

# **Διαφοροποίηση της θεραπευτικής απάντησης στην Αξονική Σπονδυλαρθριτίδα με βάση δημογραφικά χαρακτηριστικά και εργαστηριακά ευρήματα**

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# Το φάσμα των Σπονδυλαρθρίτιδων (ΣπΑ)

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Αξονική ΣπΑ  
χωρίς  
ακτινολογικά  
ευρήματα

Αγκυλοποιητική  
σπονδυλίτιδα

Αντιδραστική  
αρθρίτιδα

Ψωριασική  
αρθρίτιδα

Αρθρίτιδα των φλεγμονωδών  
νόσων του εντέρου

Αδιαφοροποίητη ΣπΑ

Κυρίως αξονική ΣπΑ

Κυρίως περιφερική ΣπΑ



## Axial spondyloarthritis – a heterogenous disease

- Degree of radiographic change varies
- Peripheral arthritis
- Enthesitis
- Anterior uveitis
- Psoriasis
- Inflammatory bowel disease
- Comorbidities

## Παράμετροι για θεραπευτική απάντηση

- ASAS 20, ASAS 40, ASDAS-PR, ASAS 5/6
- BASDAI 50
- ASDAS-CII, ASDAS-MI, ASDAS-LDA, ASDAS-ID

# Κριτήρια βελτίωσης ASAS 20

Βελτίωση  $\geq 20\%$  και  $\geq 1^*$  μονάδα σε τουλάχιστον 3 από τους 4 τομείς

Σφαιρική εκτίμηση ασθενή

Πόνος\*\*

Λειτουργικότητα

Φλεγμονή\*\*\*

Καμία επιδείνωση στον 4<sup>ο</sup> τομέα  $\geq 20\%$  και  $\geq 1$  μονάδα

\* Σε κλίμακα 0-10

\*\* Πόνος Σπονδυλικής στήλης ή ερώτηση 2 του δείκτη BASDAI

\*\*\* Μέση τιμή των ερωτήσεων 5 και 6 στο BASDAI



# Κριτήρια βελτίωσης ASAS 40

Βελτίωση  $\geq 40\%$  και  $\geq 2^*$  μονάδες σε τουλάχιστον 3 από τους 4 τομείς

Σφαιρική εκτίμηση ασθενή

Πόνος\*\*

Λειτουργικότητα

Φλεγμονή\*\*\*

Καμία επιδείνωση στον τελευταίο τομέα

\* Σε κλίμακα 0-10

\*\* Πόνος Σπονδυλικής στήλης ή ερώτηση 2 του δείκτη BASDAI

\*\*\* Μέση τιμή των ερωτήσεων 5 και 6 στο BASDAI

# Κριτήρια ASAS για μερική ύφεση της νόσου

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**Βαθμολογία όχι άνω των 2 μονάδων \* στον κάθε ένα από τους 4 τομείς**

**Σφαιρική εκτίμηση ασθενή**

**Πόνος\*\***

**Λειτουργικότητα**

**Φλεγμονή\*\*\***

\* Σε κλίμακα 0-10

\*\* Πόνος Σπονδυλικής στήλης ή ερώτηση 2 του δείκτη BASDAI

\*\*\* Μέση τιμή των ερωτήσεων 5 και 6 στο BASDAI

# Κριτήρια βελτίωσης ASAS 5/6

Βελτίωση  $\geq 20\%$  σε τουλάχιστον 5 από τους 6 τομείς

Σφαιρική εκτίμηση ασθενή

Πόνος\*

Λειτουργικότητα

Φλεγμονή\*\*

CRP

**Κινητικότητα σπονδυλικής στήλης**

\* Πόνος Σπονδυλικής στήλης ή ερώτηση 2 του δείκτη BASDAI

\*\* Μέση τιμή των ερωτήσεων 5 και 6 στο BASDAI

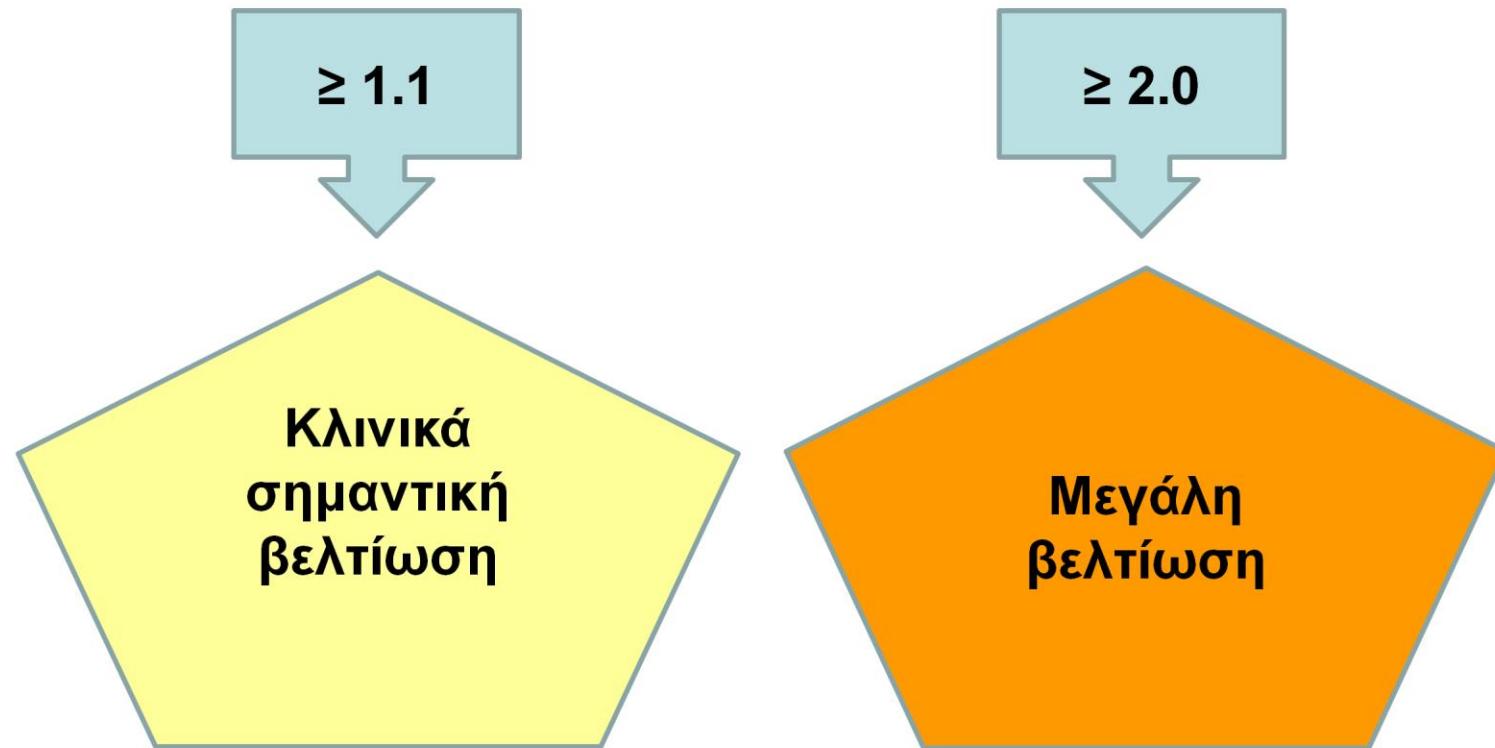
## Όρια ASDAS για εκτίμηση ενεργότητας νόσου

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# Όρια ASDAS για κριτήρια βελτίωσης νόσου

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# Ομοιότητες και διαφορές μεταξύ ΑΣ και αξονικής ΣπΑ (αξΣπΑ) χωρίς ακτινολογικά ευρήματα (μα-αξΣπΑ)

	GESPIC <sup>1</sup>		Herne-Cohort <sup>2</sup>	
	Όλες οι αξΣπΑ	ΑΣ ≤5 έτη	μα-αξΣπΑ ≤5 έτη	ΑΣ
	N=236	N=119	N=226	N=56
Ηλικία, έτη	35.6	36.1	36.1	41.2
HLA-B27 (+), %	82.2	73.1	74.7	89.1
Γυναίκες, %	36.0	34.5	57.1 <sup>§</sup>	23.2
BASDAI (0-10)	4.0	4.0	3.9	4.3
Πόνος συνολικά (0-10)	5.0	4.8	4.8	5.0
BASFI (0-10)	3.1	3.1	2.5 <sup>§</sup>	2.9
Σφαιρική αξιολόγιση ασθενούς (0-10)	5.0	5.0	4.9	4.6
Παθολογική τιμή CRP, %	51.9	49.6	29.8 <sup>§</sup>	69.1

<sup>§</sup>p < 0.05 vs ΑΣ ≤5 έτη, \*p < 0.05 vs ΑΣ

1. Rudwaleit M et al. Arthritis Rheum 2009;60:717-27

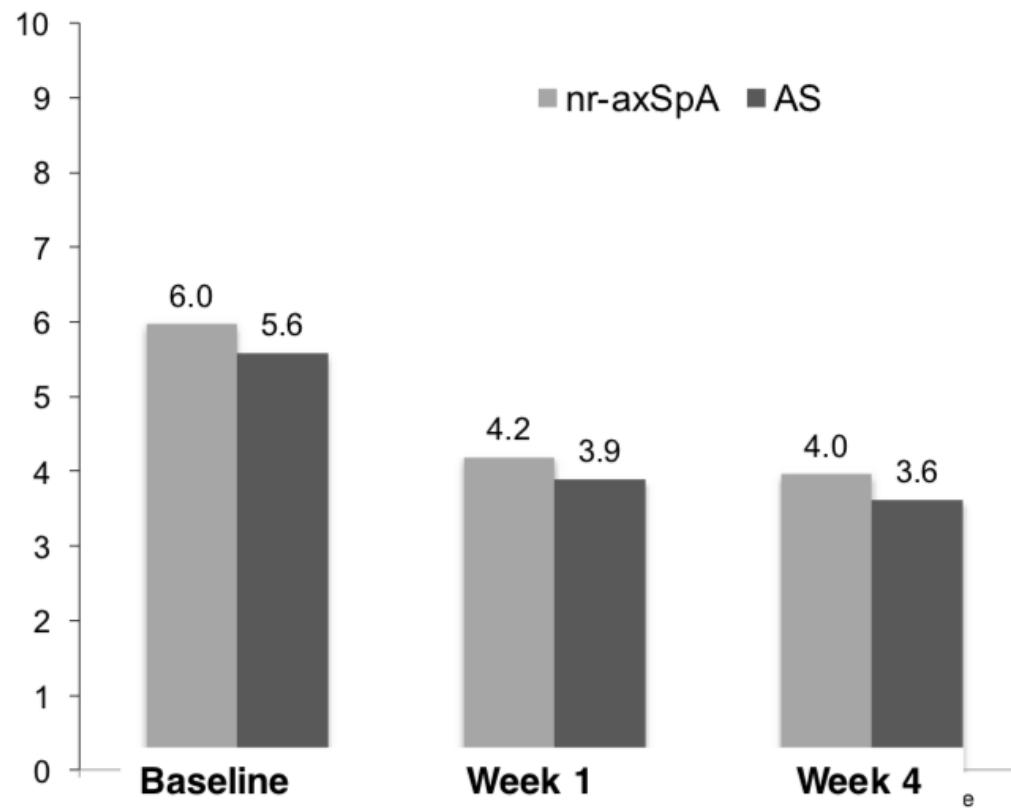
2. Kiltz U et al. Arthritis Care Res (Hoboken) 2012;64:1415-22



# Efficiency of treatment with NSAIDs according to current recommendations in patients with radiographic and non-radiographic axial spondyloarthritis – a prospective 4-week-study including magnetic resonance imaging

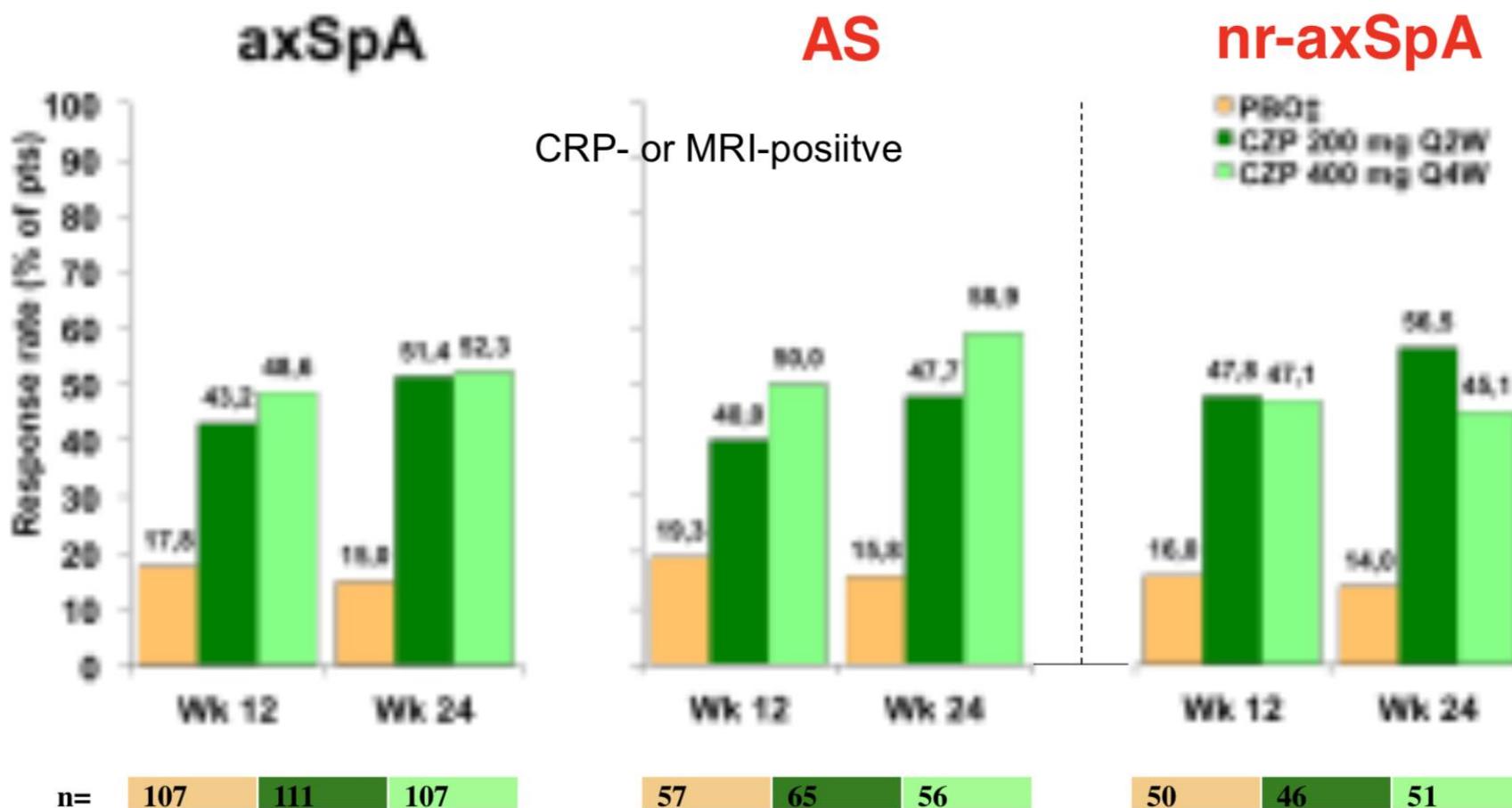
Consecutive anti-TNF-naïve patients (n=100) with nr-axSpA and AS (n=50 each) were included if their BASDAI was  $\geq 4$  and if they had not received maximal NSAID doses. Thereafter the NSAID dose was increased to maximum approved and tolerated.

	nr-axSpA (n=50)	AS (n=50)
Male gender	52%	70%
Age (years)	$37.6 \pm 11$	$41.9 \pm 12.3$
Symptom duration (years)	$7.3 \pm 9.1$	$14.6 \pm 11.8$
HLA-B27+ (%)	80%	74%
BASDAI (0-10)	$6.0 \pm 1.4$	$5.6 \pm 1.3$
NRS for back pain (0-10)	$7.1 \pm 1.7$	$6.5 \pm 2.4$
PatGA (0-10)	$6.9 \pm 1.8$	$6.5 \pm 2.3$
PhysGA (0-10)	$6.5 \pm 1.7$	$6.1 \pm 2.1$
Mean BASFI (0-10)	$4.6 \pm 2.6$	$4.8 \pm 2.4$
AS-QoL	$10.8 \pm 4.0$	$10.0 \pm 4.6$
CRP (mg/dl)	$0.6 \pm 0.9$	$1.2 \pm 1.1^*$
SIJ MRI score	$3.1 \pm 3.0$	$6.7 \pm 5.4^*$
ASDAS-CRP >2.1	76%	74%
Positive MRI of the SIJs	70%	78%
NSAID index (0-100)	$19.8 \pm 28.3$	$28.9 \pm 37.2$



# Certolizumab in axial SpA

## RAPID-axSpA ASAS40 Response

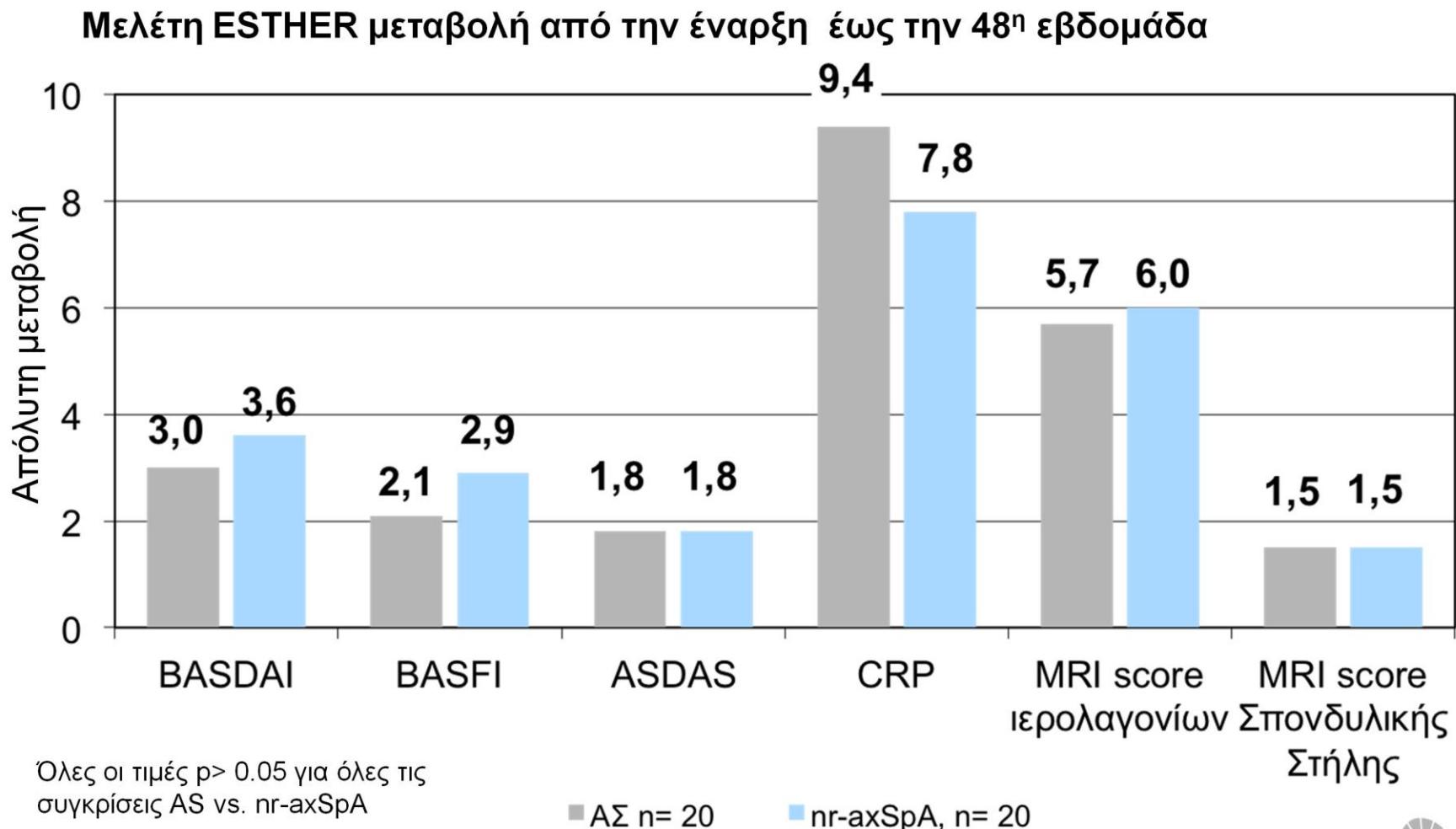


\* p < 0.001; † p < 0.05 CZP vs. PBO (2-sided Wald asymptotic test)

‡ Escaping PBO patients were considered non-responders Wk 24  
Randomized Set [NRI Imputation]

Landewé R et al. Ann Rheum 2014

# Παρόμοιος βαθμός απάντησης σε ασθενείς με ΑΣ και αξονική ΣπΑ χωρίς ακτινολογικά ευρήματα (nr-axSpA) μετά 1 έτος θεραπείας με Etanercept



Song IH et al. Ann Rheum Dis 2013;72:823-5 (with permission)



## 2016 update of the ASAS-EULAR management recommendations for axial SpA

- The use of IL-17i therapy should be avoided in patients with active IBD.
- Monoclonal antibodies are efficacious in the treatment of IBD and in preventing the recurrence of uveitis and, whereas etanercept has shown contradictory results for uveitis and no efficacy in IBD. Etanercept seems to be less efficacious for psoriatic skin involvement than other TNFi.

## 2019 Update of the ACR/ SPARTAN Recommendations for the Treatment of AS and Nonradiographic Axial SpA

- In adults with recurrent iritis, we conditionally recommend treatment with TNFi monoclonal antibodies over treatment with other biologics.
- In adults with IBD, we conditionally recommend treatment with TNFi monoclonal antibodies over treatment with other biologics.

**TABLE 1** Efficacy of cytokine and JAK inhibitors across the spondyloarthritis spectrum

Condition	Drug class				
	Monoclonal TNF inhibitors	Etanercept	IL-17A inhibitors	IL-23p19/p40 inhibitors	JAK inhibitors
AxSpA	++	++	++	--	(+)
Uveitis	++	(+)	?	?	?
IBD	++	--	--	++	CD (?/+) UC ++
Psoriasis	++	++	+++	+++	(+/++)
Hidradenitis suppurativa	++ <sup>a</sup>	(+)	(+)	(+)	?

## Sex differences in axial SpA

- Women with axSpA are found to be less often positive for the HLA- B27 allele compared with males.
- There are sex differences in other less familiar gene expressions.
- Immune processes are also influenced by sex hormones.
- IL-17A and Th17 cells were elevated in male patients but not in female patients.
- Sex hormones also influence other physiological processes, such as pain transmission.
- Sex differences in body composition influence the immune modulation indirectly, especially due to fat disposition.

# Sex differences in axial SpA

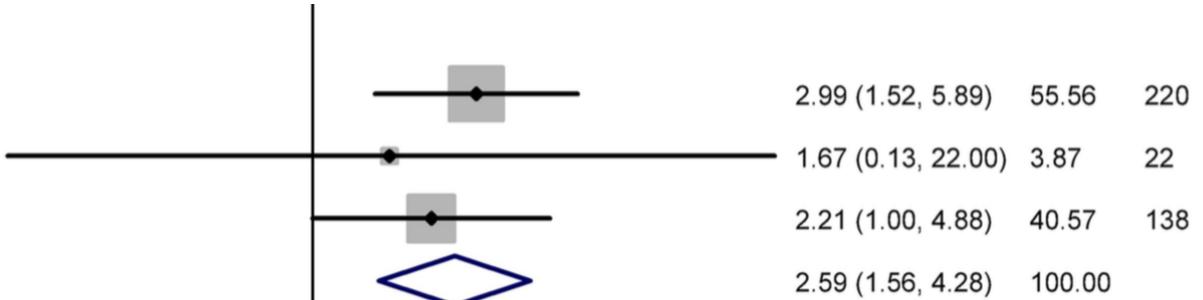
Manifestations and comorbidities	Gender differences	Disease activity at baseline	Gender differences
Extraspinal manifestations		BASDAI	↑ in women
AAU	No differences	ASDAS-CRP	No difference
Enthesitis	↑ in women	CRP-levels	↑ in men
IBD	↑ in women	ESR-levels	No difference
Psoriasis	↑ in women	Function	
Peripheral arthritis	↑ in women	BASFI	No difference
Comorbidities		Quality of life	
Cardiovascular diseases	↑ in men and post-menopausal women	ASQoL	↓ in women
Osteoporosis	Equal risk, but underdiagnosis in (young) males	ASASHI	↓ in women
		EuroQoL	No difference
		SF-36	No difference
		Physical	
		BASMI	↑ in men
		MASES	↑ in women

# Predictors of response to TNF antagonists in patients with AS: systematic review and meta-analysis

(C) Meta-analysis of gender and ASAS20 in AS. (D) Meta-analysis of gender and BASDAI50 in AS

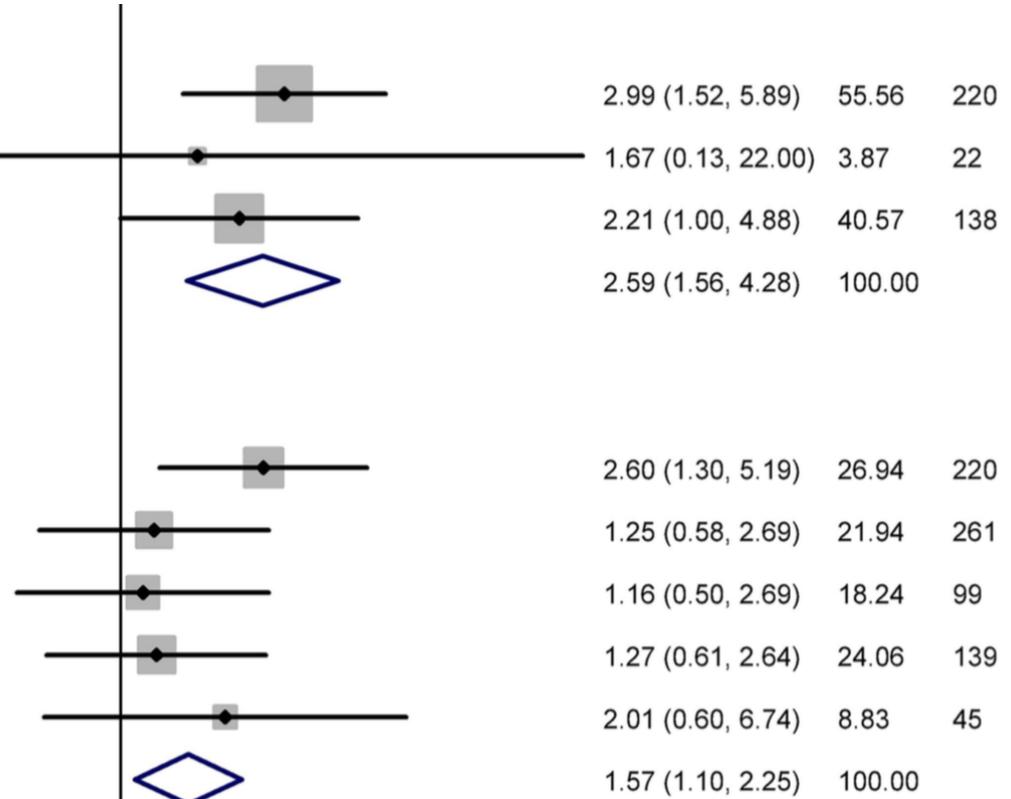
C

Arends et al (2011) IFX,ETN, ADA  
Stone et al (2004) IFX  
FDA-103795/5123 ETN  
Subtotal (I-squared = 0.0%, p = 0.803)

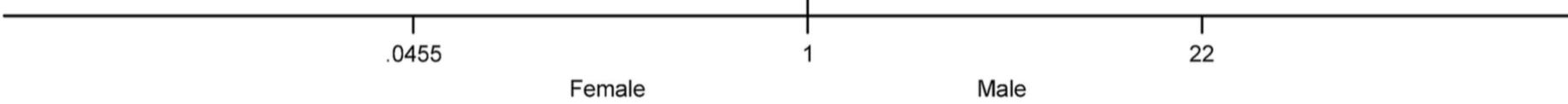


D

Arends et al (2011) IFX,ETN, ADA  
Lord et al (2010) IFX, ETN, ADA  
Rudwaleit et al (2004) IFX, ETN  
Ottaviani et al (2012) IFX  
Haibel et al (2008) ADA  
Subtotal (I-squared = 0.0%, p = 0.500)



NOTE: Weights are from random effects analysis



# Response to TNFi in Male and Female Patients with AS: Data from a Swiss Cohort

*Table 3.* Clinical outcome of women versus men after 1 year of treatment with a first TNF inhibitor (Response/Tolerance Analysis<sup>#</sup>).

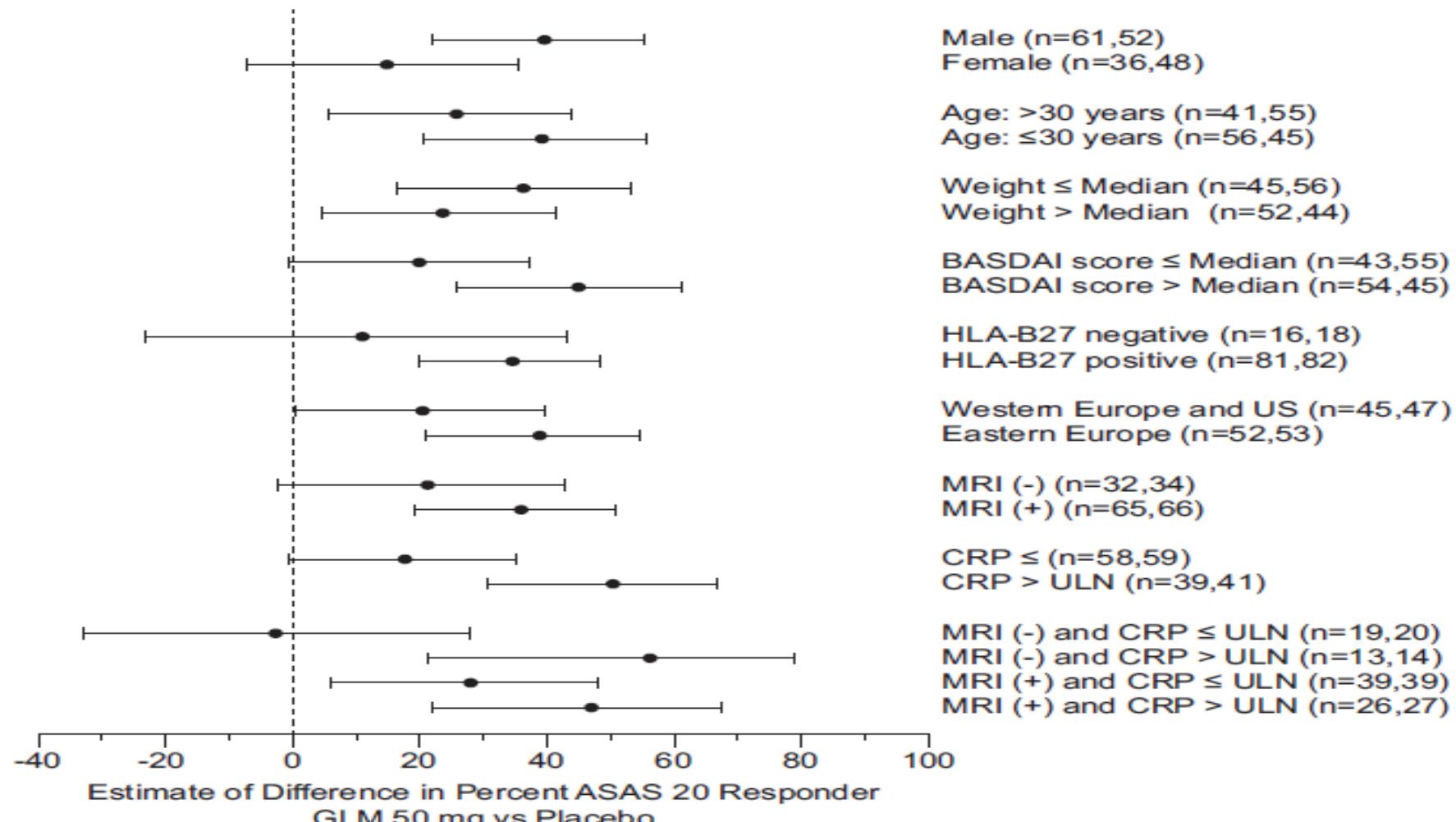
Outcome	N	Unadjusted Analyses				Adjusted Model 1*				Adjusted Model 2**				
		Women, %	Men, %	OR	95% CI	p	N	OR	95% CI	p	N	OR	95% CI	p
ASAS20	293	52	63	0.63	0.37–1.07	0.09	244	0.48	0.27–0.87	0.02	210	0.34	0.16–0.71	0.005
ASAS40	293	40	46	0.79	0.46–1.35	0.37	244	0.60	0.33–1.09	0.10	210	0.44	0.21–0.91	0.03
ASDAS improvement ≥ 1.1	262	51	61	0.69	0.38–1.22	0.21	228	0.52	0.26–1.05	0.07	196	0.27	0.10–0.67	0.006
ASDAS < 2.1	284	48	53	0.82	0.48–1.42	0.51	230	0.47	0.24–0.91	0.03	198	0.26	0.11–0.59	0.002
ASDAS improvement ≥ 2	262	23	32	0.62	0.31–1.19	0.14	228	0.48	0.22–0.99	0.05	196	0.26	0.09–0.67	0.007
ASDAS < 1.3	284	18	26	0.65	0.32–1.27	0.22	230	0.29	0.11–0.68	0.007	198	0.10	0.03–0.31	< 0.001

## Sex differences in axial SpA

Disease activity (mean)	Differences (range 6–60 months)
BASDAI	Remains higher over time in females
ASDAS-CRP	No observed differences
CRP level	Remains higher over time in males
ESR level	No observed differences
Treatment response	Differences (range 6–60 months)
BASDAI 50%	↓ in females
ASDAS-CRP <sup>a</sup>	↓ in females
ASAS20/40	↓ in females
Drug survival	Differences (range 12 weeks–10 years)
Time on drug	↓ in female patients
Switch	↑ in female patients

# GO-AHEAD: GOL 50mg vs placebo σε μη ακτινολογικά αξονική ΣΠΑ

## Διαφορά % ανταπόκρισης ASAS 20



## BMI δεν επηρεάζει το δείκτη ASDAS στην αξονική ΣΠΑ

**Table 5** Linear regression analyses explaining ASDAS by BMI in the 168 axSpA patients

$\beta$	SE	95% CI	R-squared	p Value
Without adjustments				
BMI	0.02	0.01	-0.01 to 0.04	0.01
0.18				
Adjusted for age and gender				
BMI	0.02	0.01	-0.01 to 0.04	0.03
0.13				

ASDAS, Ankylosing Spondylitis Disease Activity Score; axSpA, axial spondyloarthritis;  $\beta$ , unstandardised  $\beta$  coefficient.

**Table 4** Linear regression analyses explaining CRP by BMI according to gender in the whole population (n=428)

$\beta$	SE	95% CI	R-squared	p Value
Male (n=158)				
BMI	-0.11	0.20	-0.51 to 0.28	0.00
0.58				
Female (n=270)				
BMI	0.35	0.07	0.21 to 0.49	0.09
<0.001				

p Value in bold with statistical significance.

$\beta$ , unstandardised  $\beta$  coefficient; BMI, body mass index; CRP, C reactive protein.

# Η παχυσαρκία είναι συχνή στην αξονική ΣΠΑ και σχετίζεται φτωχή κλινική έκβαση

Παχυσαρκία: 22% αξονική ΣΠΑ vs 15% γενικό πληθυσμό

	All patients	Normal BMI< 25Kg/m <sup>2</sup>	Overweight 25Kg.m <sup>2</sup> < BMI < 30Kg/m <sup>2</sup>	Obese BMI > 30Kg/m <sup>2</sup>
BASDAI, 0–10	3.8 ± 2.3	3.8 ± 2.3	3.5 ± 2.1	4.5 ± 2.3*†
ASDAS	2.4 ± 1.0	2.3 ± 1.0	2.2 ± 0.8	2.8 ± 1.1*†
CRP, mg/l	3 (0–94)	3 (0–73)	3 (1–94)	5 (1–82)*†
ESR, mm/h	9 (1–79)	8 (1–71)	8 (2–79)	13 (2–66)*†
BASFI, 0–10	3.3 (0–9.9)	2.9 (0–9.1)	2.9 (0–9.9)	5.2 (0.1–9.7)*†
ASQoL, 0–18	6 (0–18)	5 (0–17)	4 (0–17)	8 (0–18)*†

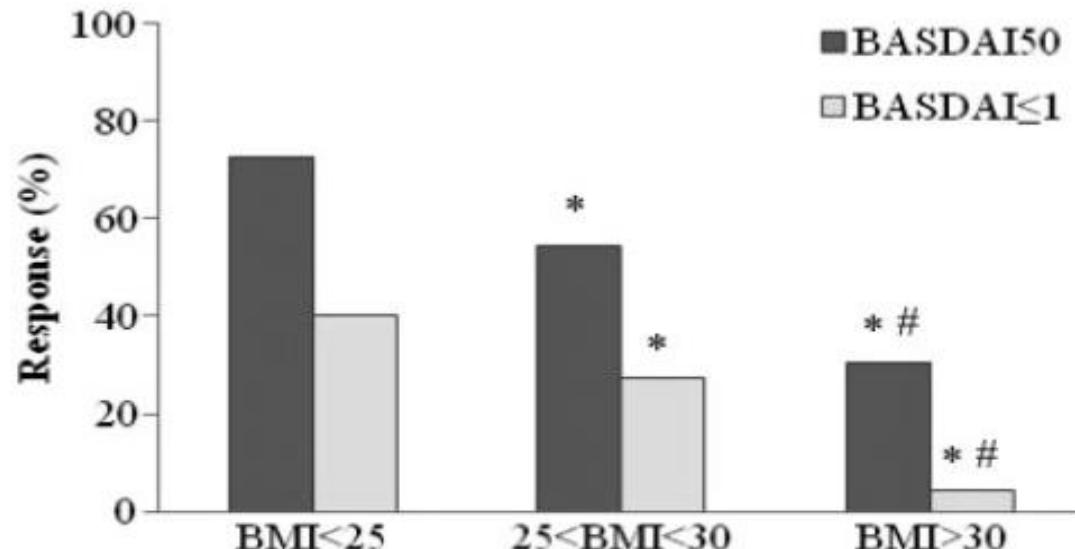
Αγωγή: 50% ΜΣΑΦ, 7% DMARDs, 44% anti-TNF

## BMI επηρεάζει την απάντηση σε INF στην ΑΣ

Πολυπαραγοντική ανάλυση: το υψηλό BMI σχετίζεται ανεξάρτητα με μη ανταπόκριση σε INF στους 6 μήνες σε ΑΣ

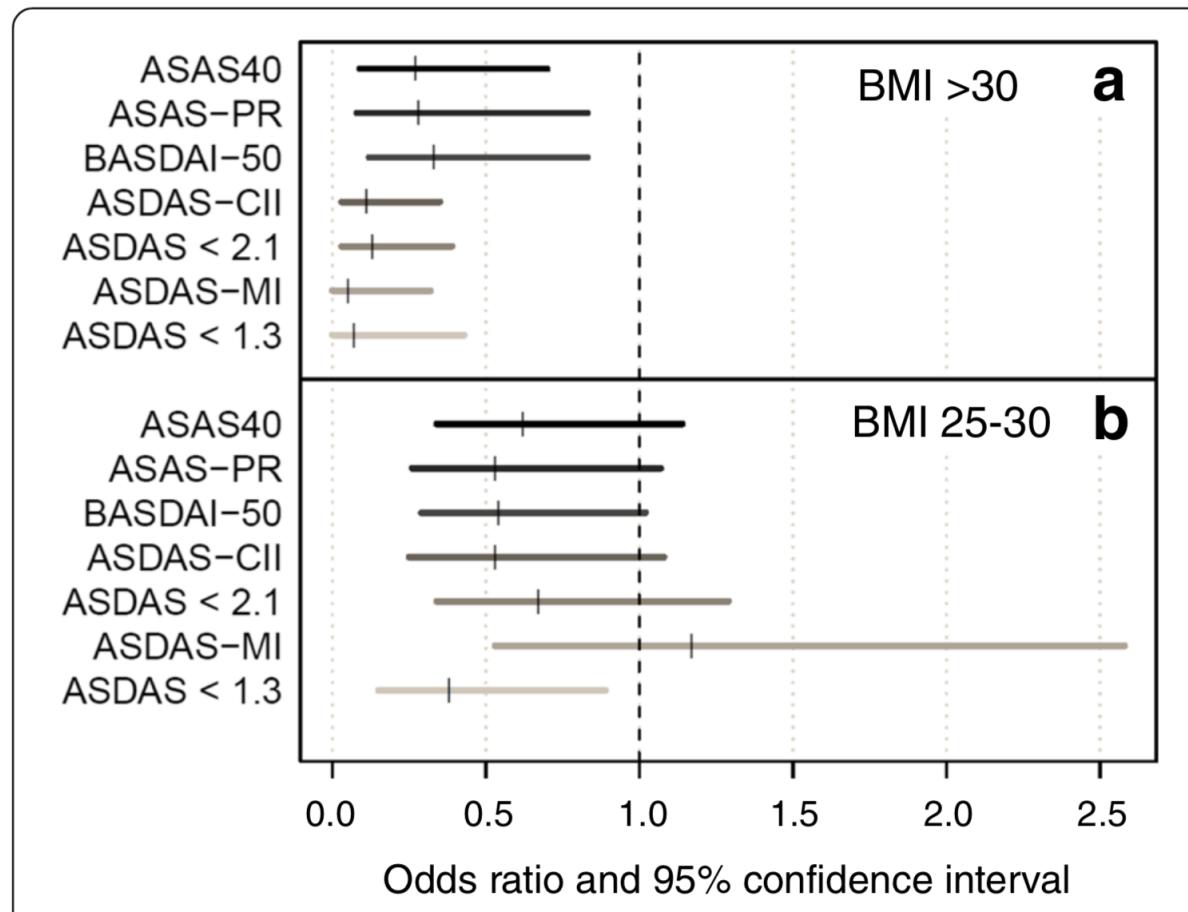
Response criteria	P value	OR (95% CI) <sup>a</sup>
BASDAI50	0.0003	0.87 (0.81-0.94)
VAS50	< 0.0001	0.87 (0.80-0.93)
CRP50	0.0279	0.93 (0.88-0.99)
NSAID50	0.0077	0.91 (0.85-0.97)

## Η παχυσαρκία σχετίζεται με λιγότερη πιθανότητα ανταπόκρισης σε αντι-TNF στην αξονική ΣΠΑ



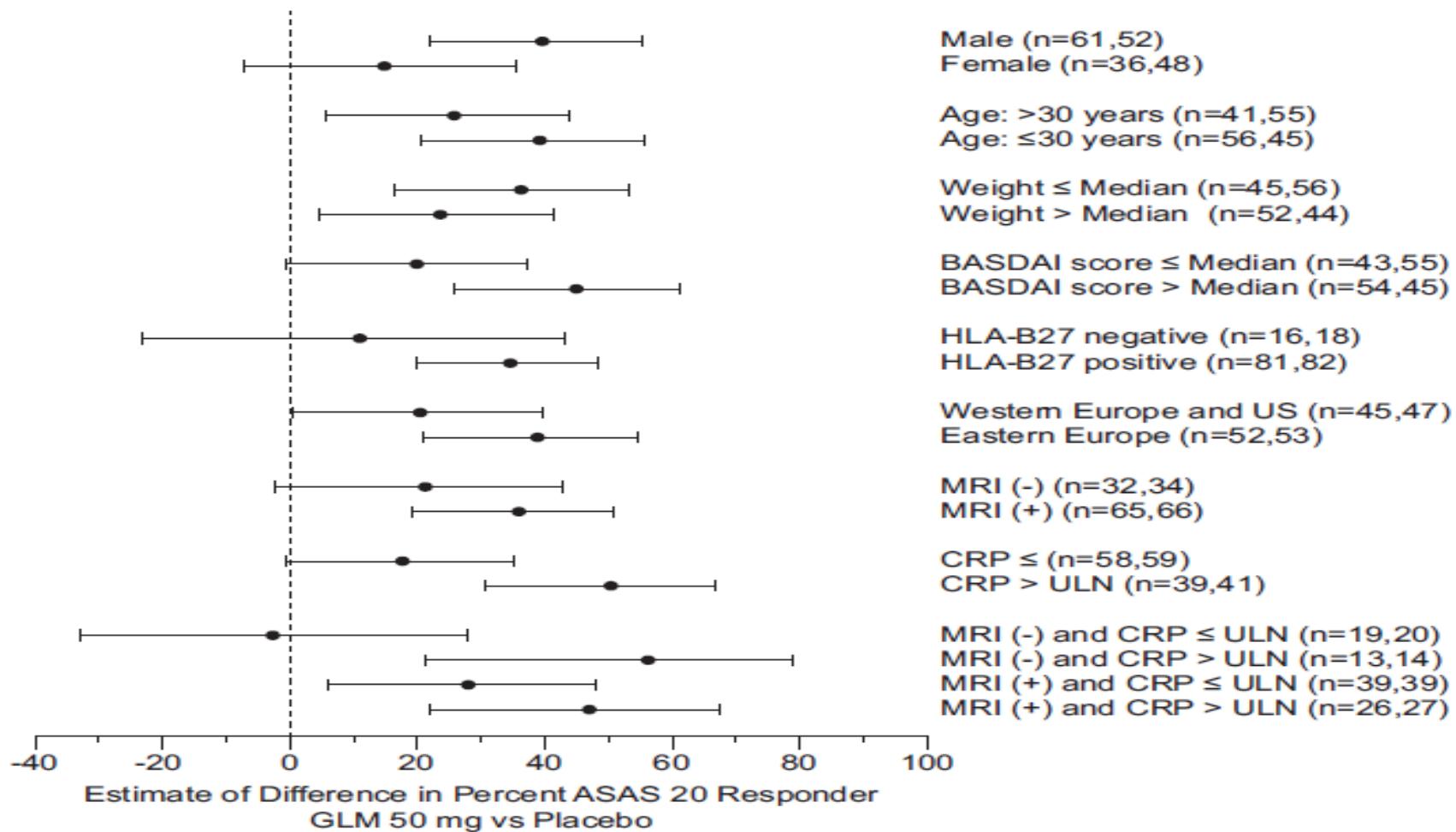
\* $P < 0.05$  vs  $BMI < 25$ ; # $P < 0.05$  vs  $BMI 25-30$ .

# Impact of obesity on the response to TNFi in axial SpA

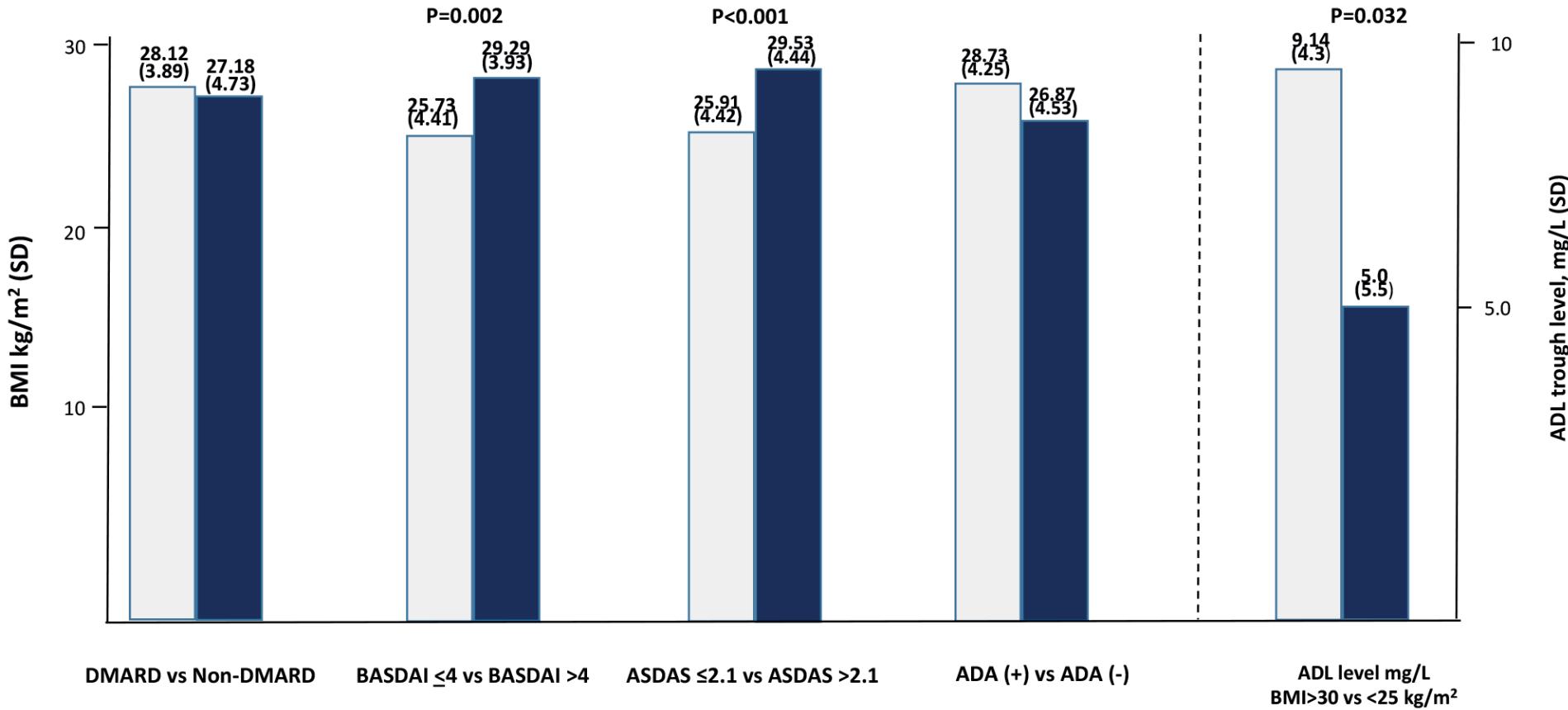


# GO-AHEAD: GOL 50mg vs placebo σε μη ακτινολογικά αξονική ΣΠΑ

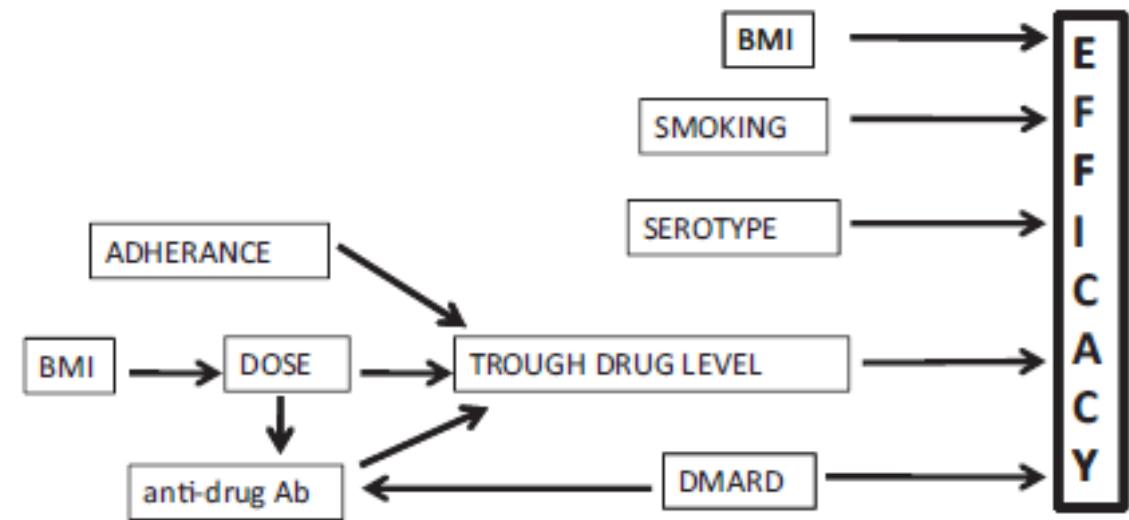
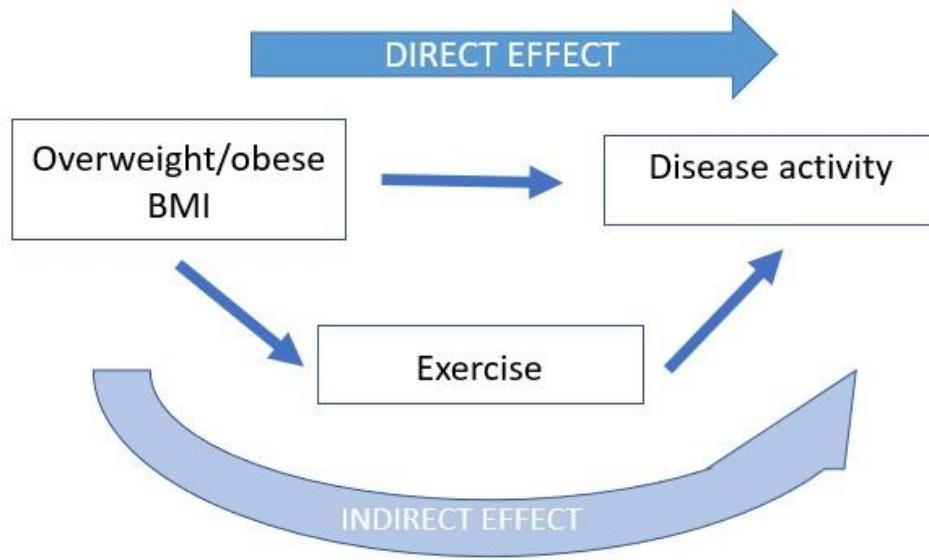
## Διαφορά % ανταπόκρισης ASAS 20



## Η παχυσαρκία ελαττώνει την κλινική αποτελεσματικότητα και τα επίπεδα του ADA στην ΑΣ

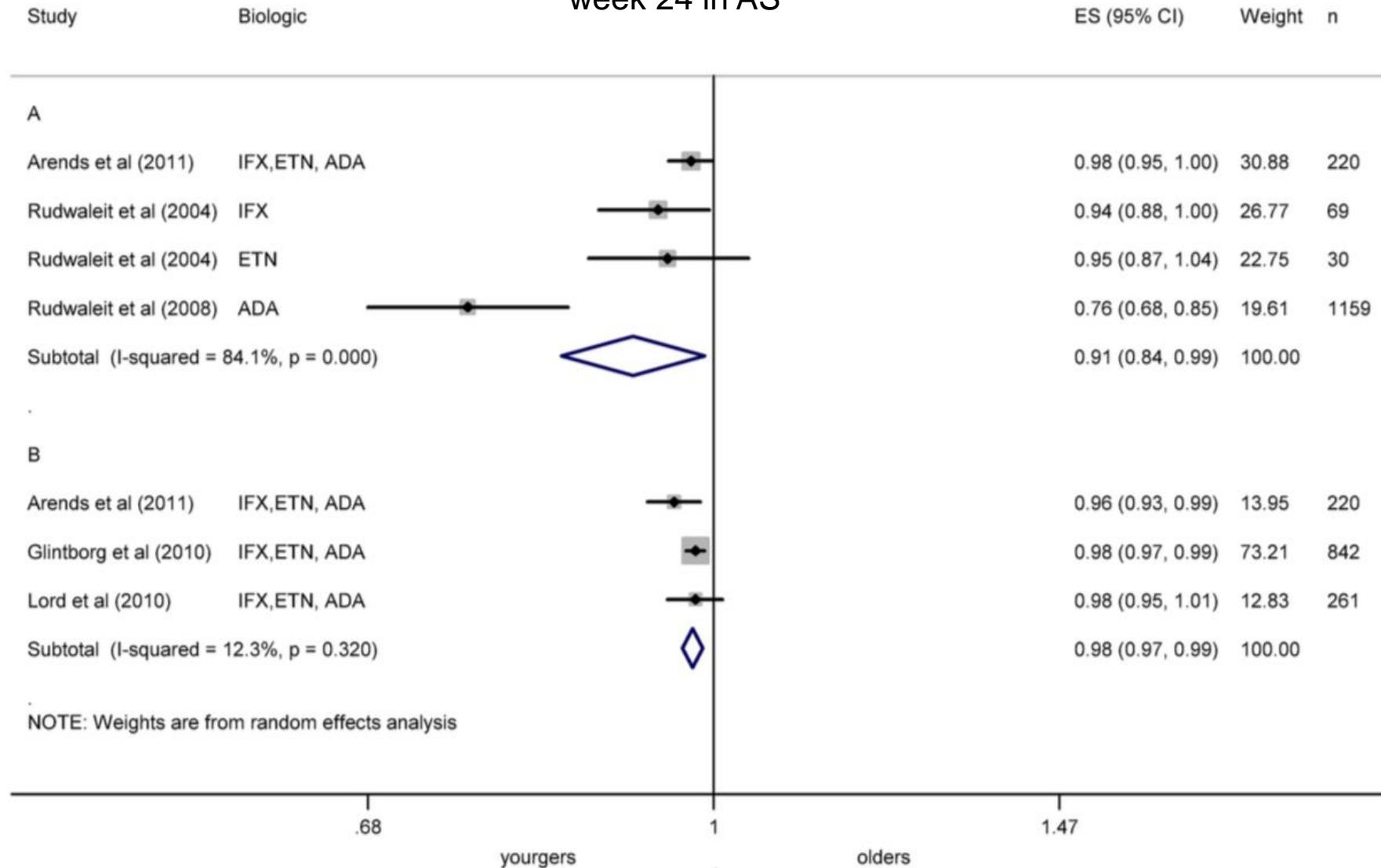


## BMI: ένας παράγοντας που θα πρέπει να λαμβάνεται υπόψη στην απόφαση βιολογικής θεραπείας



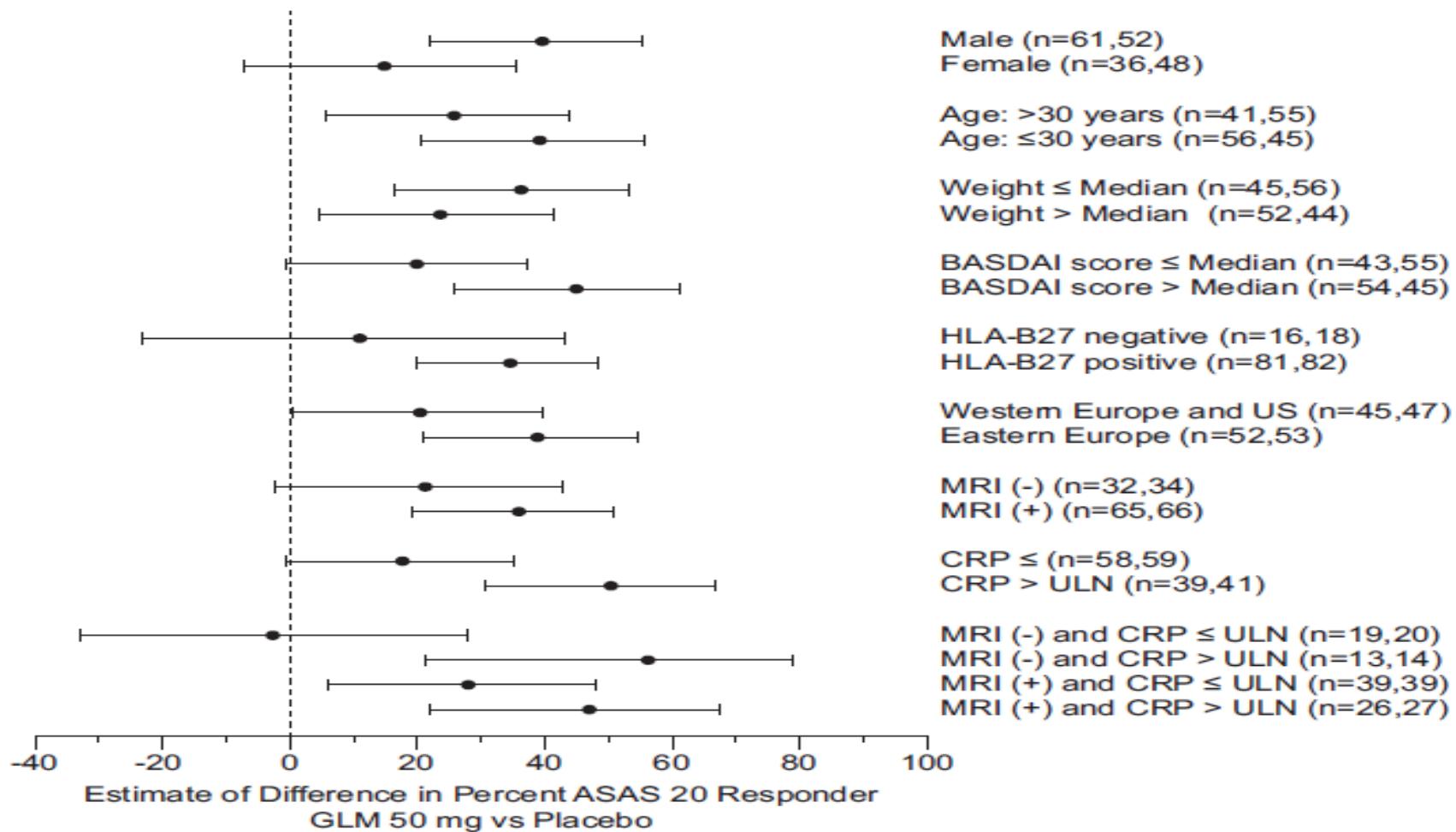
# Predictors of response to TNF antagonists in patients with AS: systematic review and meta-analysis

(A) Meta-analysis of age and BASDAI50 at week 12 in AS. (B) Meta-analysis of age and BASDAI50 at week 24 in AS

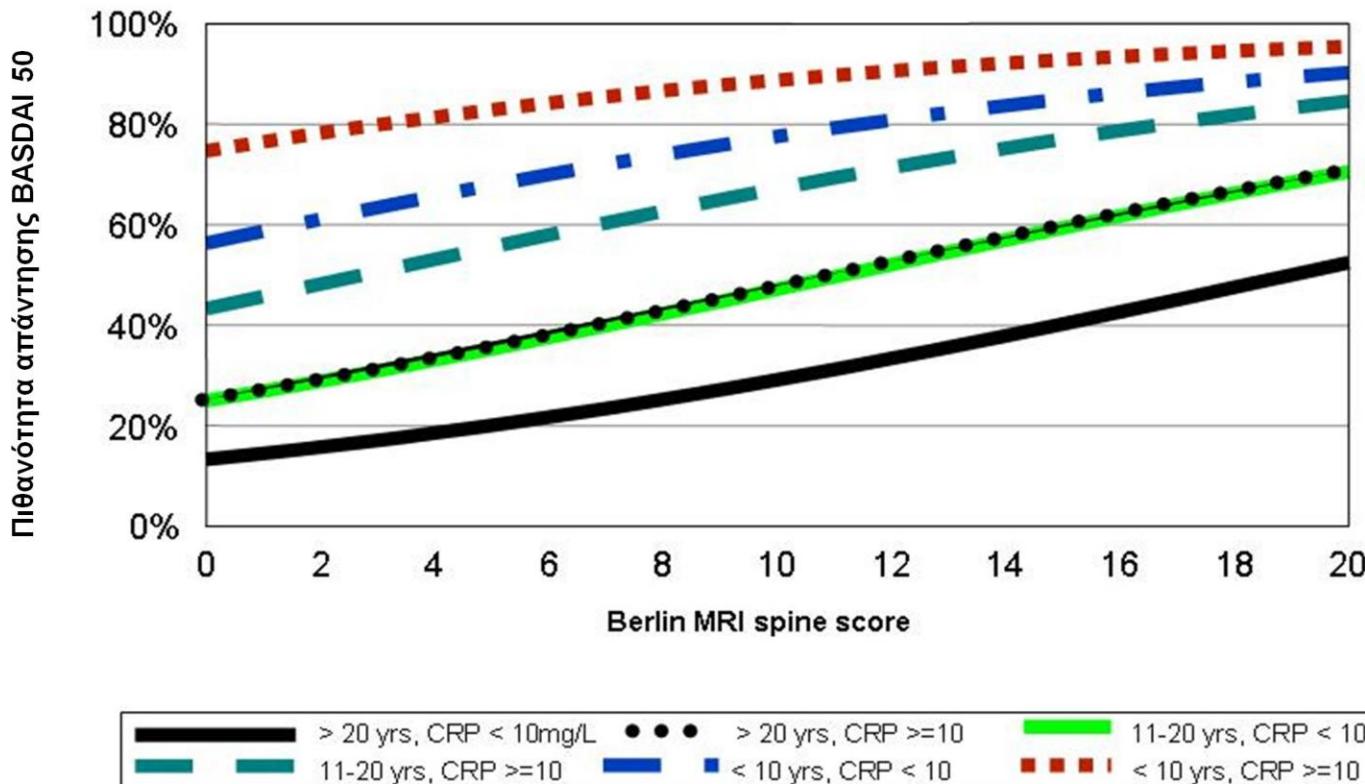


# GO-AHEAD: GOL 50mg vs placebo σε μη ακτινολογικά αξονική ΣΠΑ

## Διαφορά % ανταπόκρισης ASAS 20



# Προγνωστική συνεισφορά συνδυασμού παραμέτρων για βελτίωση BASDAI 50 στη θεραπεία με αντί-TNF $\alpha$



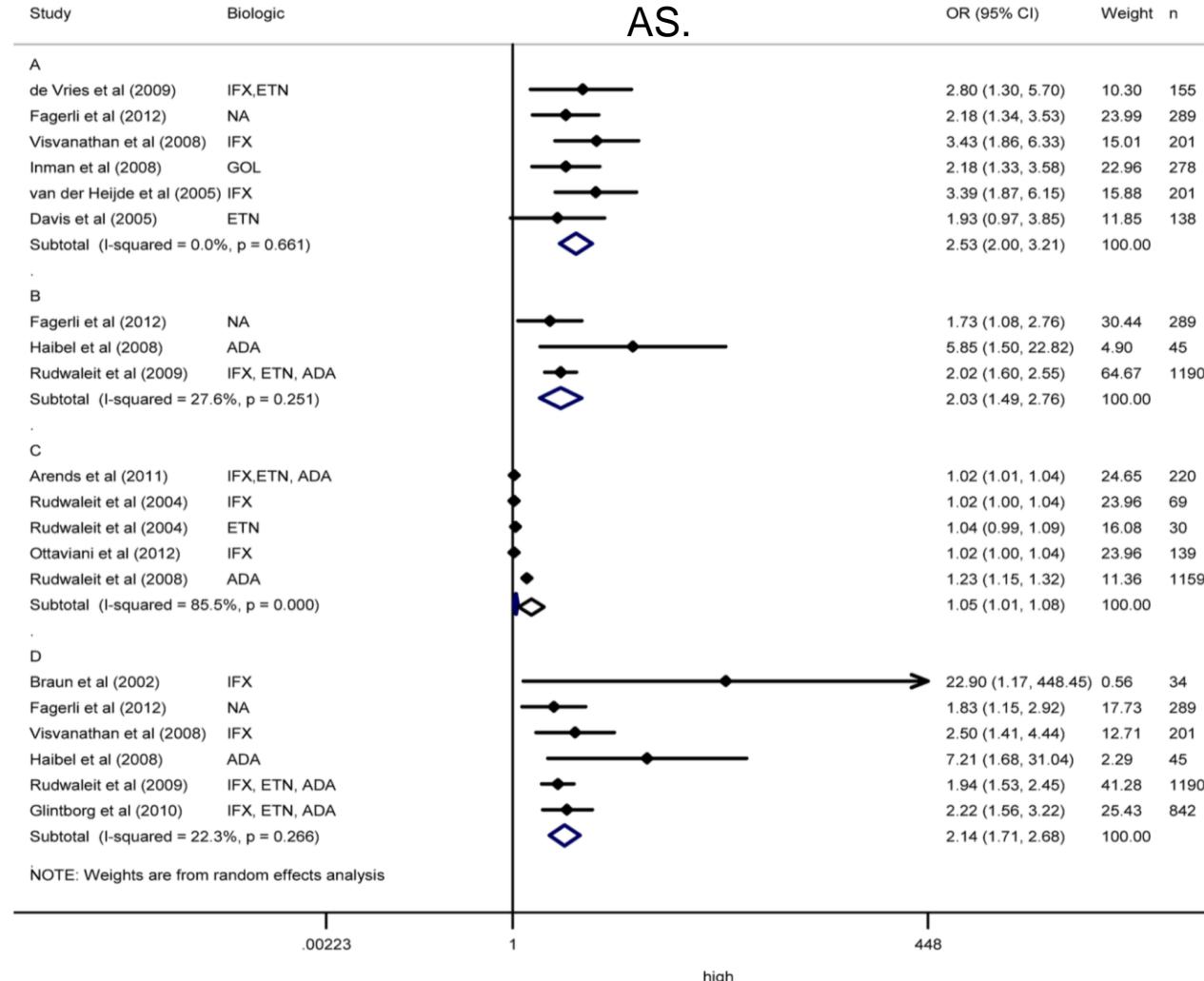
Rudwaleit M et al. Ann Rheum Dis 2008;67:1276-81 (with permission)



# Predictors of response to TNF antagonists in patients with AS: systematic review and meta-analysis

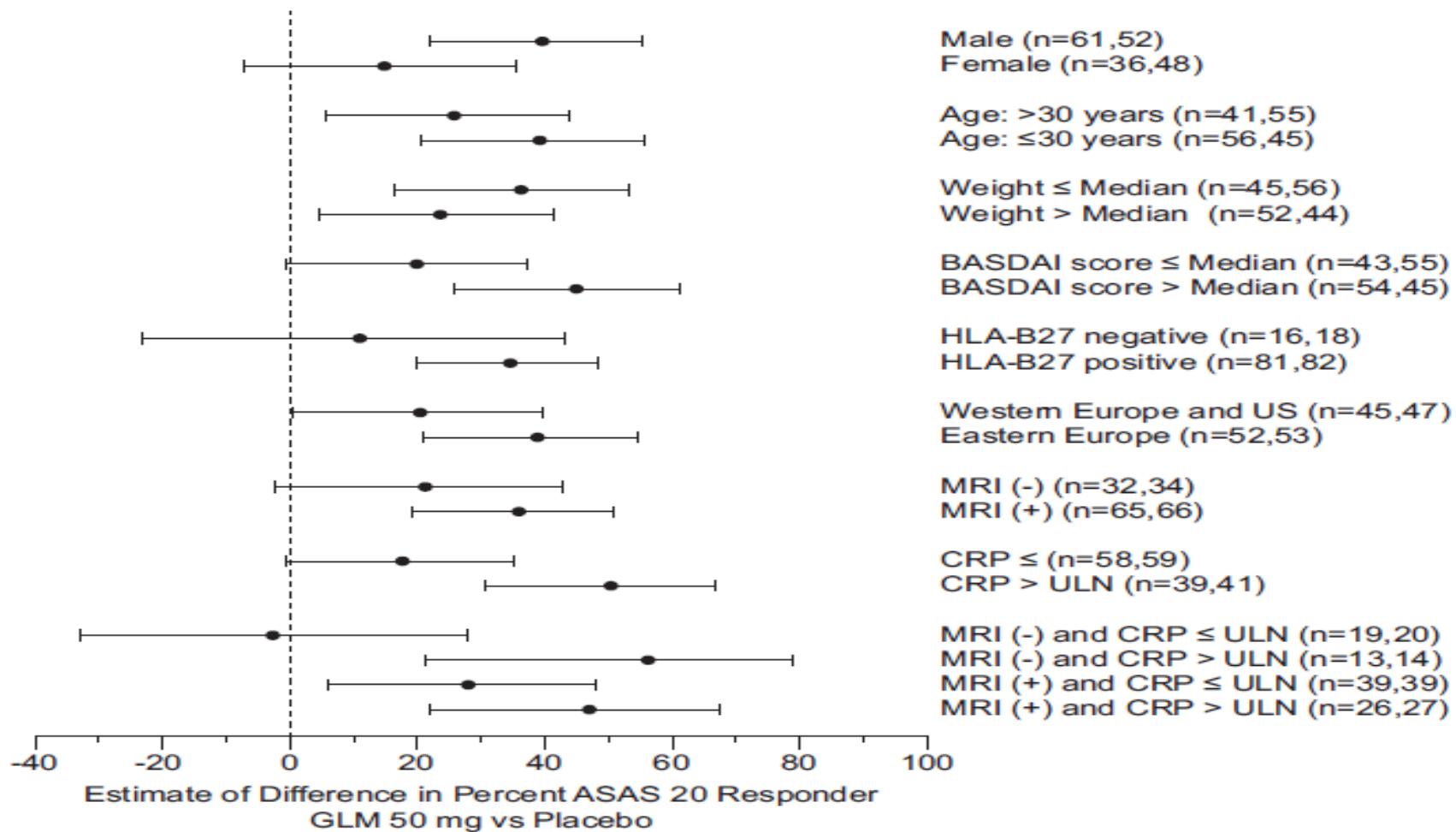
(A) Meta-analysis of dichotomous CRP and ASAS20 in AS. (B) Meta-analysis of dichotomous CRP and ASAS40 in AS.

(C) Meta-analysis of continuous CRP and BASDAI in AS. (D) Meta-analysis of dichotomous CRP and BASDAI50 in AS.



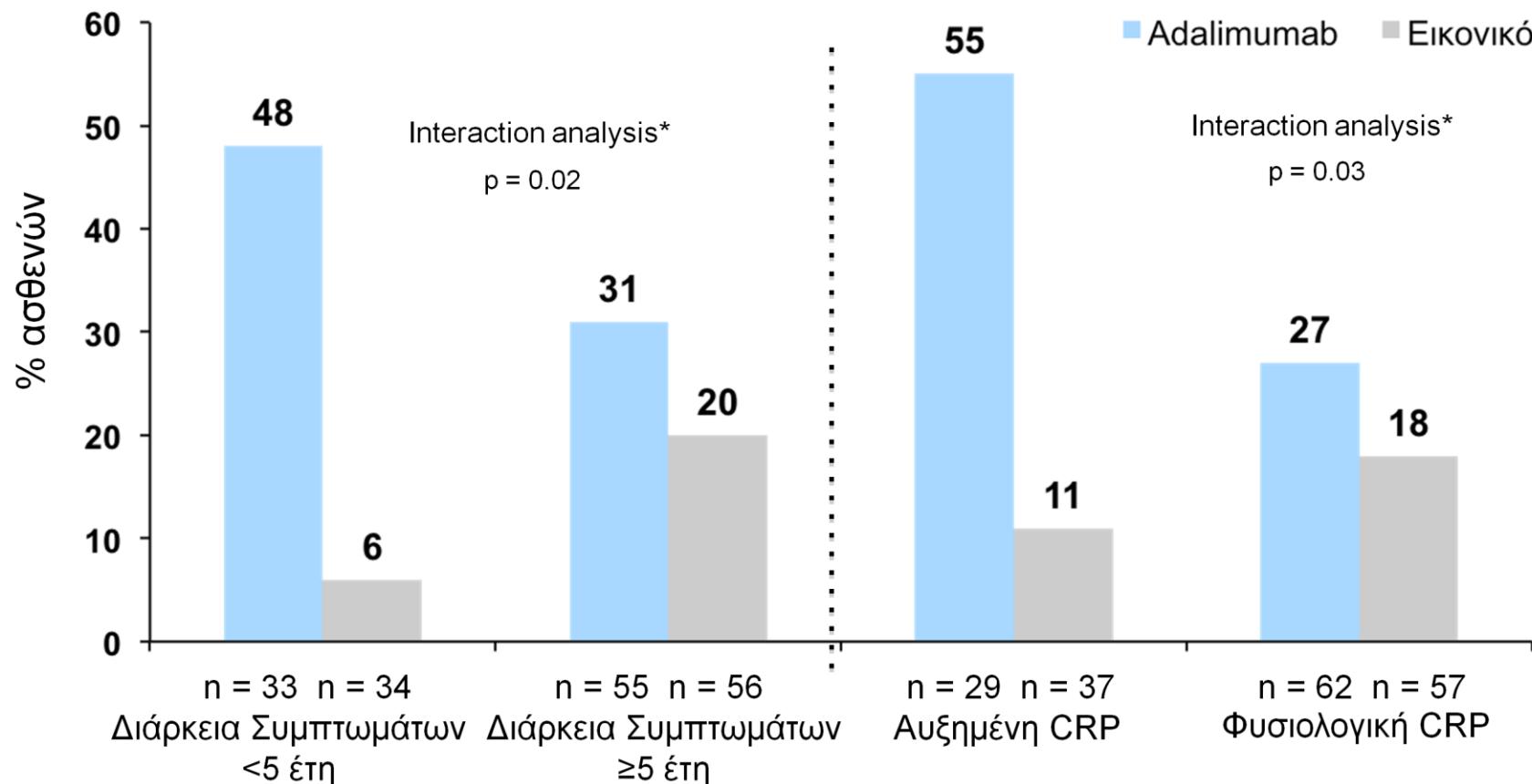
# GO-AHEAD: GOL 50mg vs placebo σε μη ακτινολογικά αξονική ΣΠΑ

## Διαφορά % ανταπόκρισης ASAS 20



**Απάντηση ASAS40 στο Adalimumab ανάλογα με τη διάρκεια των συμπτωμάτων και την αναρξης την 12<sup>η</sup> εβδομάδα σε ασθενείς με αξονική σπονδυλαρθρίτιδα χωρίς ακτινολογικά ευρήματα**

**Μελέτη ABILITY-I: 40 mg Adalimumab υ.δ./2 εβδ. vs. εικονικό σε 12 εβδομάδες**

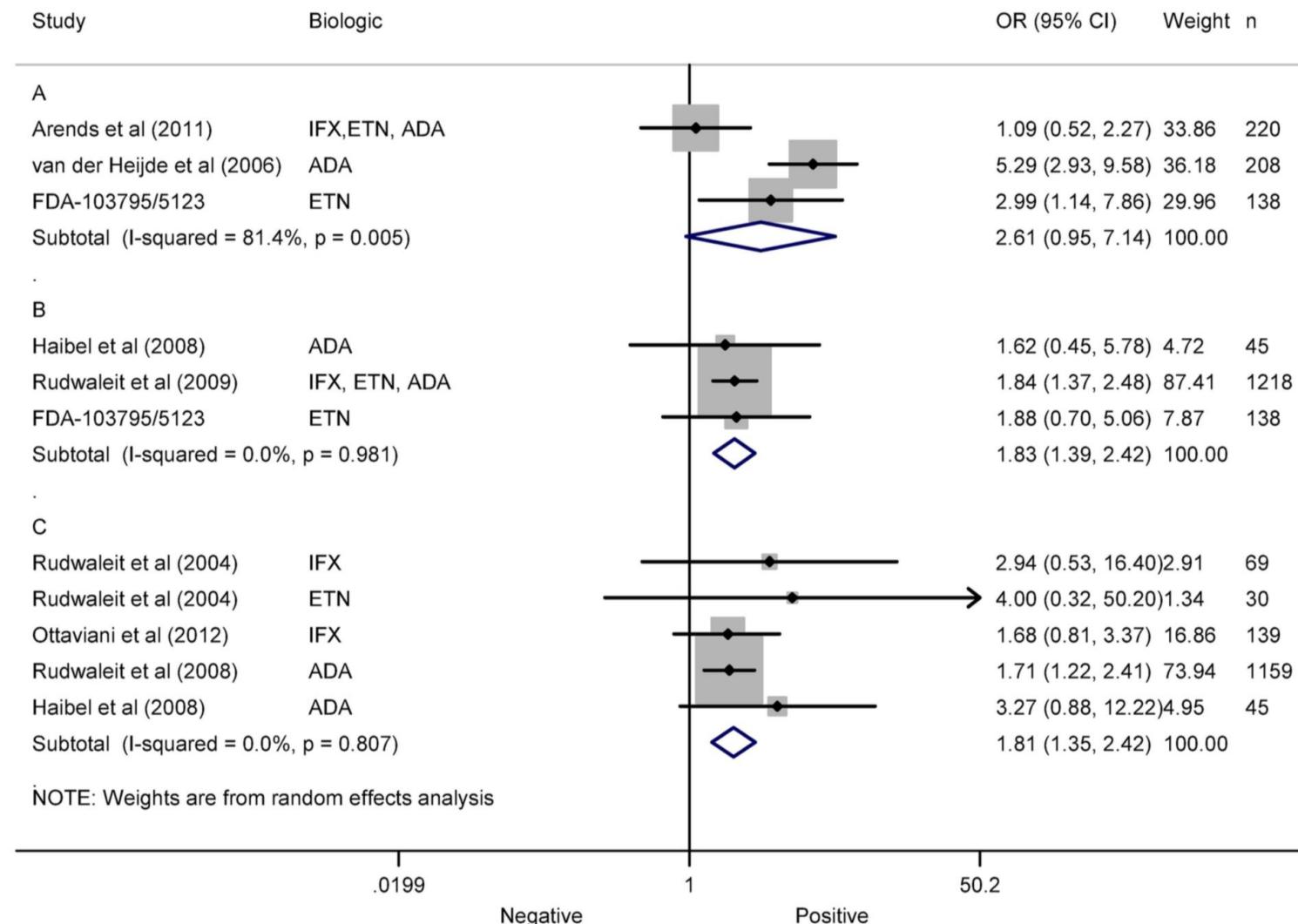


\*λογιστικό μοντέλο που χρησιμοποιήθηκε για να εκτιμηθεί η θεραπεία και η αλληλεπίδραση μεταξύ των υποομάδων, με σημαντική αλληλεπίδραση να έχει ορισθεί όταν  $p \leq 0.10$

Sieper J et al. Ann Rheum Dis 2013;72:815-22 (with permission)

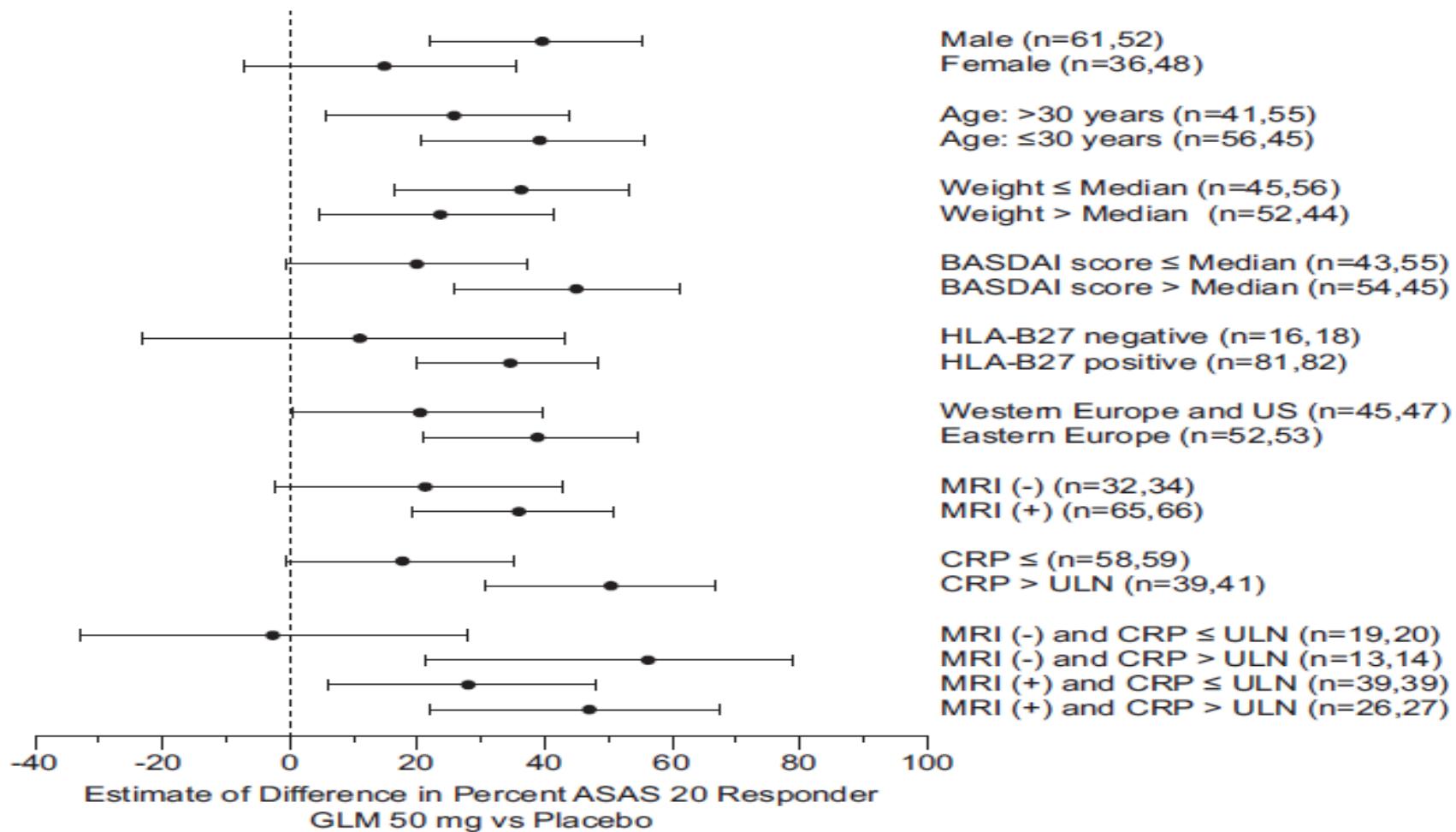
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(A) Meta-analysis of HLAB27 and ASAS20 in AS. (B) Meta-analysis of HLAB27 and ASAS40 in AS. (C) Meta-analysis of HLAB27 and BASDAI50 in AS.



# GO-AHEAD: GOL 50mg vs placebo σε μη ακτινολογικά αξονική ΣΠΑ

## Διαφορά % ανταπόκρισης ASAS 20



# The effect of smoking on clinical and radiographic variables, and acute phase reactants in patients with ankylosing spondylitis

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**Table 4** Multivariate linear regression analyses showing independent variables associated with BASDAI, BASFI and mSASSS in patients with ankylosing spondylitis (AS)

Independent variable	$\beta^a$	$B^b$ (95 % CI)	<i>p</i> value
BASDAI—Model 1			
Current smoking	0.35	14.75 (7.0, 22.49)	<0.001
ESR	0.83	4.61 (-13.13, 22.36)	0.607
CRP	0.13	5.55 (-7.72, 18.83)	0.409

# Serum levels of Dkk-1, sclerostin and VEGF in patients with ankylosing spondylitis and their association with smoking, and clinical, inflammatory and radiographic parameters

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**Table 4**

Multivariate linear regression models showing independent variables associated with serum levels of Dkk-1, sclerostin and VEGF in patients with ankylosing spondylitis (AS).

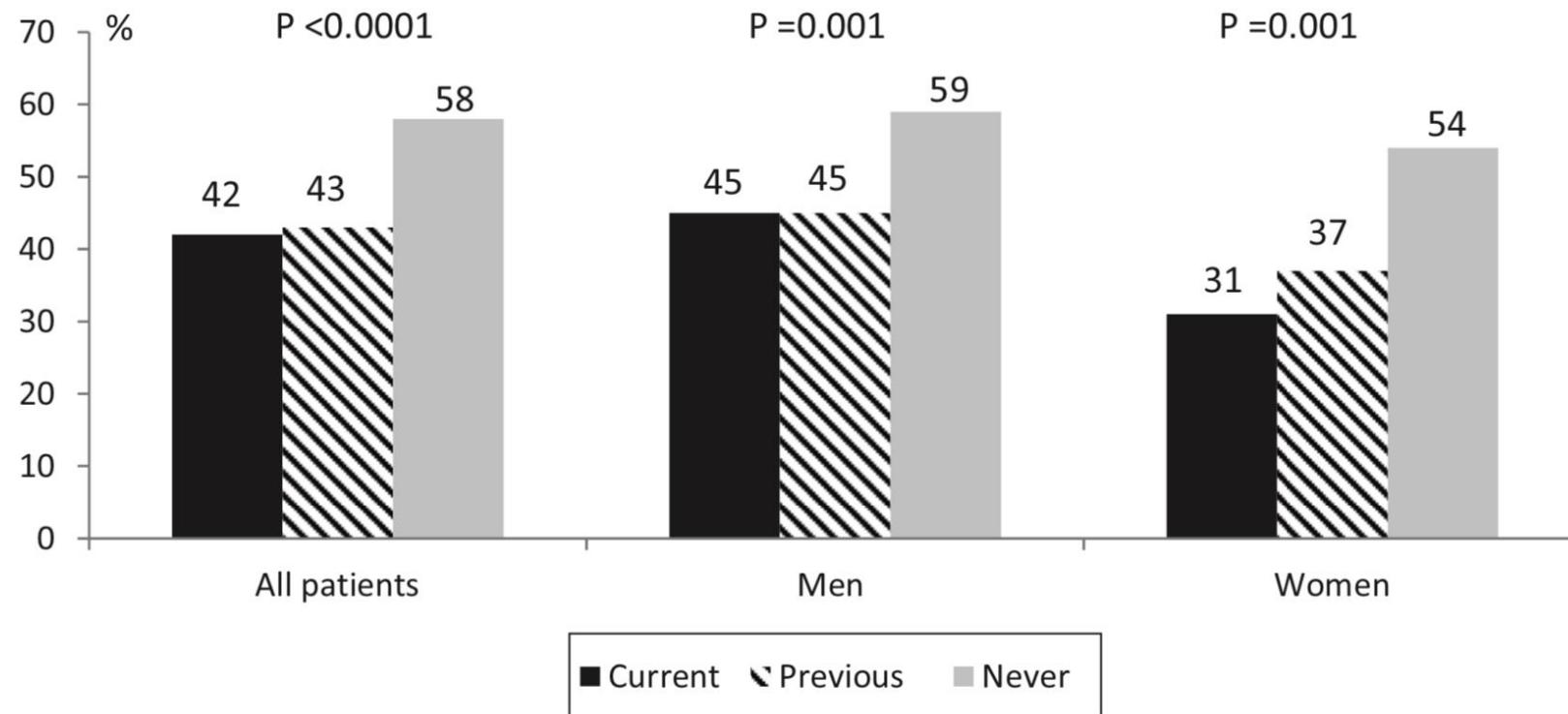
Independent variable	$\beta^a$	P-value	$\beta^a$	P-value
	Model 1		Model 2	
<i>Regression analyses for Dkk-1</i>				
Current smoking	-0.011	0.912	0.018	0.872
ESR	0.515	<0.001		
CRP			0.409	<b>0.001</b>
BASDAI	-0.338	0.064	-0.347	0.079
Syndesmophytes	-0.380	<b>0.001</b>	-0.175	0.139
Age	0.244	0.071	0.174	0.221
BMI	-0.019	0.863	-0.062	0.601
Sclerostin	0.506	<0.001	0.548	<0.001
<i>Regression analysis for sclerostin</i>				
Syndesmophytes	0.006	0.963		
Age	-0.251	0.052		
Dkk-1	0.532	<0.001		
<i>Regression analyses for VEGF</i>				
Model 1		Model 2		
Current smoking	0.240	0.088	0.269	0.059
ESR	0.227	0.090		
CRP			0.197	0.137
BASDAI	0.161	0.274	0.113	0.467
BASFI	0.106	0.431	0.181	0.163
<i>Regression analyses for VEGF</i>				
Model 1		Model 2		
Ever smoking	0.465	<0.001	0.499	<0.001
ESR	0.242	<b>0.043</b>		
CRP			0.253	<b>0.033</b>
BASDAI	0.193	0.101	0.136	0.270
BASFI	0.171	0.160	0.254	0.088

## Connection smoking and inflammation

- Smoking has an inflammatory effect through increased production of pro-inflammatory cytokines such as TNF-alpha and IL-6.
- Smoking is associated with periodontitis and its severity in a dose-dependent manner and correlated with CRP elevation .
- Smoking may also interfere with gut physiology.
- The possibility of activation of the IL-23/Th17 pathway by smoking.

# Impact of tobacco smoking on response to TNFi treatment in patients with AS: results from the Danish nationwide DANBIO registry

**FIG. 2** BASDAI50%/20 mm-response rates after 6 months' treatment according to smoking status for all patients and stratified according to gender



# Impaired response to treatment with TNFi in smokers with axial SpA

**Table 4** Estimated difference in BASDAI or ASDAS-CRP drop after initiation of a first TNF inhibitor between smokers (ever, current, previous) and non-smokers

Smokers vs non-smokers with elevated baseline CRP

Difference in $\Delta$ BASDAI				Difference in $\Delta$ BASDAI			
	BASDAI units	95% CI	p Value		BASDAI units	95% CI	p Value
Ever smokers	0.62	0.13 to 1.11	0.01	Current smokers	0.75	0.22 to 1.28	0.005
				Past smokers	0.36	-0.28 to 1.00	0.27

Difference in  $\Delta$ ASDAS-CRP

	ASDAS units	95% CI	p Value		ASDAS units	95% CI	p Value
Ever smokers	0.55	0.19 to 0.90	0.002	Current smokers	0.69	0.30 to 1.08	0.001
				Past smokers	0.30	-0.18 to 0.78	0.22

Smokers vs non-smokers with normal baseline CRP

Difference in $\Delta$ BASDAI				Difference in $\Delta$ BASDAI			
	BASDAI units	95% CI	p Value		BASDAI units	95% CI	p Value
Ever smokers	0.43	-0.05 to 0.90	0.08	Current smokers	0.30	-0.24 to 0.83	0.28
				Past smokers	0.59	0.002 to 1.18	0.05

Difference  $\Delta$ ASDAS-CRP

	ASDAS units	95% CI	p Value		ASDAS units	95% CI	p Value
Ever smokers	0.15	-0.20 to 0.49	0.40	Current smokers	0.17	-0.21 to 0.56	0.38
				Past smokers	0.12	-0.31 to 0.54	0.59

## Baseline predictors of response to TNF- $\alpha$ blocking therapy in axial SpA

- Φύλο
- Ηλικία
- Διάρκεια νόσου
- ΒΜΙ/παχυσαρκία
- Κάπνισμα
- Επίπεδα δεικτών φλεγμονής
- B27

# Evaluation of the impact of concomitant fibromyalgia on TNFi effectiveness in axial SpA

**Table 2** Effectiveness endpoints of the main analysis using the FiRST definition for fibromyalgia

Effectiveness endpoint	All patients n=508 (%)	Fibromyalgia†		Crude OR (95% CI)‡	P value*	Adjusted OR (95% CI)§	P value
		Yes n=192 (%)	No n=316 (%)				
BASDAI response¶	258/508 (50.8)	87/192 (45.3)	171/316 (54.1)	0.7 (0.5 to 1.0)	NS	0.7 (0.5 to 1.1)	NS
ASAS 40	201/508 (39.6)	55/192 (28.6)	146/316 (46.2)	0.5 (0.3 to 0.7)	<0.001	0.5 (0.3 to 0.8)	0.001
ASAS 20	268/508 (52.8)	83/192 (43.2)	185/316 (58.5)	0.5 (0.4 to 0.8)	<0.001	0.6 (0.4 to 0.9)	0.008
ASDAS MI	117/508 (23.0)	36/192 (18.7)	81/316 (56.3)	0.7 (0.4 to 1.0)	NS	0.8 (0.5 to 1.3)	NS
ASDAS CII	265/508 (52.2)	87/192 (45.3)	178/316 (56.3)	0.6 (0.5 to 0.9)	0.02	0.7 (0.5 to 1.1)	NS
ΔNSAID score ≥50%	235/508 (46.3)	69/192 (35.9)	166/316 (52.5)	0.5 (0.4 to 0.7)	<0.001	0.6 (0.4 to 0.8)	0.003
ΔCRP >0 mg/L	325/508 (64.0)	112/192 (58.3)	213/316 (67.4)	0.7 (0.5 to 1.0)	NS	0.7 (0.5 to 1.2)	NS
ASDAS MDA at 12 weeks	264/508 (52.0)	74/192 (38.5)	190/316 (60.1)	0.4 (0.3 to 0.6)	<0.001	0.5 (0.3 to 0.7)	<0.001
ASDAS ID at 12 weeks	126/508 (24.8)	28/192 (14.6)	98/316 (31.0)	0.4 (0.2 to 0.6)	<0.001	0.4 (0.3 to 0.7)	<0.001
NSAID score ≤10 at 12 weeks	401/508 (78.9)	140/192 (72.9)	261/316 (82.6)	0.6 (0.4 to 0.9)	0.01	0.6 (0.4 to 0.9)	0.02
CRP <6 mg/L at 12 weeks	392/508 (77.2)	145/192 (75.5)	247/316 (78.2)	0.9 (0.6 to 1.3)	NS	0.7 (0.5 to 1.2)	NS

# Predicting Response to Biologic Therapy in Patients with Axial SpA

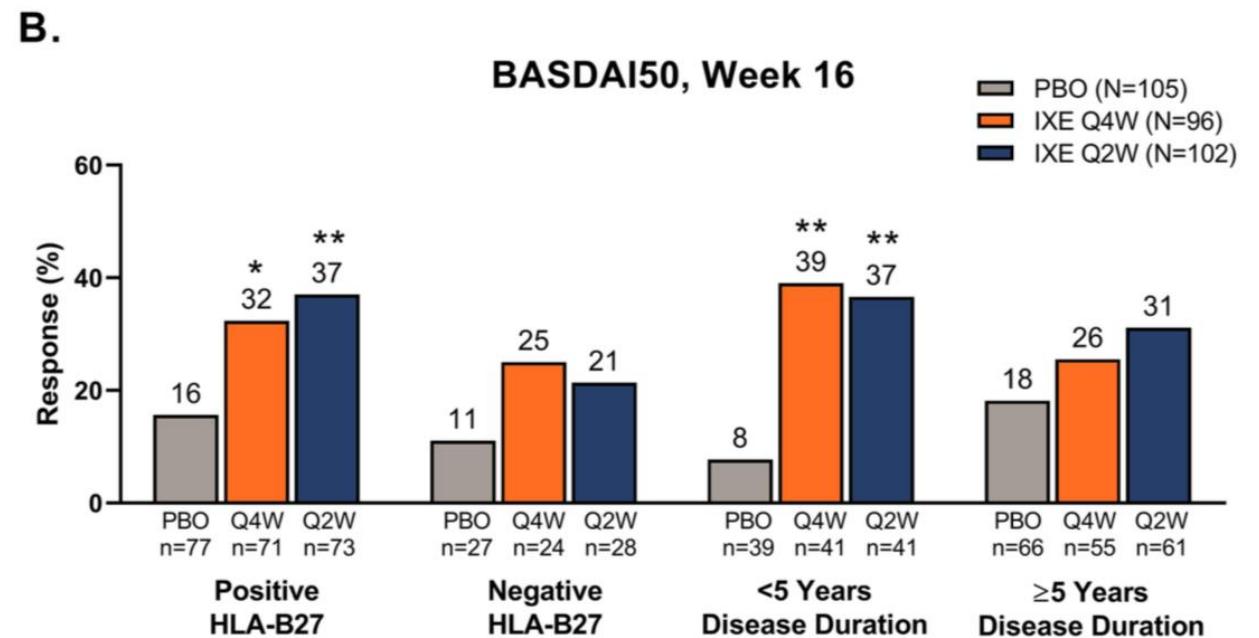
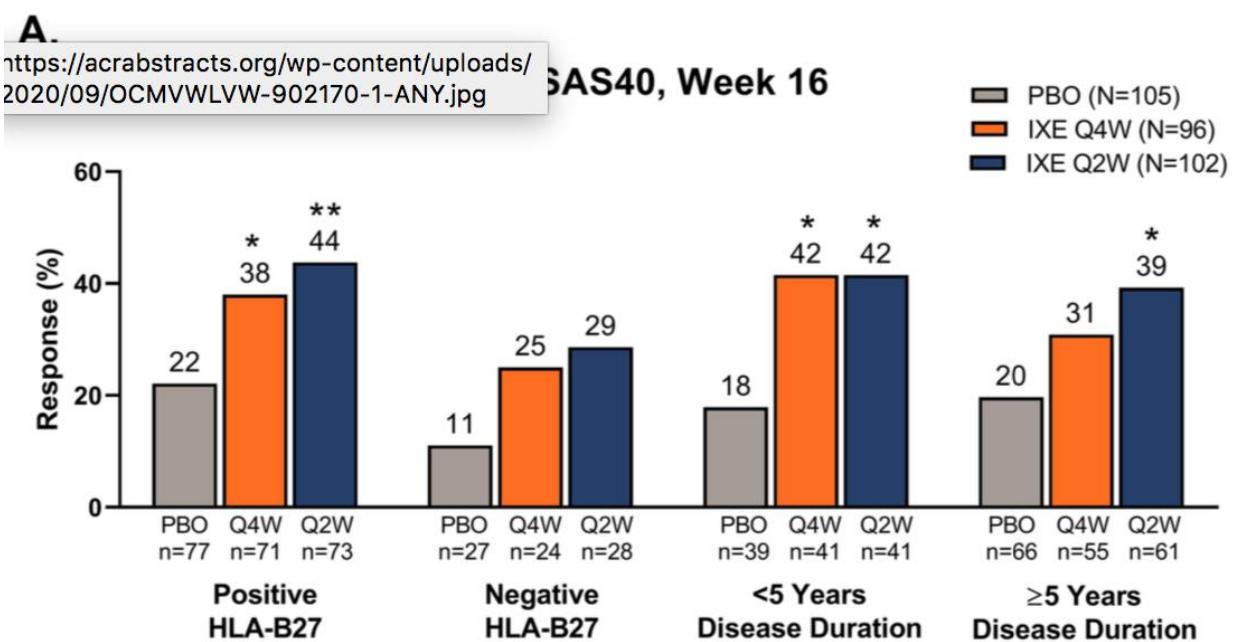
Baseline predictor <sup>1</sup>		Odds ratio (95%CI) Univariate association	Odds ratio (95%CI) Independent predictors
<i>Clinical factors</i>			
Disease activity	BASDAI	0.71 (0.60-0.85)	
	ASDAS	0.74 (0.55-0.99)	
<i>Bath indices</i>			
	Function (BASFI)	0.70 (0.61-0.81)	
	Metrology (BASMI)	0.83 (0.70-0.99)	
	Global health (BASG)	0.68 (0.57-0.81)	
Presence of extra-spinal manifestation [Reference = Absence of symptom]	Heel enthesitis	1.18 (0.51-2.73)	
	Uveitis	1.15 (0.62-2.12)	
	Dactylitis	1.63 (0.53-5.01)	
	Psoriasis	0.80 (0.33-1.93)	
	Inflammatory bowel disease	0.76 (0.32-1.81)	
	Peripheral joint disease	0.87 (0.46-1.67)	
<i>Classification criteria</i>			
[Reference = modified New York]	ASAS imaging	0.89 (0.50-1.56)	
	ASAS clinical	1.84 (0.51-6.62)	
Pain	Spinal VAS	0.84 (0.74-0.96)	
CRP (mg/dL)		0.99 (0.97-1.01)	
Comorbidity count		0.51 (0.35-0.75)	0.60 (0.38-0.95)
BMI (kg/m <sup>2</sup> )		0.94 (0.89-1.001)	
<i>Socioeconomic factors</i>			
Highest education level	Apprenticeship	1.97 (0.80-4.86)	1.43 (0.50-4.08)
[Reference = Secondary school]	College	1.17 (0.57-2.42)	1.01 (0.43-2.36)
	University	2.64 (1.26-5.53)	1.72 (0.72-4.10)
	Further degree	3.51 (1.29-9.54)	2.62 (0.82-27.5)
Deprivation (quintiles) [Reference = 1, Least deprived]	2	0.59 (0.29-1.23)	
	3	0.39 (0.17-0.85)	
	4	0.43 (0.19-0.99)	
	5, Most deprived	0.36 (0.14-0.93)	
<i>Patient-reported outcomes</i>			
Quality of life	ASQoL (range: 0-18 <sup>2</sup> )	0.82 (0.76-0.88)	
Physical health	SF12 Physical summary (range 0-100 <sup>3</sup> )	1.07 (1.03-1.10)	
Mental health	SF12 Mental summary (range 0-100 <sup>3</sup> )	1.06 (1.04-1.09)	1.05 (1.01-1.08)
	HADS anxiety (range 0-21 <sup>2</sup> )	0.87 (0.81-0.93)	
	HADS depression (range 0-21 <sup>2</sup> )	0.86 (0.80-0.93)	
<i>Fatigue/Sleep**</i>			
	Chalder Fatigue Scale (range 0-11 <sup>2</sup> )	0.87 (0.80-0.93)	
	Jenkins Sleep Scale (range 0-20 <sup>2</sup> )	0.94 (0.89-0.98)	
Smoking	Ex	0.66 (0.36-1.21)	
[Reference = Never]	Current – light	0.30 (0.10-0.97)	
	Current – heavy	0.72 (0.32-1.59)	
<i>Alcohol drinking</i>			
	Never	0.20 (0.04-0.92)	
[Reference = ≤14 units/week]	Ex	0.45 (0.21-0.96)	
	Current >14 units/week	1.30 (0.42-4.05)	

<sup>1</sup> For non-categorical variables, results are given per 1 unit increase

<sup>2</sup> High score = worse

<sup>3</sup> High score = better

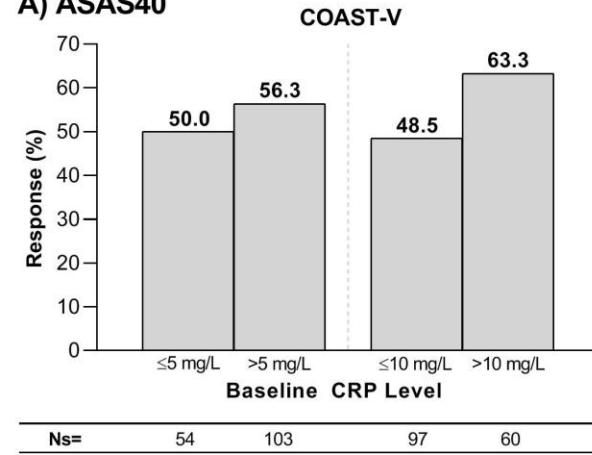
# Response to Treatment with Ixekizumab in Patients with Active Non-Radiographic Axial SpA Based on HLA-B27 Status and Disease Duration



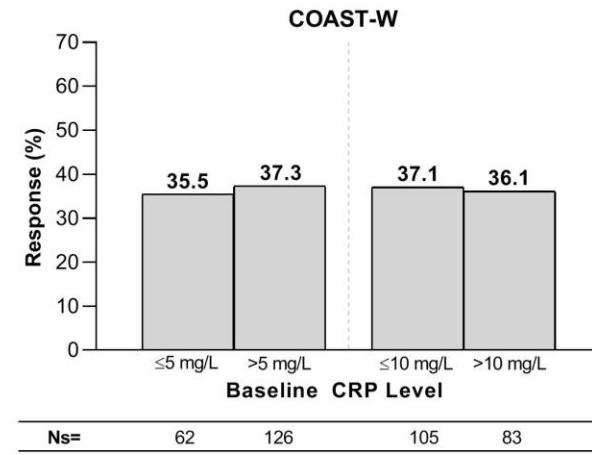
# Response to Ixekizumab by CRP Level in Patients with Radiographic Axial SpA: Results from the COAST-V (Biological-Naïve) and COAST-W (TNF Inhibitor-Experienced) Trials at 52 Weeks

Figure 2. (A) ASAS40 and (B) BASDAI50 Responses at Week 52, NRI

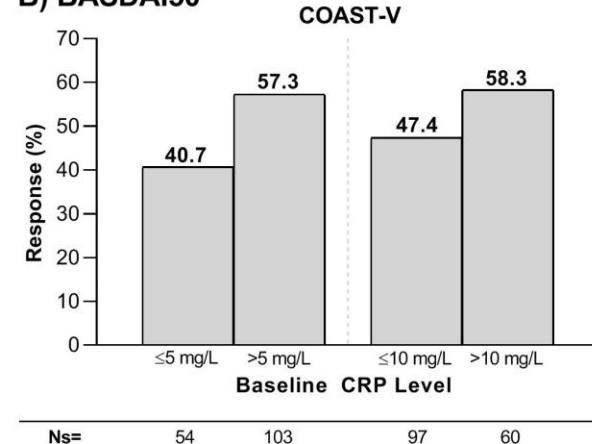
A) ASAS40



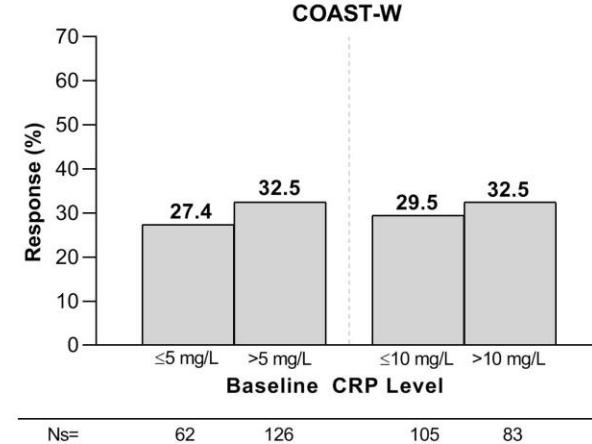
COAST-W



B) BASDAI50



COAST-W



# Response to Treatment with Secukinumab in Pooled Week 52 Data from 4 Phase 3 Studies in Patients with Ankylosing Spondylitis

		Logistic Regression Models					ANCOVA			
		ASAS20	ASAS40	ASDAS-CRP ID			Δ BASDAI	Δ BASFI	Δ BASMI	
<b>Binary predictors</b>										
Secukinumab dose: 300 vs 150 mg		Odds ratio (95% CI)	1.381 (0.704 to 2.707)	1.314 (0.749 to 2.304)	1.098 (0.584 to 2.065)					
		P value	.3473	.3414	.7717					
BMI: < 30 vs ≥ 30 kg/m <sup>2</sup>		Odds ratio (95% CI)	1.648 (0.990 to 2.746)	1.435 (0.903 to 2.282)	2.415 (1.275 to 4.576)					
		P value	.0549	.1267	.0068					
Current smoker: No vs yes		Odds ratio (95% CI)	1.368 (0.831 to 2.252)	1.641 (1.056 to 2.550)	1.536 (0.888 to 2.657)					
		P value	.2183	.0277	.1250					
hsCRP: ≥ 5 vs < 5 mg/L		Odds ratio (95% CI)	1.093 (0.668 to 1.790)	1.391 (0.907 to 2.135)	0.699 (0.380 to 1.286)					
		P value	.7232	.1306	.2496					
TNF $\alpha$ naive: No vs yes		Odds ratio (95% CI)	0.553 (0.327 to 0.933)	0.721 (0.447 to 1.165)	0.541 (0.284 to 1.028)					
		P value	.0264	.1814	.0609					
<b>Continuous predictors</b>										
Time since diagnosis of AS (years)		Odds ratio (95% CI)	1.010 (0.980 to 1.041)	0.991 (0.964 to 1.019)	0.967 (0.929 to 1.005)					
		P value	.5290	.5284	.0907					
Age (years)		Odds ratio (95% CI)	0.969 (0.947 to 0.991)	0.979 (0.960 to 0.999)	0.985 (0.962 to 1.008)					
		P value	.0063	.0401	.1984					
Baseline value (for ASDAS-CRP)		Odds ratio (95% CI)	-	-	0.804 (0.567 to 1.140)					
		P value			.2204					

# Predictors of Response in Secukinumab-treated Patients with AS: Logistic Regression and Machine Learning Analyses

Predictors*	Odds Ratio (95% CI)		
	ASAS40	ASDAS-ID	BASDAI50
Age (years)	0.98 (0.97, 0.99)	—	0.98 (0.96, 0.99)
Sex (Male vs Female)	—	1.67 (1.07, 2.41)	—
BMI (<30 kg/m <sup>2</sup> vs ≥30 kg/m <sup>2</sup> )	1.44 (1.04, 2.01)	2.35 (1.42, 3.89)	—
Current Smoker (No vs Yes)	1.41 (1.04, 1.92)	—	—
TNF status (Treatment Naïve vs Inadequate Responder)	1.58 (1.15, 2.18)	2.30 (1.42, 3.73)	—
hsCRP (Elevated ≥5 mg/L vs Normal <5 mg/L)	1.67 (1.24, 2.26)	—	1.59 (1.16, 2.18)
BL Occiput-to-wall distance	0.96 (0.94, 0.99)	0.89 (0.84, 0.93)	0.97 (0.94, 1.00)
BL PGA (every 10 unit increment on VAS 100 scale)	1.16 (1.06, 1.26)	0.82 (0.74, 0.91)	—
BL MASES Score	0.96 (0.92, 1.00)	—	0.92 (0.88, 0.96)

\* Only predictors with  $P < 0.05$  are kept in the final multivariate model

## Συμπερασματικά

- Η θεραπευτική απάντηση της μα-αξΣΠΑ και ΑΣ έναντι των ΜΣΑΦ και αντι-TNF είναι παρόμοια.
- Υπάρχει διαφορετική θεραπευτική απάντηση των εξωαρθρικών εκδηλώσεων των αξΣΠΑ έναντι των βιολογικών παραγόντων.
- Δημογραφικοί, όπως ηλικία, διάρκεια νόσου, φύλο, BMI/παχυσαρκία και κάπνισμα, καθώς και εργαστηριακοί παράγοντες, όπως δείκτες φλεγμονής και HLA-B27, φαίνεται να επηρεάζουν την θεραπευτική απάντηση των αξΣΠΑ έναντι τόσο των αντι-TNF όσο και των αντι-IL17.
- Άλλοι παράγοντες, όπως ινομυαλγία, ψυχική υγεία, μορφωτικό επίπεδο, απασχόληση, επηρεάζουν την θεραπευτική απάντηση έναντι των αντι-TNF.
- Η θεραπεία των ασθενών με αξΣΠΑ θα πρέπει να εξατομικεύεται σύμφωνα με τα χαρακτηριστικά της νόσου και του ασθενούς (σύσταση 1 της ASAS/EULAR)
- Παρεμβάσεις βελτίωσης των δυσμενών παραγόντων που μπορούν να τροποποιηθούν.