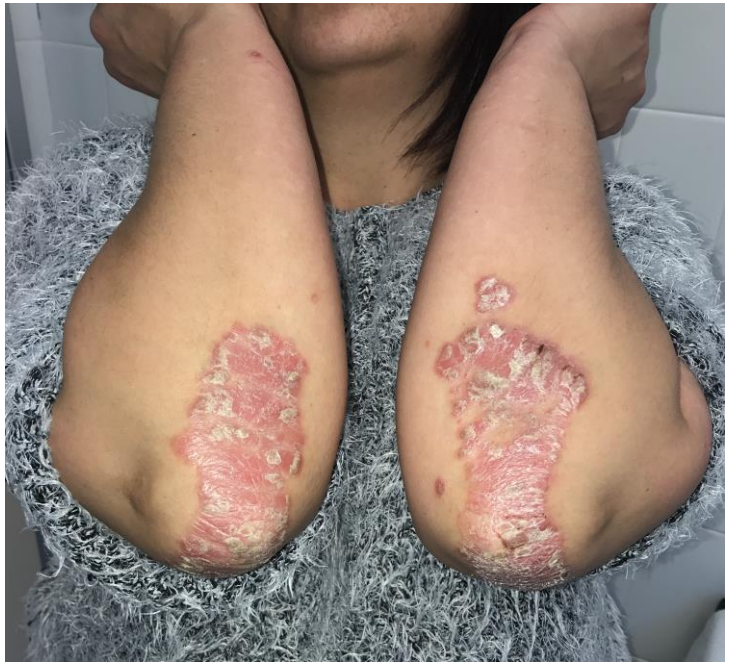
PASI 19, BASDAI 8,7

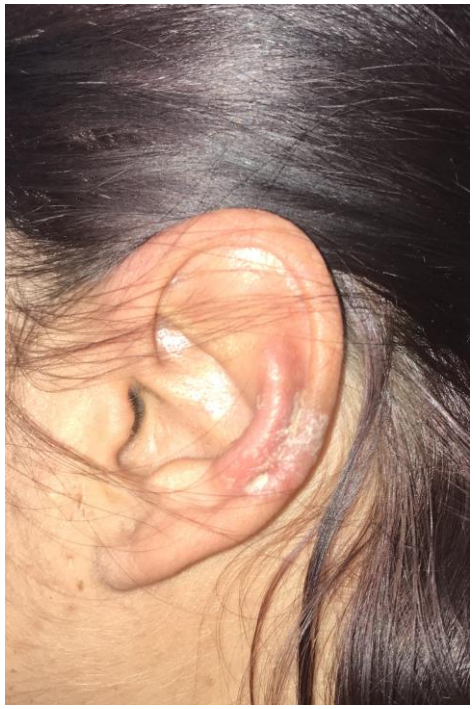


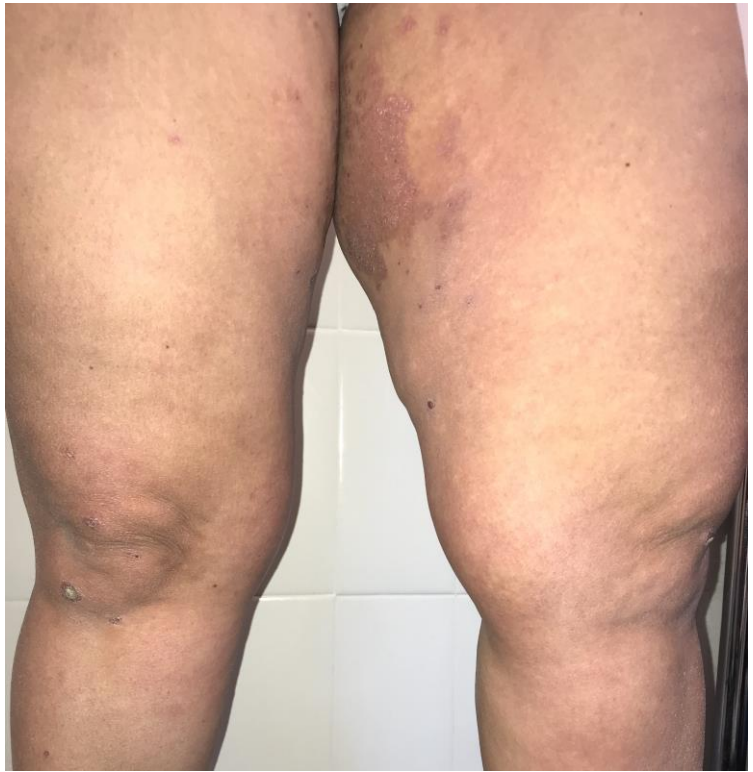
DAPSA wk0 52,8

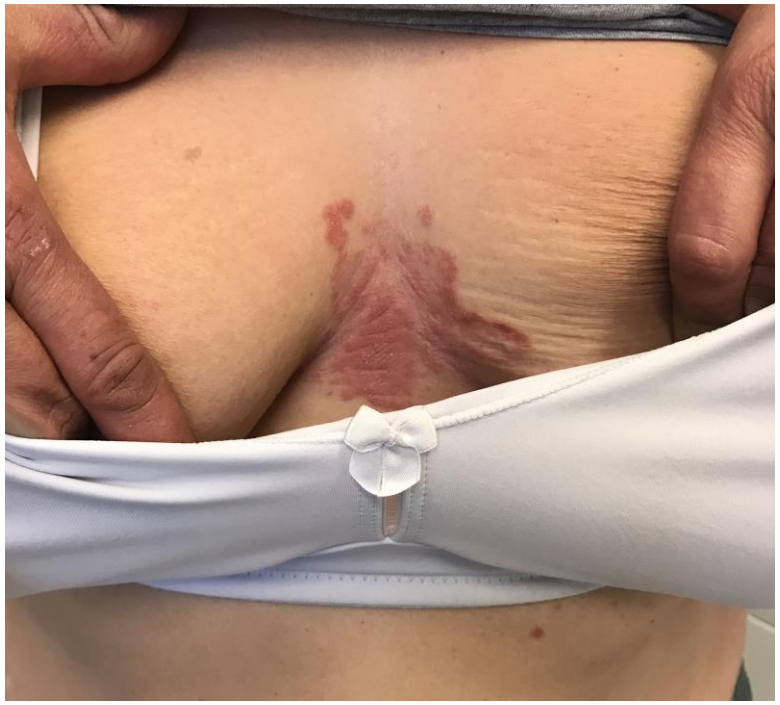
- No. ευαίσθητων αρθρώσεων = 22
- No. διογκωμένων αρθρώσεων= 10
- Γνώμη ασθενούς (0-10) = 10
- Γνώμη ιατρού (0-10) = 10
- CRP (mg/L). = 8

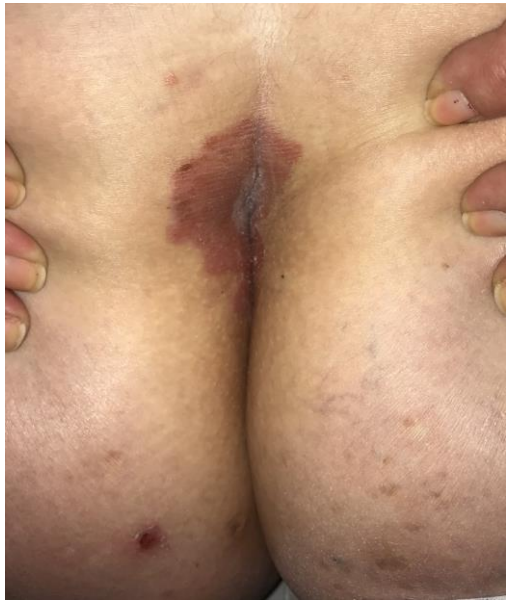












Guselkumab 100mg/8wks

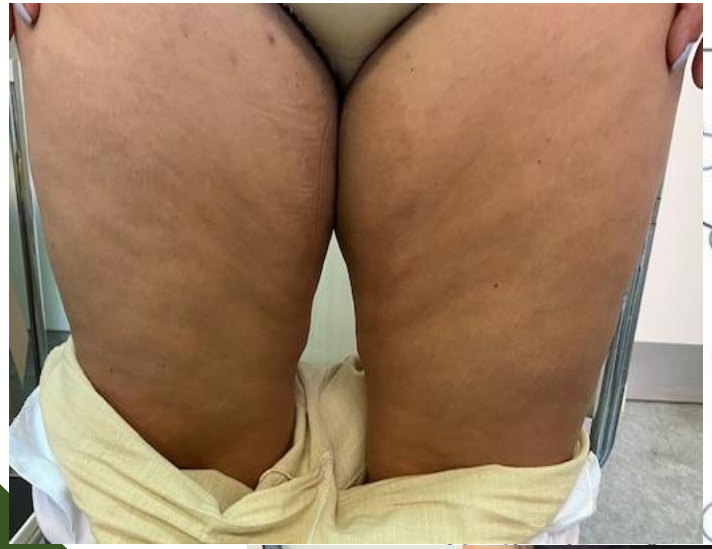
6 months later

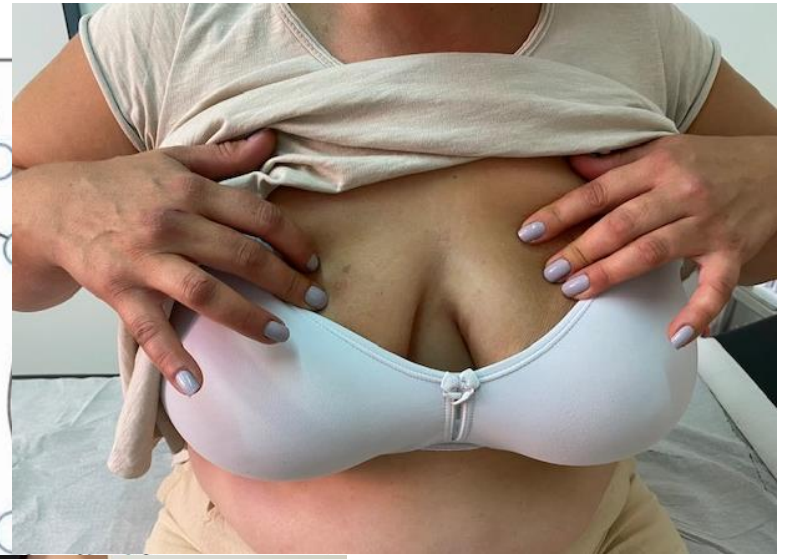
T 12
S 4
VAS p 2/10
VAS g 5/10
CRP 5mg/l

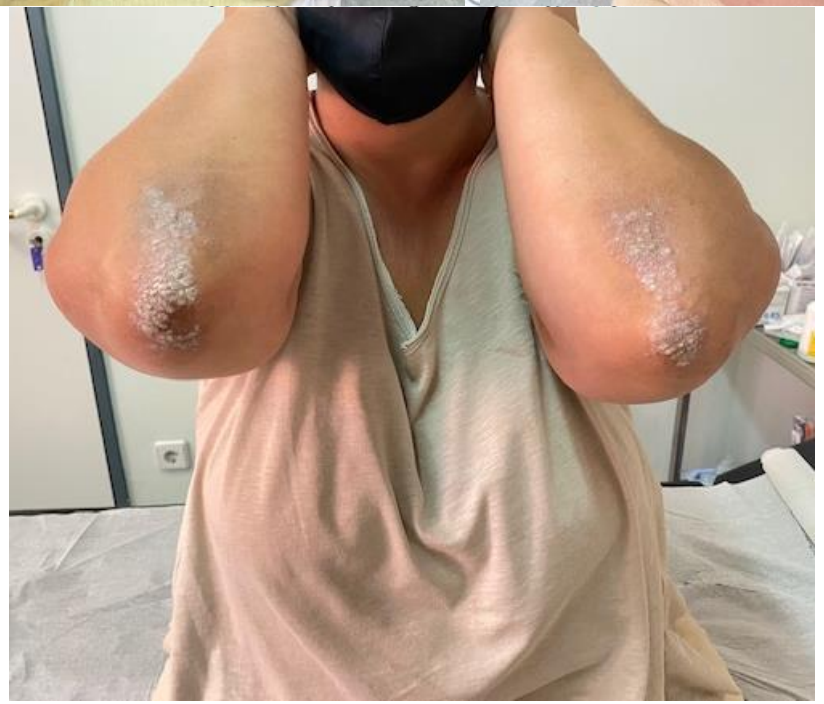
DAPSA 52 → 23,5

Skin : PASI 1,2 BSA 1, PGA 1

Enthesitis : none







Shift in Enthesitis Severity from BL to Week 52

Mild enthesitis (LEI=1) at BL (n=181)

Enthesitis at Week 24

	Resolved	Stable or partially improved	Worse
PBO (n=61)	42.6	31.1	24.6
GUS q8w (n=64)	65.6	17.2	14.1
GUS q4w (n=56)	67.9	23.2	8.9

Enthesitis at Week 52

	Resolved	Stable or partially improved	Worse
PBO → GUS q4w (n=61)	80.3	11.5	-
GUS q8w (n=64)	70.3	10.9	6.3
GUS q4w (n=56)	75.0	16.1	5.4

Moderate enthesitis (LEI=2) at BL (n=188)

Enthesitis at Week 24

	Resolved	Stable or partially improved	Worse
PBO (n=74)	37.8	44.6	16.2
GUS q8w (n=60)	56.7	33.3	8.3
GUS q4w (n=54)	53.7	37.0	7.4

Enthesitis at Week 52

	Resolved	Stable or partially improved	Worse
PBO → GUS q4w (n=74)	67.6	18.9	5.4
GUS q8w (n=60)	73.3	23.3	1.7
GUS q4w (n=54)	68.5	14.8	9.3

Severe enthesitis (LEI=3-6) at BL (n=351)

Enthesitis at Week 24

	Resolved	Stable or partially improved	Worse
PBO (n=117)	21.4	68.4	7.7
GUS q8w (n=105)	38.1	51.4	8.6
GUS q4w (n=129)	30.2	62.8	4.7

Enthesitis at Week 52

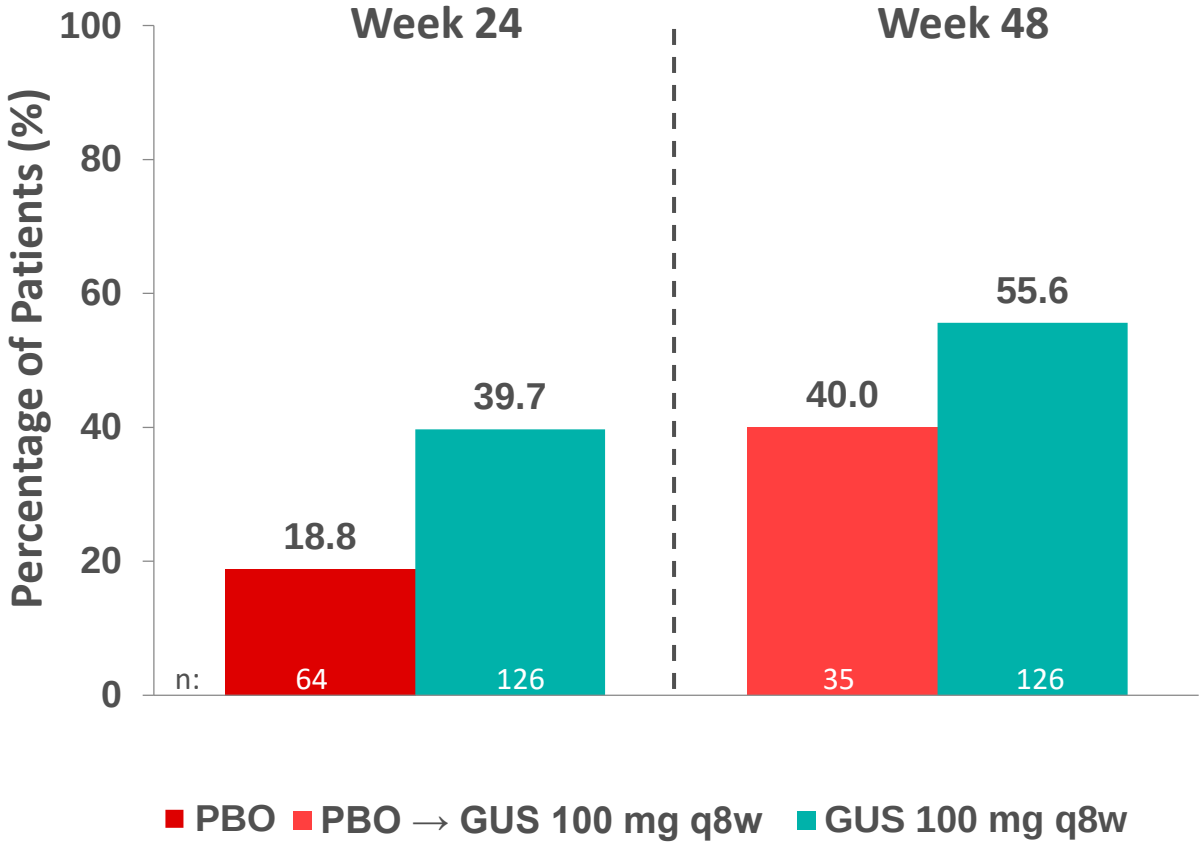
	Resolved	Stable or partially improved	Worse
PBO → GUS q4w (n=117)	47.9	40.2	1.7
GUS q8w (n=105)	41.9	47.6	1.9
GUS q4w (n=129)	44.2	47.3	3.1

Observed post-BL status was categorized as resolved (post-BL LEI score=0), stable or partially improved (0 < post-BL LEI score ≤ BL LEI score), or worse (post-BL LEI score > BL LEI score)

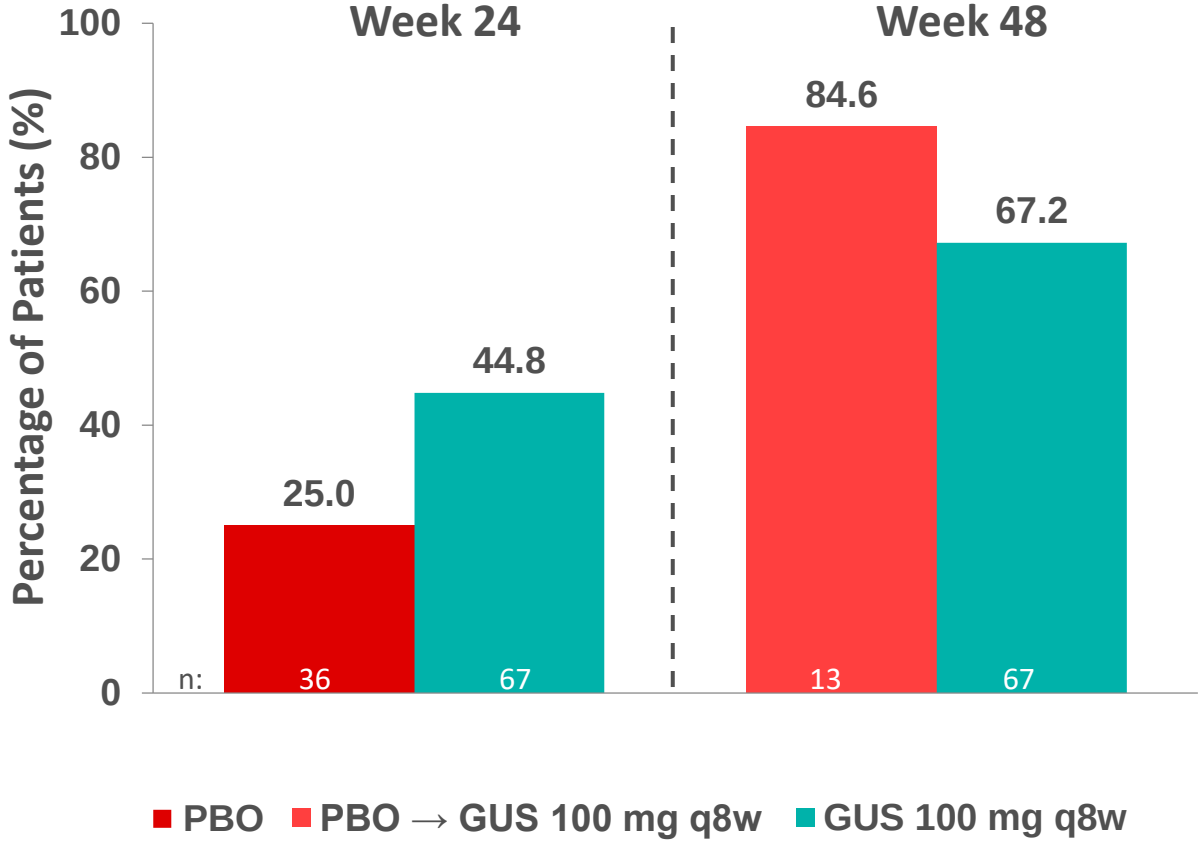
Supplement to McGonagle et al. Rheumatology 2021; epub 06APR doi: 10.1093/rheumatology/keab285.

Resolution of Enthesitis and Dactylitis through 1 Year

67% of pts had enthesitis at BL



37% of pts had dactylitis at BL

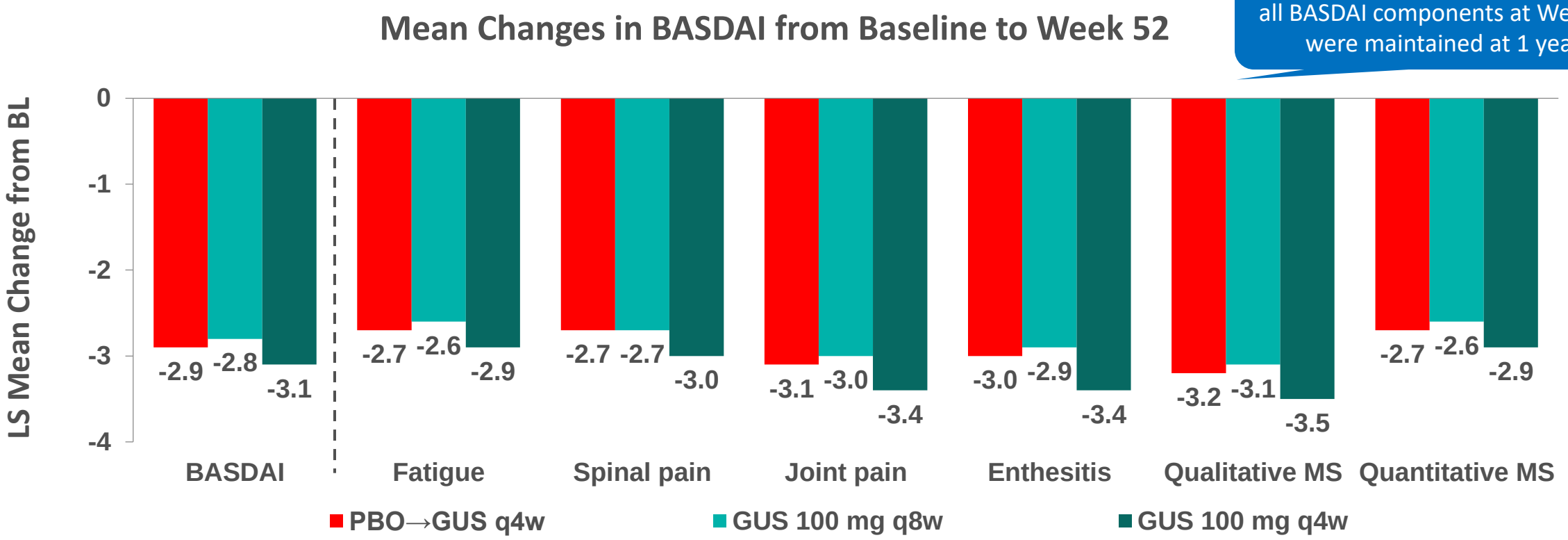


GUS: Guselkumab; NRI: Non-responder imputation

Coates et al. EULAR 2021 #OP0230.

Changes in Total BASDAI and Components from BL to Week 52

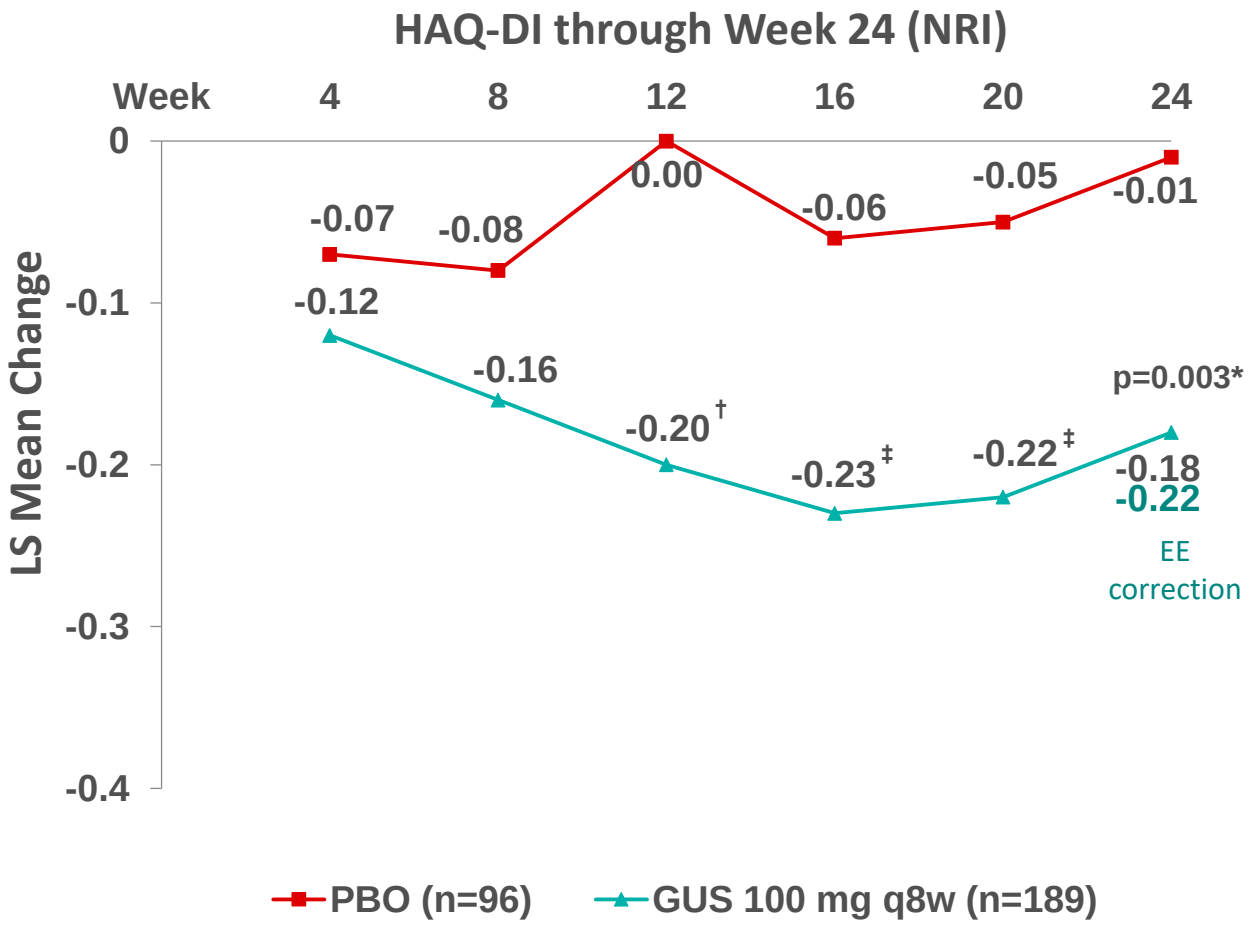
The benefits that GUS provided in all BASDAI components at Week 24 were maintained at 1 year

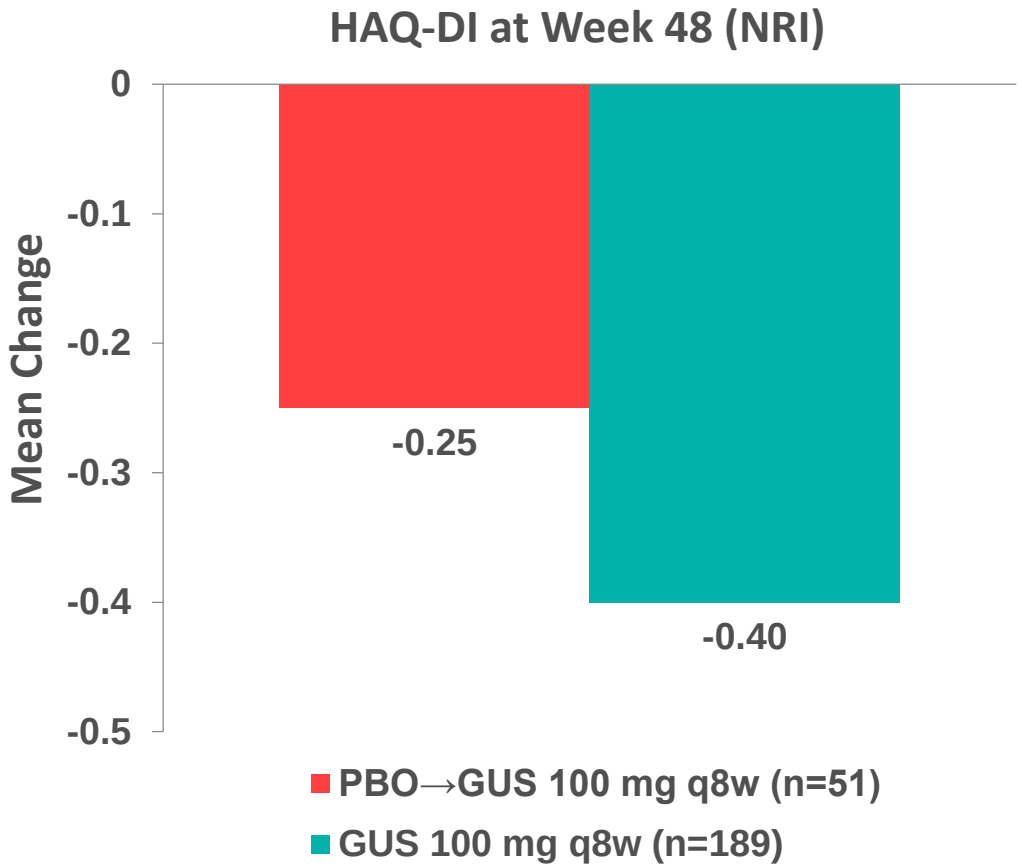


Least squares mean values were calculated using mixed-effect repeated measures where the number of patients included in the model: n=95 for GUS q4w, n=82 for GUS q8w, and n=110 for PBO→GUS q4w. AS: ankylosing spondylitis; BASDAI: Bath AS disease activity index; BL: baseline; LS: least squares; MS: morning stiffness

Supplement to Mease et al. Lancet Rheum 2021;https://doi.org/10.1016/s2665-9913(21)00105-3

Physical Function through 1 Year

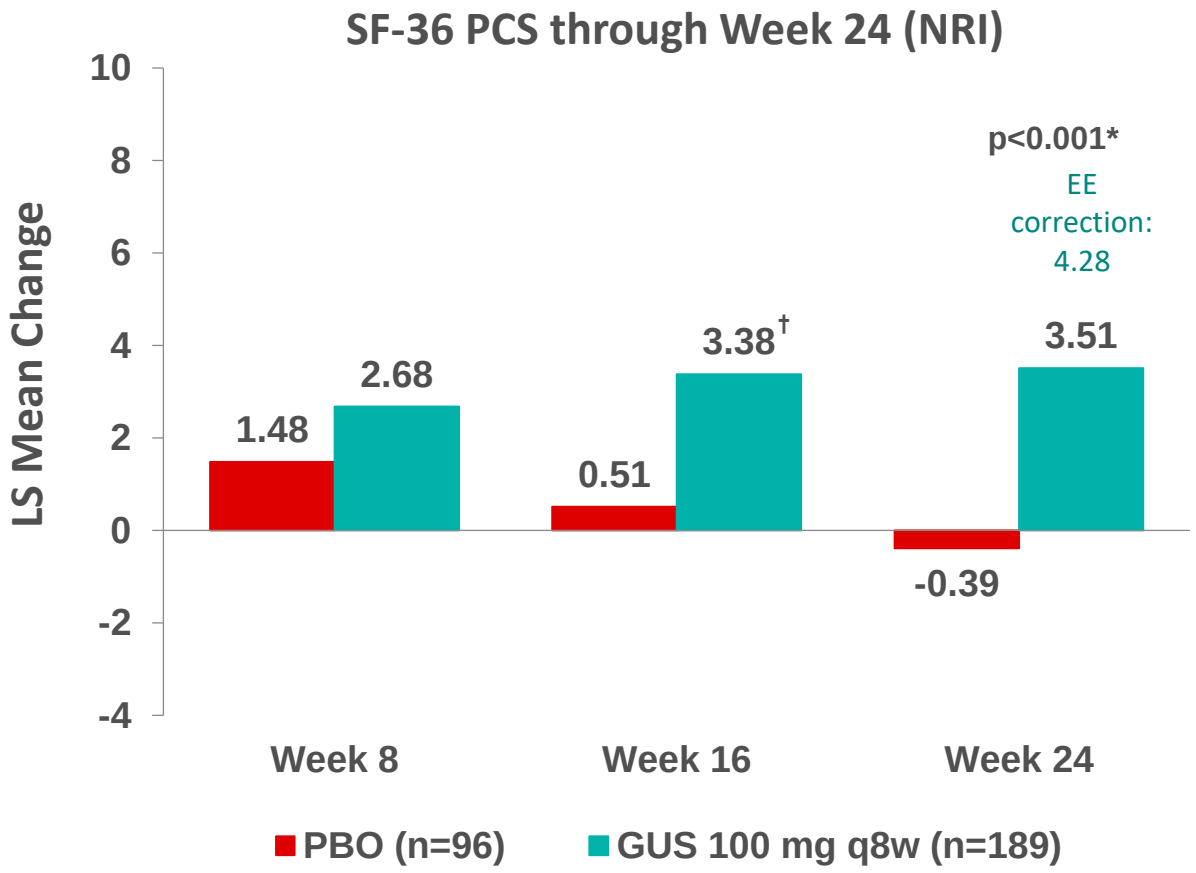


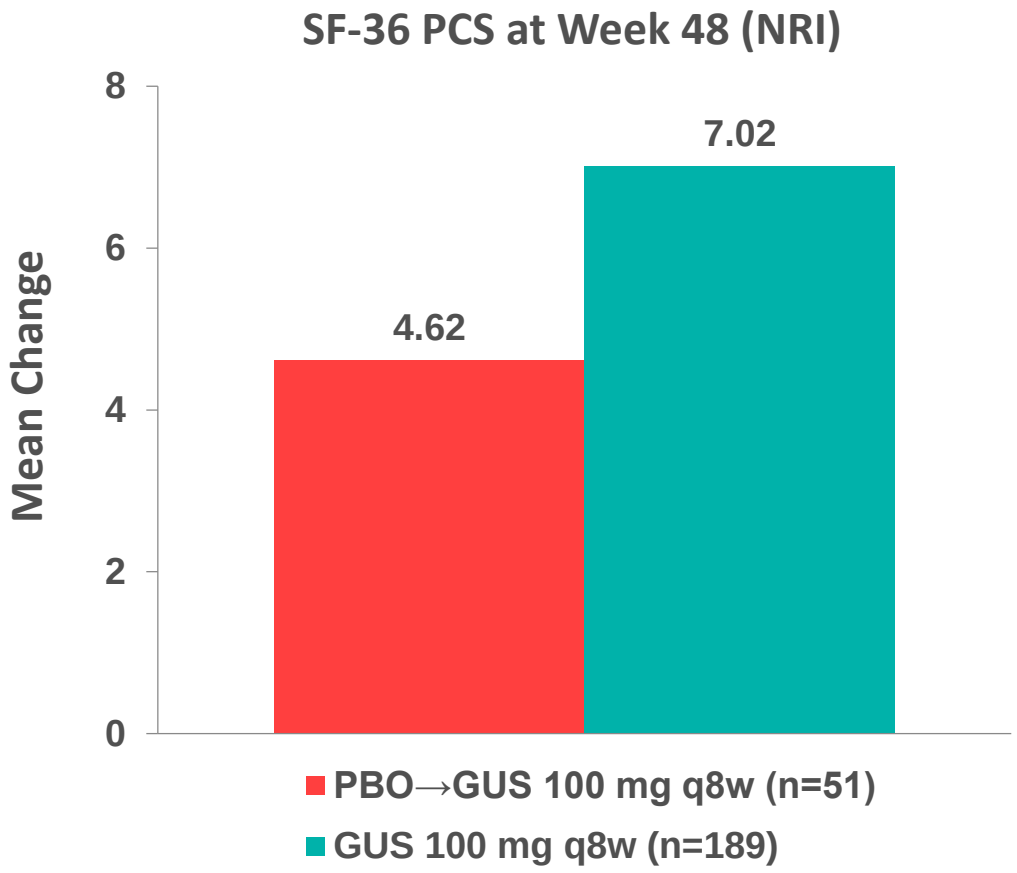


*p=0.003 adjusted for multiplicity testing; †p<0.001 and ‡p<0.01 nominal (not adjusted for multiplicity testing); GUS: Guselkumab

Coates et al. EULAR 2021 #OP0230.

Quality of Life through 1 Year





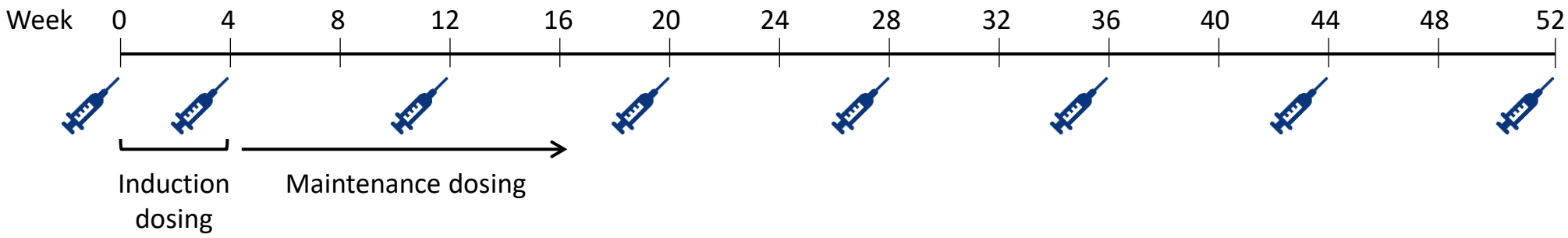
*p<0.001 adjusted for multiplicity testing; †p<0.001 nominal (not adjusted for multiplicity testing); GUS: Guselkumab

Coates et al. EULAR 2021 #OP0230.

Guselkumab dosing in PsA

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, November 2020.

Συμπεράσματα

Το guselkumab στοχεύει ένα νέο μονοπάτι στη θεραπεία της ψωριασικής νόσου.

Το guselkumab πετυχαίνει σημαντική βελτίωση σε όλες τις εκδηλώσεις της ψωριασικής αρθρίτιδας (ψωρίαση δέρματος, ενθεσίτιδα, δακτυλίτιδα, αρθρίτιδα ΚΑΙ αξονική συμμετοχή).

Η αποτελεσματικότητα του guselkumab διατηρείται σε βάθος χρόνου και είναι ανεξάρτητη από τη προηγούμενη λήψη TNFi.