ΕΠΙΣΤΗΜΟΝΙΚΗ ΕΤΑΙΡΕΙΑ ΓΙΑ ΤΗ ΜΥΟΣΚΕΛΕΤΙΚΗ ΥΓΕΙΑ

ΣΥΝΕΔΡΙΑ ΣΠΟΝΔΥΛΑΡΘΡΙΤΙΔΩΝ

«Σε ποιους ασθενείς με Αξονική Σπονδυλαρθρίτιδα βελτιστοποιούμε το αποτέλεσμα με τους αναστολείς των IL-17»

Ιωάννης Καλλιτσάκης
Ρευματολόγος

Lilly ΦΑΡΜΑΣΕΡΒ

Δήλωση σύγκρουσης συμφερόντων

- Τιμητική αμοιβή από την Φαρμασέρβ-Lilly

Παρουσίαση περίπτωσης ασθενούς

- Άντρας 24 ετών ,ελεύθερο Α/Α
  - Οδηγός εταιρείας Courier.
- Φλεγμονώδης οσφυαλγία με αμφοτερόπλευρη ιερολαγονίτιδα (επιβεβαιωμένη με ΜΤ/2023).
- HLA B27 (+)
- Ιριδοκυκλίτιδες ΔΟ από 18 ετών.
- Πελματιαία απονευρωσίτιδα (ΔΕ) / 2022.
- Υψηλούς δείκτες φλεγμονής σε όλη τη διάρκεια των συμπτωμάτων.(CRP 8-12 mg/dl)
- **BASDAI** : 7 **ASDAS** : 4,1

ESSG-Classification Criteria

(European Spondylarthropathy Study Group)

Inflammatory Back Pain

or

Synovitis

- **asymmetric or**
- **predominantly in the lower limbs**

plus one of the following:

- **enthesitis (heel)**
- **positive family history**
- **psoriasis**
- **Crohn‘s disease, Colitis ulcerosa**
- **urethritis / cervicitis or acute diarrhea within one month before arthritis**
- **buttock pain (alternating between right and left gluteal areas)**
- **sacroiliitis**

Dougados M et al. Arthritis Rheum 1991;34:1218

ASAS

Παρουσίαση περίπτωσης ασθενούς

- Αστοχία σε meloxicam/ibubrofen.
- Έγχυση στεροειδούς+wet needling στην πελματιαία απονεύρωση.
- Έναρξη ADALIMUMAB τον **2ο/2023.**

  - **6ος/2023 :** Δεν περιγράφει πρωινή οσφυαλγία, χωρίς επεισόδιο ιριδοκυκλίτιδας.

  ❑BASDAI 4,8

  ❑CRP : 8 mg/dl

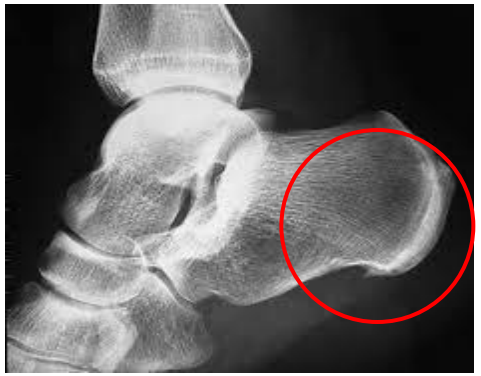
  - Δυσκολεύεται σημαντικά στην οδήγηση και περιγράφει άλγος πελμάτων στα 20-30’ βάδισμα στην ευθεία αλλά και πρωινή δυσκαμψία στα πέλματα του.

    - Δεύτερη έγχυση στεροειδούς λήψη ΜΣΑΦ και ΦΘ για πελματιαία απονευρωσίτιδα.

Παρουσίαση περίπτωσης ασθενούς

11ος/2023 :

- Επανεμφάνιση πρωινής οσφυαλγίας
- Σημαντική δυσκολία στην οδήγηση
- Ενθεσόφυτο στην πρόσφυση της ΠΑ



- **ΚΛΙΝΙΚΑ :** Ιερολαγονίτιδα αμφοτερόπλευρα
  - SCHOBER TEST : 4 cm

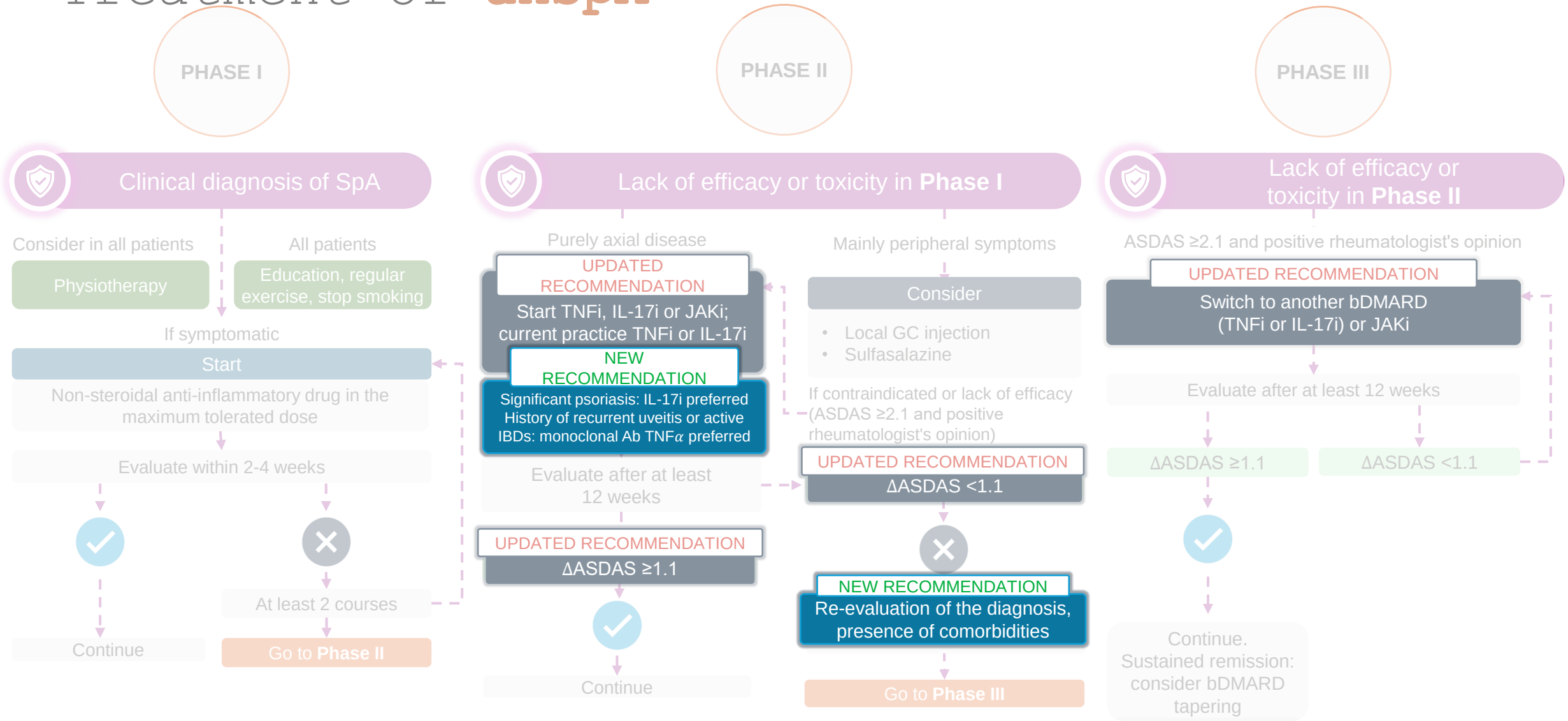
Πελματιαία απονευρωσίτιδα

Αρθρίτιδα ΜΤΦ

- **BASDAI : 5,5**
- **CRP : 7,2 mg/dl**

ΔΕΥΤΕΡΟΓΕΝΗΣ ΑΣΤΟΧΙΑ ΣΤΟΝ ΠΡΩΤΟ ΑΝΤΙ-TNF

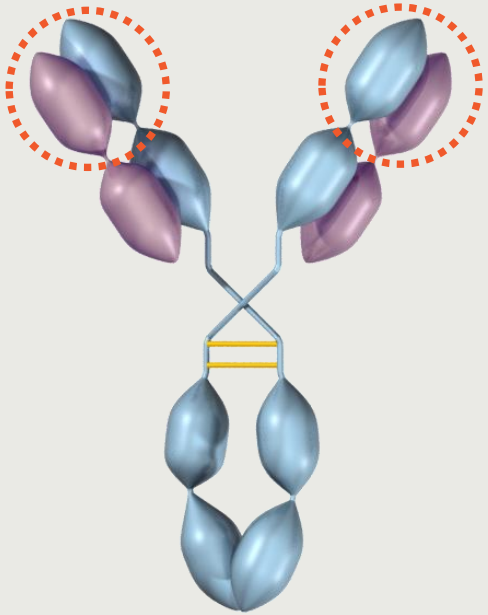
2022 ASAS/EULAR Algorithm for the Treatment of axSpA



See speaker notes for full list of abbreviations. 1. Ramiro S, et al. *Ann Rheum Dis*. 2023;82(1):19-34. 2. van der Heijde D, et al. *Ann Rheum Dis*. 2017;76(6):978-991.

IL-17A Inhibition in axSpA

Ixekizumab Molecule



Variable region

Half-life = 13 days[2]
Binding affinity = 1.8 pM[3]

Light chain

Heavy chain

Image adapted from The Immune System.
3rd ed. Garland Science 2009.

- Ixekizumab is an IgG4 monoclonal antibody that targets IL-17A with hi binding affinity[1]
- Inhibition of IL-17A may effectively prevent joint and entheseal inflammation, cartilage and bone degradation, and possibly, ectopic bone formation[4-15]

Note: MoA model is based on pre-clinical laboratory observations. Currently there are no data linking these observations to clinical efficacy or safety results. Any implications are hypotheses only.

axSpA=Axial Spondyloarthritis; IgG=Immunoglobulin G; IL=Interleukin.

1. Krueger JG, et al. *J Allergy Clin Immunol*. 2012;130:145-154. 2 Taltz PI. Available from: https://pi.lilly.com/us/taltz-uspi.pdf (Accessed June 2023). 3. Liu L, et al. *J Inflamm Res*. 2016;9:39-50. 4. Raychaudhuri SK, et al. *Clin Rheumatol*. 2015;34:1019-1023. 5. Taams LS, et al. *Nat Rev Rheumatol*. 2018;14:453-466. 6. Raychaudhuri SP, et al. *Mol Cell Biochem*. 2012;359:419-429. 7. De Vlam K, et al. *Acta Derm Venereol*. 2014;94:627-634. 8. Mease P, et al. *EMJ Rheumatol*. 2015;2:55-64. 9. Kehl AS, et al. *Arthritis Rheumatol*. 2016;68:312-322. 10. Raychaudhuri SP, Raychaudhuri SK. *Arthritis Res Ther*. 2017;19:51. 11. Suzuki E, et al. *Autoimmun Rev*. 2014;13:496-502. 12. Osta B, et al. *Front Immunol*. 2014;5:48. 13. Lee Y. *BMB Rep*. 2013;46:479-483. 14. Onishi RM, Gaffen SL. *Immunology*. 2010;129:311-321. 15. Caetano-Lopes J, et al. *Autoimmun Rev*. 2009;8:250-255.

Clinical Trials Overview: Ixekizumab in axSpA

COAST-V
AS/r-axSpA, bDMARD-naïve[1]
N=341

- Placebo-controlled
- Q4W, Q2W, adalimumab[a]
- 16 & 52 weeks[b]

Study dosing
Initial 160 mg or 80 mg, followed by 80 mg Q4W or Q2W[d]

Outcomes
Signs, symptoms, function, imaging (X-ray and MRI), quality of life

331 patients (97%) completed Week 16

COAST-W
AS/r-axSpA, TNFi-experienced[2]
N=316

- Placebo-controlled
- Q4W, Q2W
- 16 & 52 weeks[b]

Study dosing
Initial 160 mg or 80 mg, followed by 80 mg Q4W or Q2W[d]

Outcomes
Signs, symptoms, function, imaging (MRI), quality of life

282 patients (89%) completed Week 16

COAST-X
nr-axSpA, bDMARD-naïve[3]
N=303

- Placebo-controlled
- Q4W, Q2W
- 16 & 52 weeks[c]

Study dosing
Initial 160 mg or 80 mg, followed by 80 mg Q4W or Q2W[d]

Outcomes
Signs, symptoms, function, imaging (MRI), quality of life

290 patients (96%) completed Week 16 and 265 patients (87%) completed Week 52

COAST-Y
axSpA, completed COAST-V, -W, or -X[4,5]
N=773 (RWP, N=155)

- Open-label[e]
- Q4W, Q2W
- 104 weeks

Study dosing
80 mg Q4W or Q2W[d]

Outcomes[4,5]
Signs, symptoms, function, imaging (X-ray and MRI), quality of life

644 patients (83%) completed Week 104[5]

Patients who complete 52 weeks in the 3 registration trials (COAST-V, -W, and -X) had the option to enroll in the long-term trial (COAST-Y)[4]

[a]Adalimumab 40 mg Q2W treatment arm served as active reference for comparison with placebo. [b]Primary endpoint at 16 weeks, trial extension through 52 weeks, followed by long-term trial COAST-Y. [c]Primary endpoint at 52 weeks for US, at 16 weeks for other countries, followed by long-term trial COAST-Y. [d]Label dose for AS in the US is Q4W.[6] [e]The RWP (starting at Week 24) is placebo-controlled. AS=Ankylosing Spondylitis; r-axSpA=Radiographic Axial Spondyloarthritis; axSpA=Axial Spondyloarthritis; bDMARD=Biological Disease-Modifying Anti-Rheumatic Drug; IXE=Ixekizumab; Q2W=Every 2 Weeks; IXE Q4W=Every 4 Weeks; nr-axSpA=Non-Radiographic Axial Spondyloarthritis; RWP=Randomized Withdrawal-Retreatment Period; TNFi=Tumor Necrosis Factor Inhibitor.

1. van der Heijde D, et al. *Lancet.* 2018;392(10163):2441-2451. 2. Deodhar A, et al. *Arthritis Rheumatol.* 2019;71(4):599-611. 3. Deodhar A, et al. *Lancet.* 2020;395(10217):53-64. 4. Landewé RB, et al. *Ann Rheum Dis.* 2021;80(8):1022-1030. 5. Landewé RBM, et al. *Ann Rheum Dis.* 2023;82(2):212-216. 6. Taltz PI. Available from: https://pi.lilly.com/us/taltz-uspi.pdf (Accessed April 2023).

Greater Proportion of Ixekizumab-Treated Patients Achieved Low Disease Activity at Week 16[1-3]

	COAST-V		COAST-W	
	PBO N=87	IXE Q4W N=83	PBO N=104	IXE Q4W N=114
ASDAS at Week 16				
LS mean change in ASDAS from baseline, MMRM	-0.5	-1.4*	-0.1	-1.1*
ASDAS <2.1 (low disease activity), %	13	43*	4.8	18†
ASDAS <1.3 (inactive disease), %	2.0	16†	1.0	3.5
BASDAI at Week 16				
Mean change in BASDAI from baseline, MMRM	-1.4	-2.9*	-0.9	-2.2*
BASDAI50 response, %	17	42*	9.6	22‡

Ixekizumab was superior to PBO in reducing disease activity in COAST-V and COAST-W

*p<.001 vs. PBO; †p<.01 vs. PBO; ‡p<.05 vs. PBO.

1. van der Heijde D, et al. *Lancet*. 2018;392:2441-2451. 2. Deodhar A, et al. *Arthritis Rheumatol*. 2019;71:599-611.

Παρουσίαση περίπτωσης ασθενούς

- Αλλαγή του βιολογικού παράγοντα σε IXEKIZUMAB τον 12ο/2023
- Στεροειδή σε χαμηλή δόση για 6 εβδομάδες.

➢ ***…ο ασθενής μας τηλεφώνησε 2 ημέρες μετά την 5η έγχυση TALTZ αναφέροντας πως η κατάσταση του έχει βελτιωθεί εντυπωσιακά και για πρώτη φορά μετά από 3 χρόνια οδηγεί την μοτοσυκλέτα του χωρίς παραμικρή ενόχληση…***

Παρουσίαση περίπτωσης ασθενούς

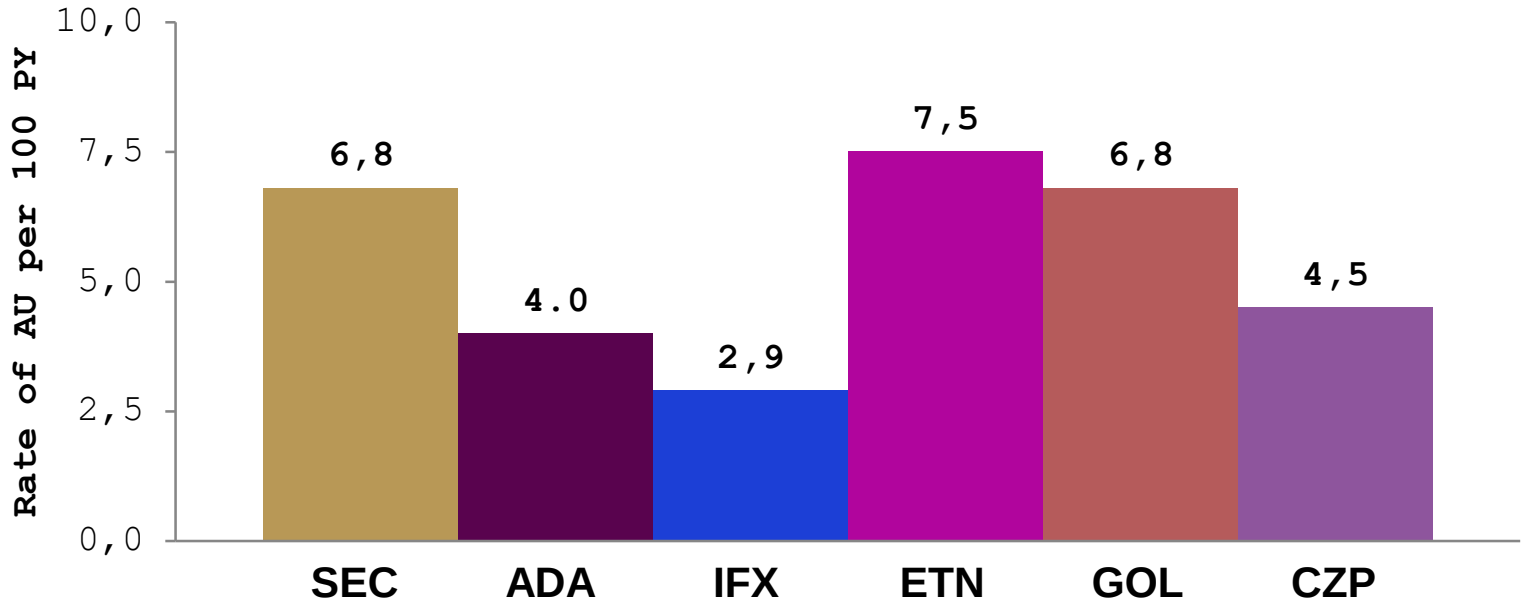
- **Μάρτιος 2025 :**
  - Πρωινή οσφυαλγία 10’.
  - Λειτουργικός στην εργασία του χωρίς περιορισμό στην οδήγηση.
  - Χωρίς ευαισθησία ΙΛ, απουσία Πελματιαίας Απονευρωσίτιδας κλινικά και υπερηχογραφικά.
  - Απουσία επεισοδίου **ιριδοκυκλίτιδας.**

  - **CRP : < 5 mg/dl**
  - **BASDAI : 2,5**

Incidence per 100 Patient Years:

Swedish Rheumatology Quality Register

TNFi- or SEC-treated Patients with r-axSpA or Undifferentiated SpA



	SEC	ADA	IFX	ETN	GOL	CZP
N	456	1006	783	1800	500	306
Previous AU, n (%)[a]	63 (14)	179 (18)	204 (11)	96 (12)	88 (18)	50 (16)

- [a]Any registration of AU in outpatient ophthalmology care since start of the outpatient register in 2001. Note: Includes patients with a diagnosis of r-axSpA (42%) or undifferentiated SpA (58%).
ADA=Adalimumab; AU=Anterior Uveitis; CZP=Certolizumab Pegol; ETN=Etanercept; GOL=Golimumab; IFX=Infliximab; PY=Patient Years; r-axSpA=Radiographic Axial Spondyloarthritis; SEC=Secukinumab; SpA=Spondyloarthritis; TNFi= Tumor Necrosis Factor Inhibitors. Lindström U, et al. *Ann Rheum Dis.* 2021;80(11):1445-1452.

Anterior Uveitis in IXE Trials

SPIRIT program (PsA)

Patients were excluded from enrolling in the SPIRIT program if they had evidence of active uveitis within 4 weeks[1]

0 cases of uveitis were reported during the SPIRIT program[2]

COAST Program (axSpA)[1]

Patients with evidence of active anterior uveitis ≤4 weeks prior to baseline randomization were excluded from entering any of the originating studies (COAST-V, -W, and -X)[a]

Incidence rate of anterior uveitis or uveitis flares was collected as secondary endpoint data in all studies in the COAST program

Participants were **assessed at each study visit for symptoms of uveitis[b]**

Events of anterior uveitis or uveitis flare were **confirmed by an ophthalmologist (for patients with no prior history), or a physician (for patients with prior history)**

- [a]Patients with evidence of active anterior uveitis could be rescreened only one time ≥4 weeks after resolution of acute symptoms.[1] [b]Defined as eye pain or discomfort, eye redness, blurring of vision, or any other symptoms suggestive of anterior uveitis.[1] axSpA=Axial Spondyloarthritis; IXE=Ixekizumab; PsA=Psoriatic Arthritis.

Deodhar AA, et al. *Ann Rheum Dis*. 2022;81(7):944-950.

New Onset and Exacerbation

- of Uveitis in axSpA and PsA

All PsA and axSpA IXE Trials: All IXE Trials Exposure Datasets

	All PsA IXE[1] Through March 2021	All axSpA IXE[2,3] Through April 2023
Total number of patients, N	1401	932
Patients with history of uveitis, n	NR	173
Total patients with ≥1 TE-uveitis, n (IR/100 PY, 95% CI)	**0**	**58 (2.8, 2.1-3.6)**
Patients with ≥1 TE-uveitis and a history of uveitis, n (IR/100 PY, 95% CI)	0	41 (10.7, 7.9-14.6)
Patients with ≥1 TE-uveitis and no history of uveitis, n (IR/100 PY, 95% CI)	0	17 (1.0, 0.6-1.6)

- There were 58 axSpA patients with anterior uveitis (IR 2.8 per 100 PY), the majority of which were mild (IR 1.2 per 100 PY) or moderate (IR 1.5 per 100 PY) in severity[2]
- Of the 173 axSpA patients who had a previous history of anterior uveitis, 41 patients had an episode of flare (IR 10.7 per 100 PY); of the 755 patients with no anterior uveitis, 17 patients were new onset (1.0 per 100 PYs)[2]

Notes: Dates indicate the most recent database lock for each disease state. CIs are from likelihood ratio test of treatment effect from the Poisson regression model. Data are reported by Preferred Term.
axSpA=Axial Spondyloarthritis; CI=Confidence Interval; IR=Incidence Rate; IXE=Ixekizumab; NR=Not Reported; PsA=Psoriatic Arthritis; PY=Patient Years; TE=Treatment-emergent.

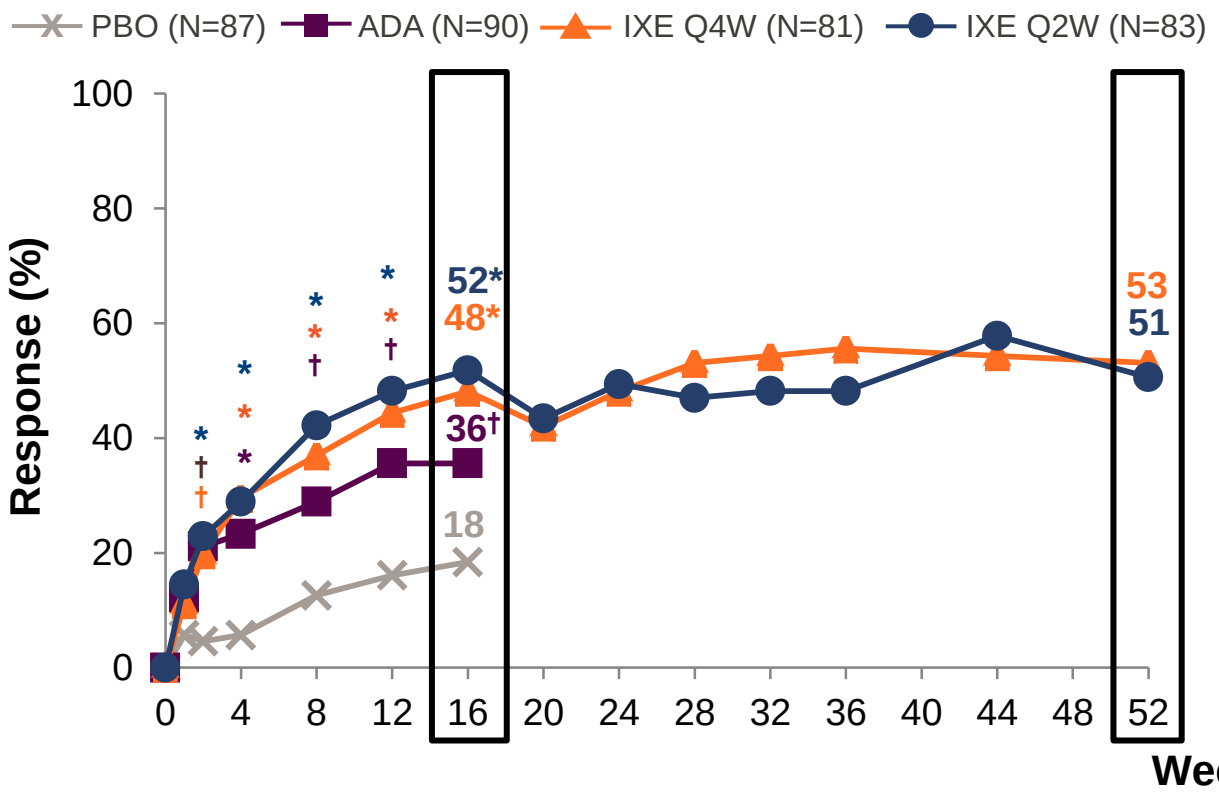
1. Deodhar AA, et al. *Arthritis Res Ther*. 2024;26(1):49. 2. Deodhar AA, et al. *J Rheumatol*. 2023;50(8):1020-1028

ASAS40 Response Rates Through Week 52, NRI[1-4]

Double-Blind PBO-Controlled and Dose Double-Blind Extended Treatment Periods, ITT Populations

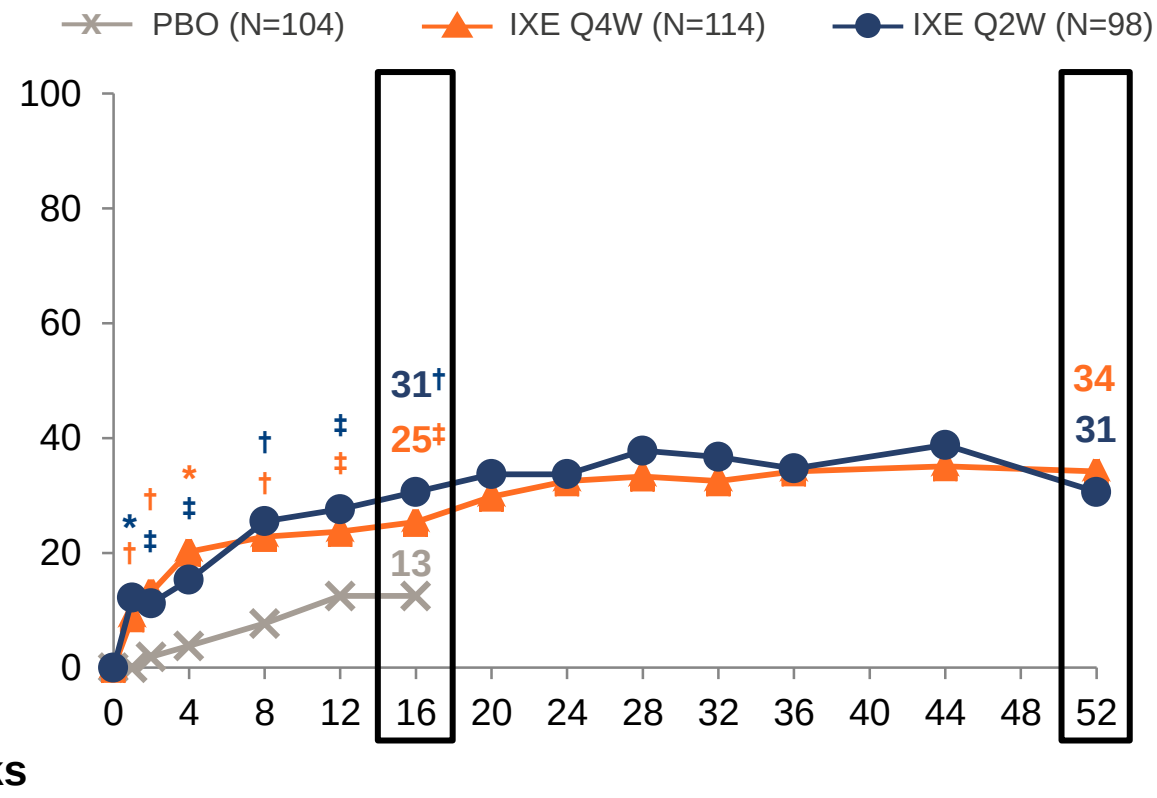
COAST-V

(bDMARD-naïve, AS/r-axSpA)[1-3]



COAST-W

(TNFi-experienced, AS/r-axSpA)[3,4]



Statistically significant improvements in ASAS40 response rate vs. PBO were seen as early as Week 2 in COAST-V, and Week 1 in COAST-W. Responses were maintained through Week 52.

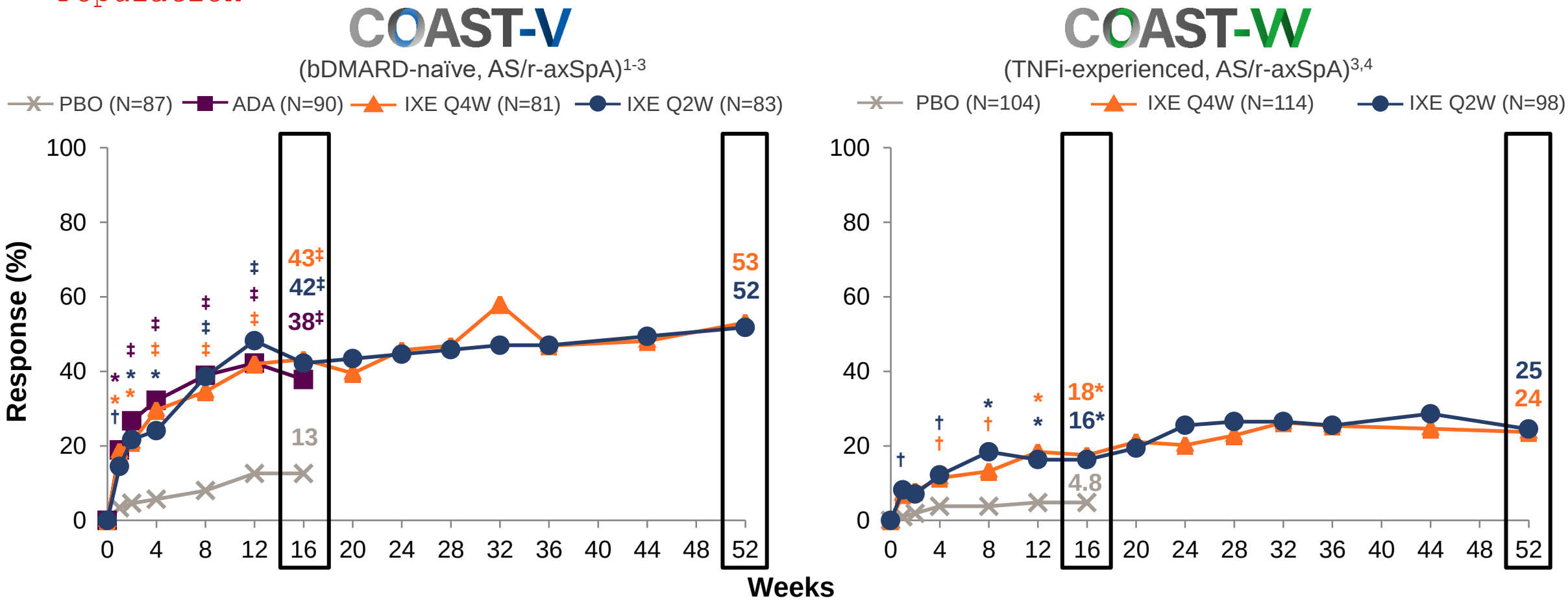
*p<.001 vs. PBO; †p<.01 vs. PBO; ‡p<.05 vs. PBO. Note: When logistical regression did not converge, Fisher's exact test was used where appropriate.

Note: ADA represents an active reference; COAST-V was not powered to test equivalence or noninferiority of active treatment groups to each other, including IXE vs. ADA.[1]

1. van der Heijde D, et al. *Lancet.* 2018;392:2441-2451. 2. van der Heijde D, et al. Presented at the *2018 ACR Annual Meeting*. Poster 1864. 3. Dougados M, et al. *Ann Rheum Dis.* 2020;79:176-185. 4. Deodhar A, et al. *Arthritis Rheumatol.* 2019;71:599-611.

ASDAS <2.1 (Low Disease Activity) Response Rates Through Week 52, NRI[1-4]

Double-Blind PBO-Controlled and Dose Double-Blind Extended Treatment Periods, ITT Population



The proportion of IXE-treated patients achieving ASDAS Low Disease Activity at Week 16 was significantly higher than PBO. Responses were maintained through Week 52

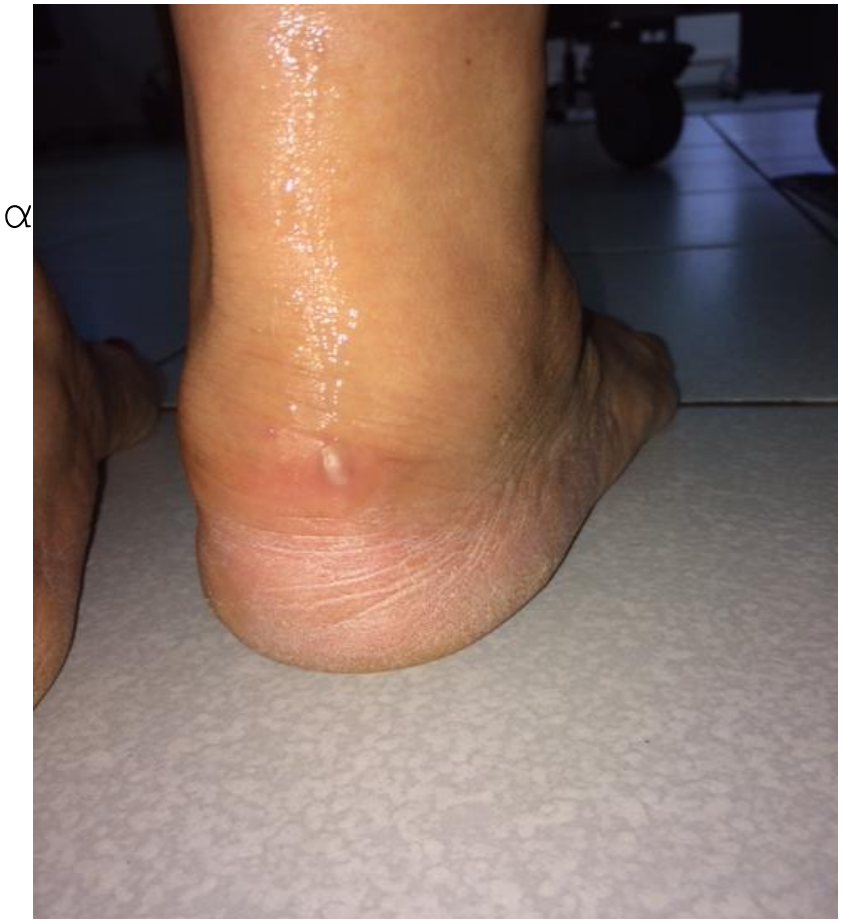
*p<.01 vs. PBO; †p<.05 vs. PBO; ‡p<.001 vs. PBO. ASDAS Low Disease Activity/Inactive Disease = ASDAS Score of <2.1. Post-hoc analysis in COAST-V: ASDAS <2.1 response was not a prespecified major secondary endpoint in COAST-V.

Note: ADA represents an active reference arm; the study was not powered to test equivalence or noninferiority of active treatment groups to each other, including IXE vs. ADA.[1]

1. van der Heijde D, et al. *Lancet*. 2008;392:2441-2451. 2. Dougados M, et al. *Ann Rheum Dis*. 2020;79:176-185. 3. Deodhar A, et al. *Arthritis Rheumatol*. 2019;71:599-611.

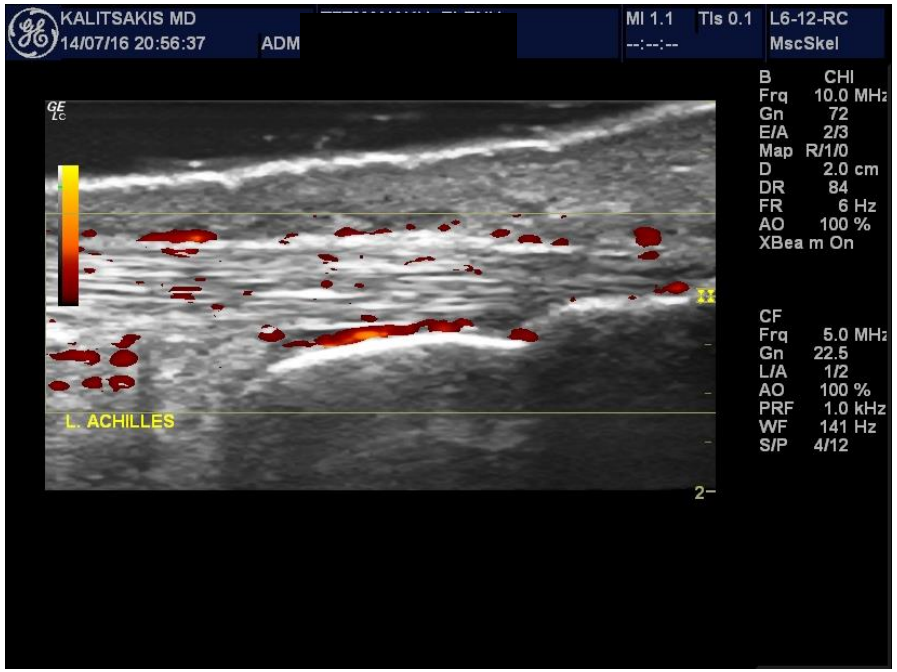
Αξονική Σπονδυλαρθρίτιδα
2η Περίπτωση ασθενούς

- **Άντρας 38 ετών, Βουλγαρικής καταγωγής.**
  - Οικοδόμος.
- Οσφυαλγία από 25 ετών.
  - Πατέρας με Αγκυλοποιητική Σπονδυλαρθρίτιδα
- Συχνή χρήση ΜΣΑΦ με μικρή ανακούφιση.

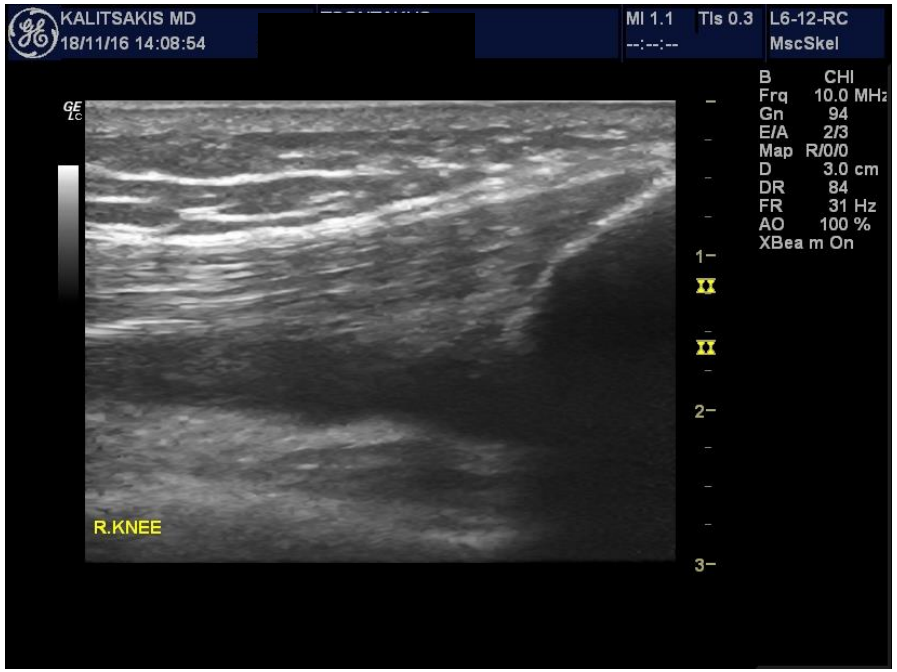


- **12ος 2024**
  - Επώδυνος αριστερός Αχίλλειος τένοντας .
  - Αρθρίτιδα με ύγραρθρο γονάτων.
  - Δεκατική πυρετική κίνηση.
  - Οσφυαλγία με πρωινή δυσκαμψία 1 ώρας.
  - CRP : 25 mg/dl
  - Φυσιολογικές α/α ΟΜΣΣ, ΙΛ.

Αγκυλοποιητική Σπονδυλαρθρίτιδα
2η Περίπτωση ασθενούς



Ενθεσίτιδα και θυλακίτιδα αρ. Αχιλλείου τένοντα.



Αρθρίτιδα με ύγραρθρο δεξιού γόνατος.

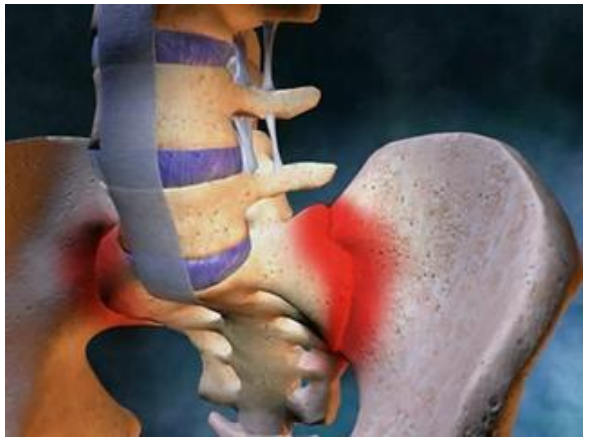
Αγκυλοποιητική Σπονδυλαρθρίτιδα
2η Περίπτωση ασθενούς

- Εγχύσεις στεροειδούς στην ένθεση του Αχιλλείου και ενδοαρθρικά στα γόνατα.
- Μεθοτρεξάτη 15 mg/wk και p.o. Στεροειδή για 2 μήνες.

- **Αξονική Σπονδυλαρθρίτιδα (nr-Axial SpA)**
  - Φλεγμονώδης Οσφυαλγία
  - HLAB27 +
  - Πατέρας με ΑΣ
  - Ενθεσίτιδα Αχιλλείου
  - CRP +

Αγκυλοποιητική Σπονδυλαρθρίτιδα
2η Περίπτωση ασθενούς

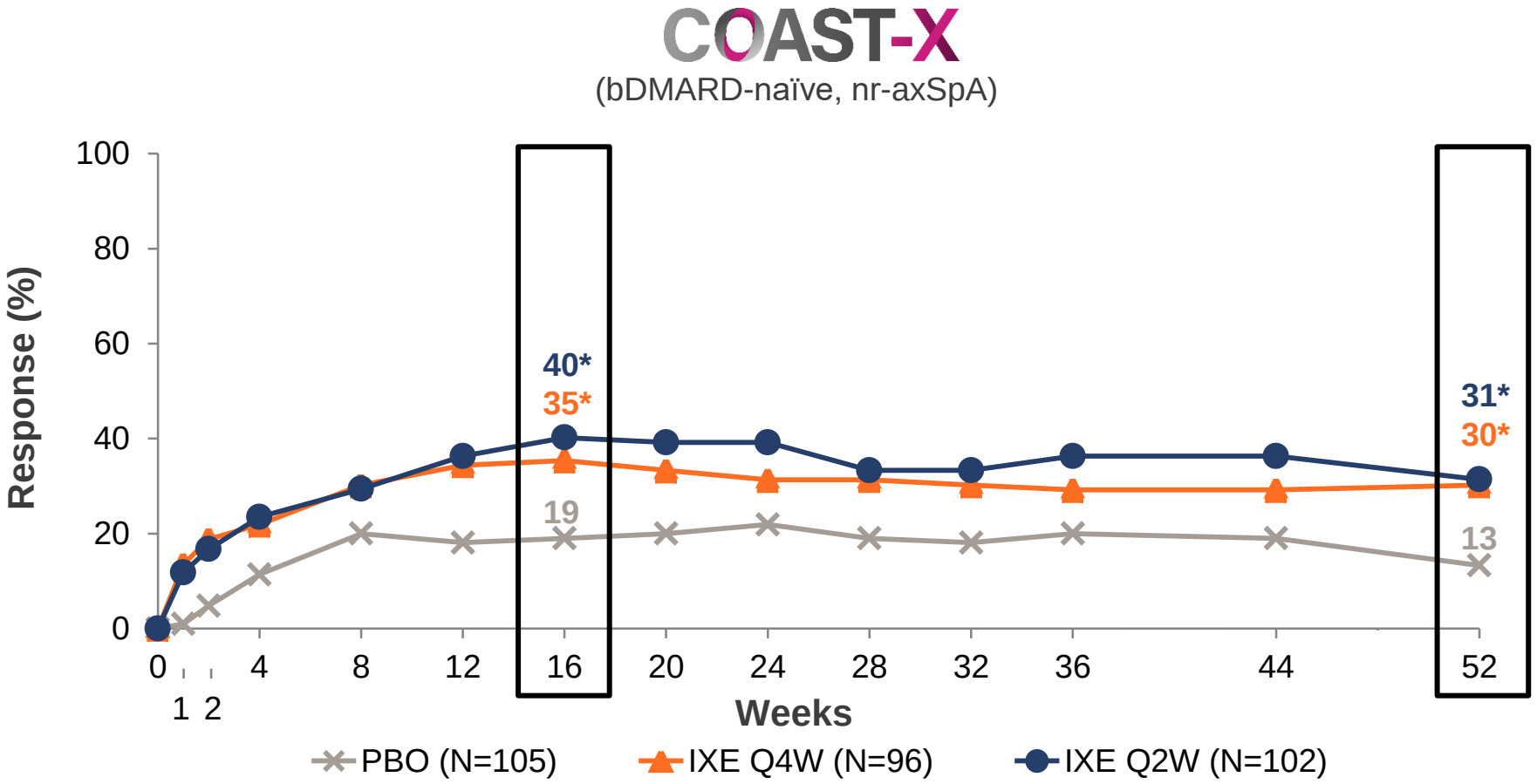
- **Μάρτιος 2025 :**
  - Βελτίωση της αρθρίτιδας στα γόνατα.
  - Παραμένει η πρωινή οσφυαλγία και η δυσκολία στη
  - BASDAI : 5,3
  - CRP : 12 mg/dl



- **Αποφασίστηκε η έναρξη βιολογικού παράγοντα.**
  - Mantoux : 8 mm
    - *Αγωγή για latent-TB.*
  - HBV-DNA : Μη ανιχνεύσιμο.
    - SGOT/SGPT : κφ

ASAS40 Response Through Week 52, NRI

Blinded Dosing Period Prior to Open-Label Switch to IXE Q2W, ITT Population



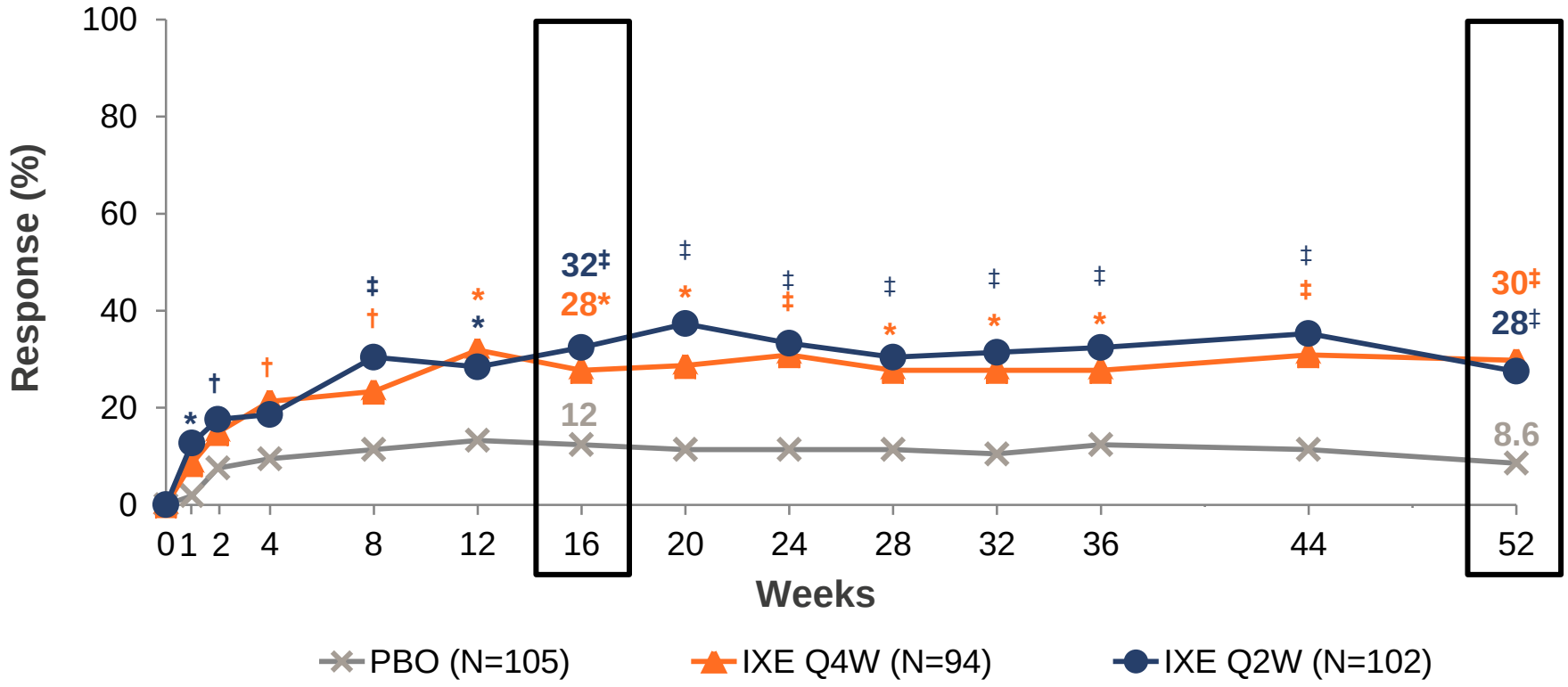
Significantly higher proportion of patients achieved ASAS40 response for each IXE regimen vs. PBO at Weeks 16 and 52

*p<.01 vs. PBO.
Note: NRI analysis was used for imputation of missing data including the whole switched treatment population.
Deodhar A, et al. *Lancet.* 2020;395:53-64.

ASDAS <2.1 (Low Disease Activity) Response Through Week 52, NRI[1,2]

Blinded Dosing Period Prior to Open-Label Switch to IXE Q2W, ITT Population With Baseline ASDAS ≥2.1

COAST-X
(bDMARD-naïve, nr-axSpA)



Baseline mean: PBO=3.8; IXE Q4W=3.8; IXE Q2W=3.9

Significantly higher proportion of patients achieved ASDAS LDA response for each IXE regimen vs. PBO at Weeks 16 and 52

*p<.01 vs. PBO; †p<.05 vs. PBO; ‡p≤.001 vs. PBO.

1. Deodhar A, et al. *Lancet*. 2020;395:53-64.

Safety Outcomes at Week 156

Safety Population (N=932[a]): Table 1

	IXE Q4W N=454 PY=878.2		IXE Q2W N=604 PY=1219.5		Total IXE N=932[a] PY=2097.7	
	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)
TEAE[b]	380 (83.7)	43.3 (39.1, 47.8)	462 (76.5)	37.9 (34.6, 41.5)	798 (85.6)	38.0 (35.5, 40.8)
Mild	141 (31.1)	16.1 (13.6, 18.9)	161 (26.7)	13.2 (11.3, 15.4)	276 (29.6)	13.2 (11.7, 14.8)
Moderate	198 (43.6)	22.5 (19.6, 25.9)	238 (39.4)	19.5 (17.2, 22.2)	419 (45.0)	20.0 (18.2, 22.0)
Severe	41 (9.0)	4.7 (3.4, 6.3)	63 (10.4)	5.2 (4.0, 6.6)	103 (11.1)	4.9 (4.0, 6.0)
Death	2 (0.4)	0.2 (0.1, 0.9)	1 (0.2)	0.1 (0.0, 0.6)	3 (0.3)	0.1 (0.0, 0.4)
Discontinuation due to AE	26 (5.7)	3.0 (2.0, 4.3)	40 (6.6)	3.3 (2.4, 4.5)	66 (7.1)	3.1 (2.5, 4.0)
SAE[c]	44 (9.7)	5.0 (3.7, 6.7)	57 (9.4)	4.7 (3.6, 6.1)	101 (10.8)	4.8 (4.0, 5.9)

- A total of 3 deaths occurred: 2 while patients were receiving IXE Q4W, and 1 while the patient was receiving IXE Q2W; 1 patient died by homicide, 1 patient died by suicide, and the third patient developed sepsis (probable pneumonia with multiorgan failure)

[a]126 patients were switched from IXE Q4W to IXE Q2W, these patients were counted in both IXE Q4W and IXE Q2W columns but were only counted once in the total safety population. [b]Patients with multiple occurrences of the same event are counted under the highest severity. [c]The data collection for the clinical trial database does not contain specification on when events become serious, the numbers may represent more events considered serious than what was actually serious during the treatment period.
Note: Data while patients were on IXE Q4W were reported in IXE Q4W group; data while patients were on IXE Q2W are reported in the IXE Q2W group. Observed data while on placebo or adalimumab are excluded. Percentage is calculated by n/N*100%. CIs of incidence rate are from likelihood ratio test of treatment effect from the Poisson regression.
AE=Adverse Event; CI=Confidence Interval; IR=Incidence Rate per 100 Patient-years; IXE=Ixekizumab; IXE Q2W=80 mg of Ixekizumab Every 2 Weeks; IXE Q4W=80 mg of Ixekizumab Every 4 Weeks; N=Number Of Patients In The Analysis Population; n=Number of Patients With At Least One Treatment-emergent Adverse Event In The Specified Category; PY=Patient-years; SAE=Serious Adverse Event; TEAE=Treatment-emergent Adverse Event.
Deodhar A, et al. *J Rheumatol.* 2023;50(8):1020-1028.

Επιλεγμένες παραμέτρους μακροχρόνιας ασφάλειας

Όλες οι μελέτες σε PsO, PsA, axSpA IXE μέχρι το 2019

	PsO N=5898 n (%) [IR/100 PY, 95% CI]	PsA N=1401 n (%) [IR/100 PY, 95% CI]	AxSpA N=929 n (%) [IR/100 PY, 95% CI]
Σοβαρές λοιμώξεις	225 (**3.8**) [1.3, 1.1-1.5]	28 (**2.0**) [1.3, 0.9-1.8]	17 (**1.8**) [1.3, 0.8-2.0]
Αντιδράσεις στη θέση της ένεσης[α]	892 (**15.1**) [5.1, 4.8-5.5]	259 (**18.5**) [11.6, 10.3-13.1]	154 (**16.6**) [11.5, 9.8-13.5]
Κακοήθειες	134 (**2.3**) [0.8, 0.7-0.9]	15 (**1.1**) [0.7, 0.4-1.1]	6 (**0.6**) [0.4, 0.2-1.0]
NMSC	51 (**0.9**) [0.3, 0.2-0.4]	9 (**0.6**) [0.4, 0.2-2.8]	0 (**0**) [0.0, 0.0-0.6]
Άλλες κακοήθειες πλην NMSC	89 (**1.5**) [0.5, 0.4-0.6]	7 (**0.5**) [0.3, 0.1-0.7]	6 (**0.6**) [0.4, 0.2-1.0]
Φλεγμονώδης νόσος του εντέρου (κριθείσα)	29 (**0.5**) [0.2, 0.1-0.2]	3 (**0.2**) [0.1, 0.0-0.4]	13 (**1.4**) [1.0, 0.6-1.7]
Ελκώδης κολίτιδα	12 (**0.2**) [0.1, 0.0-0.1]	2 (**0.1**) [0.1, 0.0-0.4]	7 (**0.8**) [0.5, 0.2-1.1]
Νόσος του Crohn (κριθείσα)	17 (**0.3**) [0.1, 0.1-0.2]	1 (**0.1**) [0.0, 0.0-0.3]	6 (**0.6**) [0.4, 0.2-1.0]
Κατάθλιψη	203 (**3.4**) [1.2, 1.0-1.3]	37 (**2.6**) [1.7, 1.2-2.3]	13 (**1.4**) [1.0, 0.6-1.7]

[a]The data represents externally adjudicated cases. IR was calculated as the total of "definite" and "probable" cases/total PY multiplied by 100. [b]In the axSpA program, 1 patient with an event of ulcerative colitis was reported in the placebo group and later adjudicated as Crohn's disease; and another placebo patient with history of ulcerative colitis had a reported event of ulcerative colitis but was later adjudicated as 'insufficient information'. [c]In the PsA program, 1 patient had a reported event of anal abscess and anal fistula; this event was considered consistent with inflammatory bowel disease but was not adjudicated as Crohn's disease or ulcerative colitis due to insufficient information. [d]Broad definition according to SMQ or sub-SMQ classification.

Genovese MC, et al. *Rheumatology (Oxford).*2020; doi:10.1093/rheumatology/keaa189 (Ahead of print).

Επιλεγμένες παραμέτρους μακροχρόνιας ασφάλειας

Όλες οι μελέτες σε PsO, PsA, axSpA IXE μέχρι το 2019

	PsO N=5898 n (%) [IR/100 PY, 95% CI]	PsA N=1401 n (%) [IR/100 PY, 95% CI]	AxSpA N=929 n (%) [IR/100 PY, 95% CI]
Ιρίτιδα	3 (<**0.1**) [<0.1, 0.0-0.1]	1 (**0.1**) [<0.1, 0.0-0.3]	6 (**0.6**) [0.4, 0.2-1.0]
Ιριδοκυκλίτιδα	2 (<**0.1**) [<0.1, 0.0 to <0.1]	0 (**0.0**) [0.0, NA]	42 (**4.5**) [3.1, 2.3-4.3]
Ευκαιριακές λοιμώξεις	512 (**8.7**) [3.0, 2.7-3.2]	86 (**6.1**) [3.9, 3.1-4.8]	23 (**2.5**) [1.7, 1.1-2.6]
Στοματική καντιντίαση	140 (**2.4**) [0.8, 0.7-1.0]	16 (**1.1**) [0.7, 0.4-1.2]	1 (**0.1**) [0.1, 0.0-0.5]
Καντιντίαση οισοφάγου	13 (**0.2**) [0.1, 0.0-0.1]	2 (**0.1**) [0.1, 0.0-0.4]	3 (**0.3**) [0.2, 0.1-0.7]
Έρπης ζωστήρας	110 (**1.9**) [0.6, 0.5-0.8]	16 (**1.1**) [0.7, 0.4-1.2]	11 (**1.2**) [0.8, 0.5-1.5]
Λανθάνουσες ΤΒ λοιμώξεις	105 (**1.8**) [0.6, 0.5-0.7]	22 (**1.6**) [1.0, 0.6-1.5]	1 (**0.1**) [0.1, 0.0-0.5]
Έμφραγμα του μυοκαρδίου, μη θανατηφόρο	45 (**0.8**) [0.3, 0.2-0.4]	6 (**0.4**) [0.3, 0.1-0.6]	2 (**0.2**) [0.1, 0.0-0.6]
Εγκεφαλικό επεισόδιο, μη θανατηφόρο	21 (**0.4**) [0.1, 0.1-0.2]	4 (**0.3**) [0.2, 0.1-0.5]	0 (**0.0**) [0.0, 0.0-0.6]
MACE	85 (**1.5**) [0.5, 0.4-0.6]	12 (**0.9**) [0.5, 0.3-0.9]	**2 (0.2)** [0.1, 0.0-0.6]

[a]The data represents externally adjudicated cases. IR was calculated as the total of "definite" and "probable" cases/total PY multiplied by 100. [b]In the axSpA program, 1 patient with an event of ulcerative colitis was reported in the placebo group and later adjudicated as Crohn's disease; and another placebo patient with history of ulcerative colitis had a reported event of ulcerative colitis but was later adjudicated as 'insufficient information'. [c]In the PsA program, 1 patient had a reported event of anal abscess and anal fistula; this event was considered consistent with inflammatory bowel disease but was not adjudicated as Crohn's disease or ulcerative colitis due to insufficient information. [d]Broad definition according to SMQ or sub-SMQ classification.

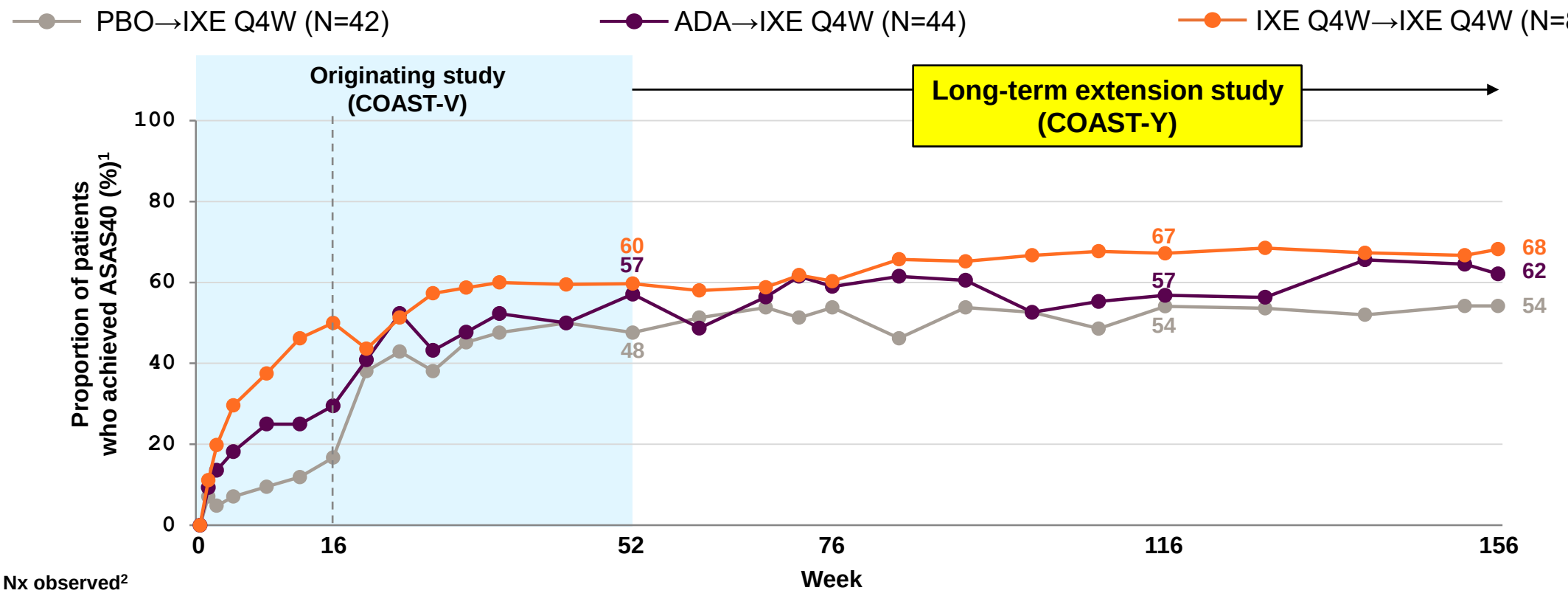
Genovese MC, et al. *Rheumatology (Oxford).*2020; doi:10.1093/rheumatology/keaa189 (Ahead of print).

Αγκυλοποιητική Σπονδυλαρθρίτιδα
2η Περίπτωση ασθενούς

- **Ιούνιος 2025**
  - BASDAI : 0
  - CRP : <0,5 mg/dl
- Χωρίς σημεία ενεργού ΑΣ από τον αξονικό σκελετό και τις περιφερικές αρθρώσεις.
- Χωρίς ακτινολογική εξέλιξη.
- Φυσιολογική ηπατική βιολογία.
- Απουσία λοιμώξεων.
- Χωρίς εκδηλώσεις από το έντερο.

ASAS40 Response Through Week 156, Observed

Efficacy Population (COAST-V, -Y): Figure 4[illegible]



Nx observed[2]

PBO→IXE Q4W	42		42		42		39		37		24	
ADA→IXE Q4W	44		44		42		39		37		29	
IXE Q4W→IXE Q4W	81		78		72		68		64		44	

Note: Observed data while on IXE Q2W escalated dose are excluded. At Week 16, patients receiving either PBO (gray) or ADA (purple) were switched to IXE Q4W (orange). ADA→IXE Q4W are patients who were on washout period from Weeks 14 to 20 and started the first ixekizumab injection of IXE Q4W on Week 20.[1]

ADA=Adalimumab; ASAS40=40% Improvement in the Assessment of Spondyloarthritis International Society; IXE Q2W=80 mg of Ixekizumab Every 2 Weeks; IXE Q4W=80 mg of Ixekizumab Every 4 Weeks; PBO=Placebo.

1. Deodhar A, et al. *J Rheumatol.* 2023;50(8):1020-1028. 2. Data on file, Eli Lilly and Company for Nx table.

Συμπεράσματα

- Η **IL-17A** διαδραματίζει βασικό ρόλο στην επαγωγή της φλεγμονής, στην καταστροφή και στον σχηματισμό νέου οστού. Είναι η κύρια κυτταροκίνη της οικογένειας IL-17 που οδηγεί σε χρόνια φλεγμονή στις ΣπΑ.
- Το **IXEKIZUMAB** δείχνει άμεση, παρατεταμένη ανακούφιση από τα σημεία και τα συμπτώματα: Ανταπόκριση κατά **ASAS.**

➢ Ο τυπικός ασθενής με Αξονική ΣπΑ (r/nr) ,

- Εμφανίζει άμεση και παρατεταμένη μείωση στην ενεργότητα της νόσου: Βελτίωση των δεικτών **BASDAI/ASDAS από την 16 η εβδομάδα με διατήρηση της ανταπόκρισης μέχρι και την 156 εβδομάδα.**

➢ **Προφίλ ασφάλειας** αντίστοιχο με εκείνο των anti-TNFa παραγόντων.

➢ Απουσία αναφοράς για αναζωπύρωση TB/HBV.

- Ευχαριστώ θερμά…