

10:00-11:00 ΠΑΡΑΛΛΗΛΑ ΔΟΥΡΥΦΟΡΙΚΑ ΣΕΜΙΝΑΡΙΑ II

Κεντρική αίθουσα «Athinais I»

I. «Διευρύνοντας τις θεραπευτικές επιλογές στις φλεγμονώδεις αρθρίτιδες: Η θέση των εκλεκτικών JAK αναστολέων»

abbvie  
Ρευματολογία

# Αξονική σπονδυλαρθρίτιδα υπό το πρίσμα της σύγχρονης θεραπευτικής προσέγγισης: μία ή περισσότερες αποχρώσεις;

Χρήστος Κουτσιανάς MD, PhD

Ρευματολόγος - Ειδικός Παθολόγος, Ακαδημαϊκός υπότροφος, Μονάδα Κλινικής Ανοσολογίας - Ρευματολογίας, Β Πανεπιστημιακή Παθολογική Κλινική και Ομώνυμο Εργαστήριο ΓΝΑ «Ιπποκράτειο»

Honorary Consultant, Research & Development Department, The Dudley Group NHS Foundation Trust

NHS

The Dudley Group  
NHS Foundation Trust

JAKa-GR-00096-E June 2022

# Disclosures

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## Τιμητική αμοιβή από την Abbvie για αυτή την ομιλία

- Honoraria for lectures:  
Roche, Genesis Pharma, Abbvie, Novartis
  - Honoraria for advisory boards:  
Genesis Pharma
  - Hospitality:  
Eli-Lilly, Novartis, Viartis, UCB, Abbvie
  - Research:  
Sub-investigator: Roche, UCB, Eli-Lilly, Novartis, BMS, Pfizer, Genesis Pharma, AMGEN, MSD, Abbvie
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# Outline

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- Introduction
  - Case presentation
  - Current management in AxSpA: choices, choices, choices
  - Which colour of the rainbow should we stand on?
    - efficacy
    - safety
    - patient preference
  - Case presentation
-

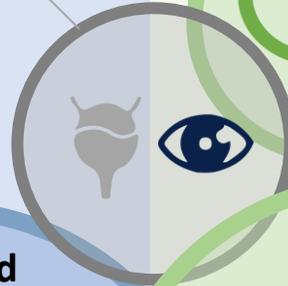
# SpA: Clinical disease and spectrum

## Relationships among the Spondyloarthritis



**Axial manifestations**

Reactive arthritis

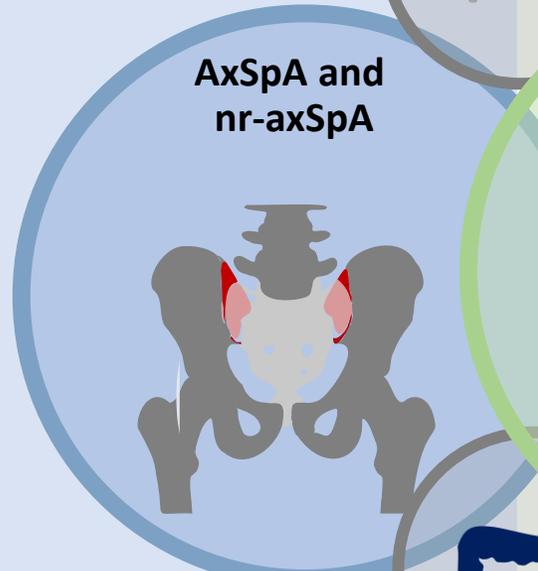


Undifferentiated peripheral SpA

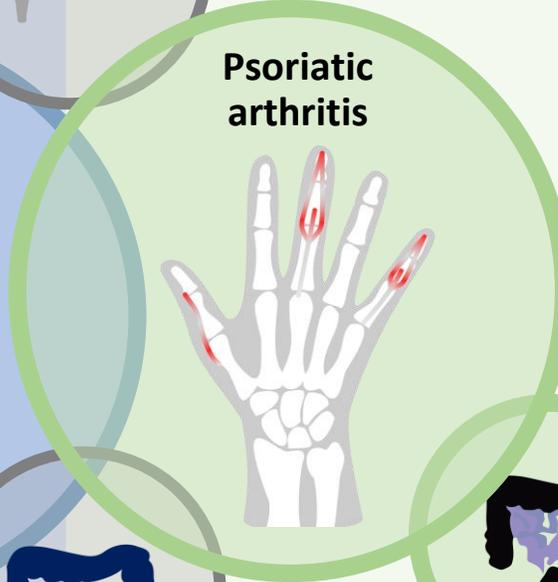


**Peripheral manifestations**

AxSpA and nr-axSpA



Psoriatic arthritis



SpA with associated IBD



Enteropathic arthritis



# AxSpA: Effect of inflammation over time

Sacroiliac joint inflammation

Erosions, ankylosis

Early axSpA or mild axSpA

Late axSpA or severe axSpA



Non-radiographic axSpA

Radiographic axSpA (AS)

- Clinical manifestations of axSpA but no radiographic evidence of structural damage
- MRI might show active sacroiliitis

Radiographic sacroiliitis

Syndesmophytes

Time (years)

PROOF

nr-AxSpA → r-AxSpA

16%

after a mean of 2.4 yrs

- Male gender
- HLA-B27 +
- Inflammation on MRI
- Good response to NSAIDs

Poddubnyy et al. EULAR 2022 OP149

# AxSpA: treatment goals

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**Control symptoms and reduce inflammation**



**Prevent structural damage**



**Normalise / preserve functional status**



**Maximise health-related quality of life**

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# Case presentation: history

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- Θωμάς, 32 ετών
- Εργάζεται σε κατασκευαστική εταιρεία και εποπτεύει έργα σε διάφορες περιοχές της Ελλάδας και του εξωτερικού
- Από «μικρή ηλικία»: άλγος στην οσφύ χαμηλά αρχικά χειρότερα αριστερά, κατόπιν και συμμετοχή της ΑΜΣΣ και της ΟΜΣΣ
  - επιδείνωση με την ανάπαυση
  - νυχτερινή αφύπνιση
  - πρωινή δυσκαμψία που διαρκεί περίπου 20-30 λεπτά
  - ανταπόκριση στα ΜΣΑΦ που διαρκεί για λίγες ώρες
- Ηπίως αυξημένη ΤΚΕ και CRP διαπιστωμένα από παλιά, χωρίς σαφή εξήγηση
- ΕΑΜs: PsO (-), uveitis (-), enthesitis (-), dactylitis (-)



# Case presentation: clinical examination - labs

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ΑΠ=110/70mmHg, Σφύξεις=86/min,

Θ=36.4°C, Αναπνοές=12/min

SatO<sub>2</sub>=98% (FiO<sub>2</sub> 21%)

Hb: 13.6 g/dl, MCV: 92 fL, WBC: 6480 (Π 69%, Λ 22%), PLT: 367000

Cr:1.0 mg/dl UR: 36mg/dL, Glu: 101 mg/dl

AST/ALT: 18/9 U/L (<34/<55), CK: 175 mg/dL

TChol: 197 mg/dL, HDL: 45mg/dL, LDL: 112 mg/dL, TGs: 90mg/dL

**CRP: 8.6 (<5 mg/dl), TKE 42 mm/h,**

Γενική ούρων : RBC: 0-1, WBC: 0-1, Λευκ: (-)

HLA-B27 (-)

## Κλινική εξέταση

Χωρίς εικόνα περιφερικής αρθρίτιδας

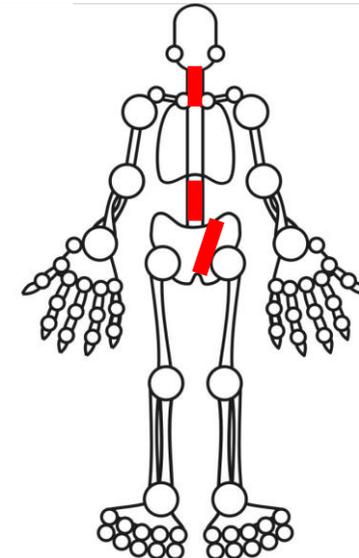
Χωρίς εικόνα ενθεσίτιδας

**FABER (+) αριστερά**

**Μειωμένη ROM στην εκατέρωθεν στροφή της**

**ΑΜΣΣ (ΔΕ: 65°, ΑΡ 60°) και στην πρόσθια**

**κάμψη της ΟΜΣΣ (Schober 15 -> 19.5 cm)**



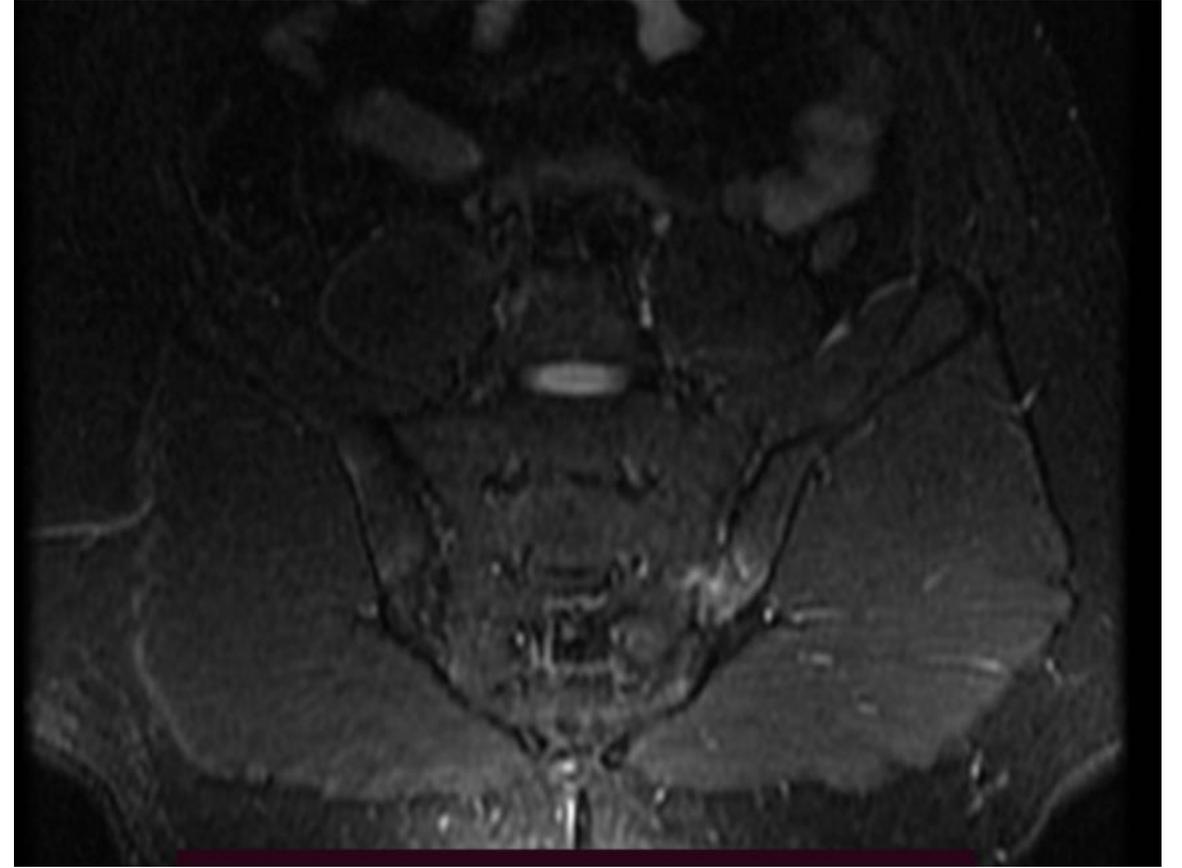
# Case presentation: imaging

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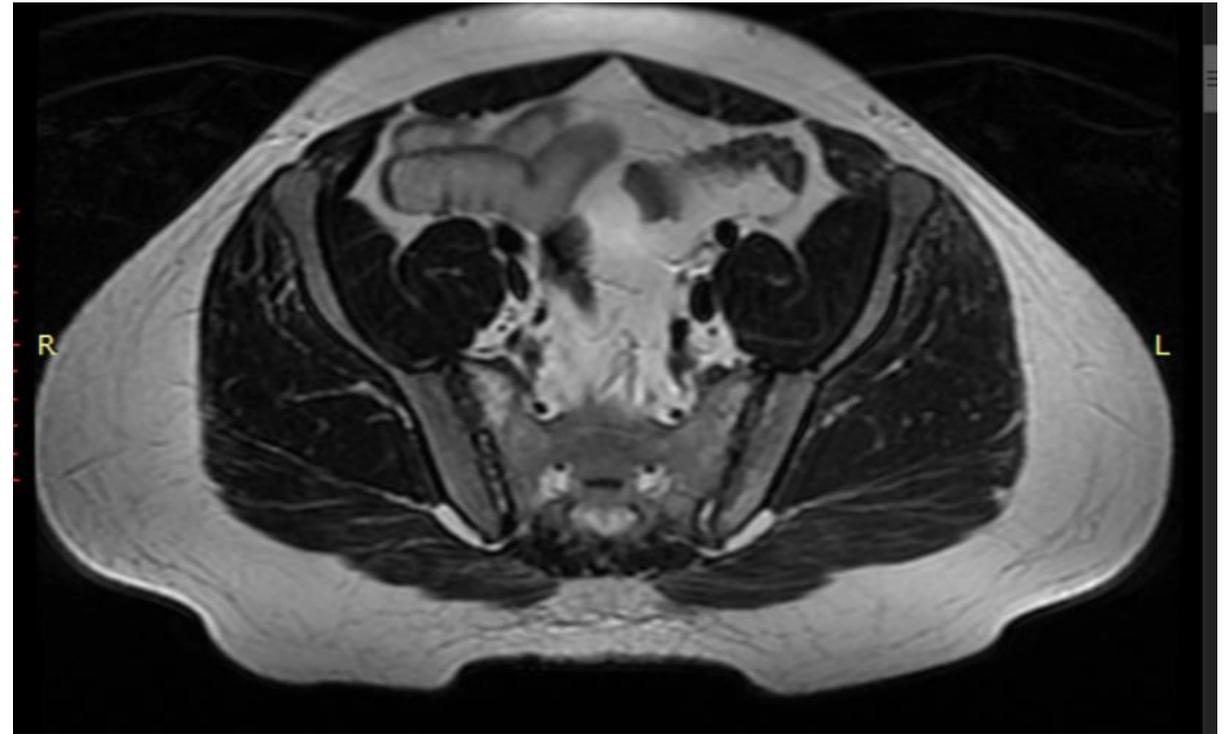
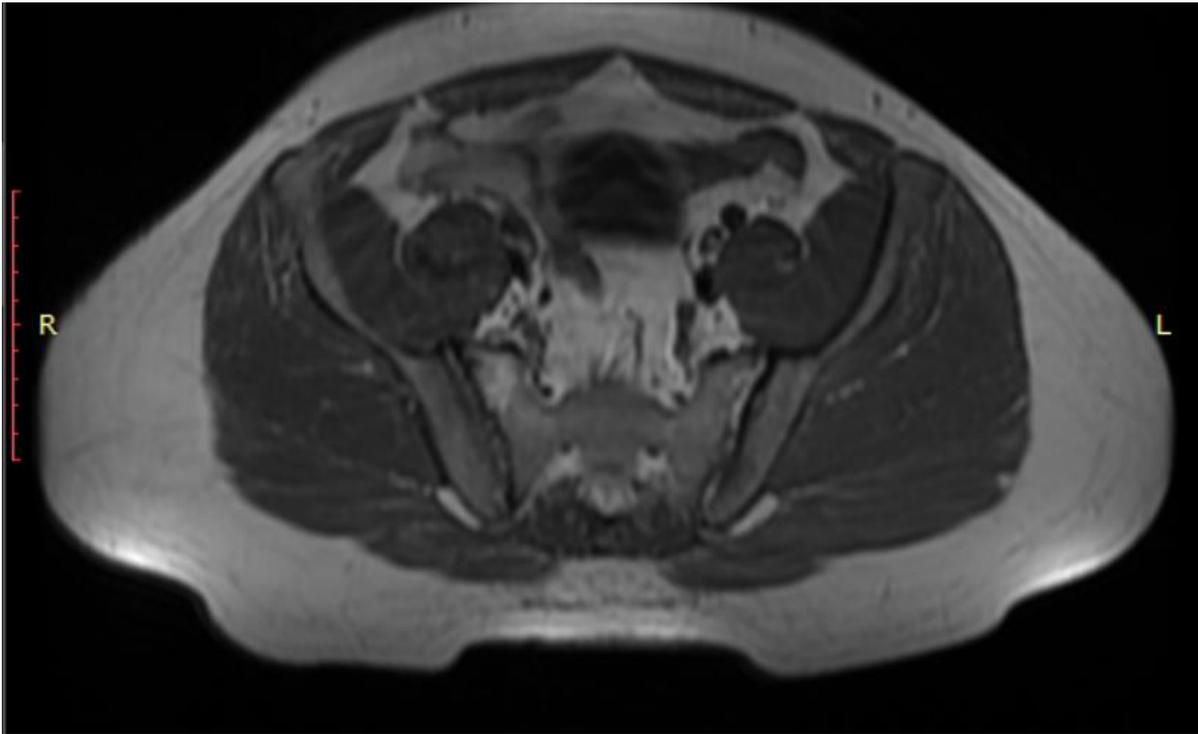
# Case presentation: imaging

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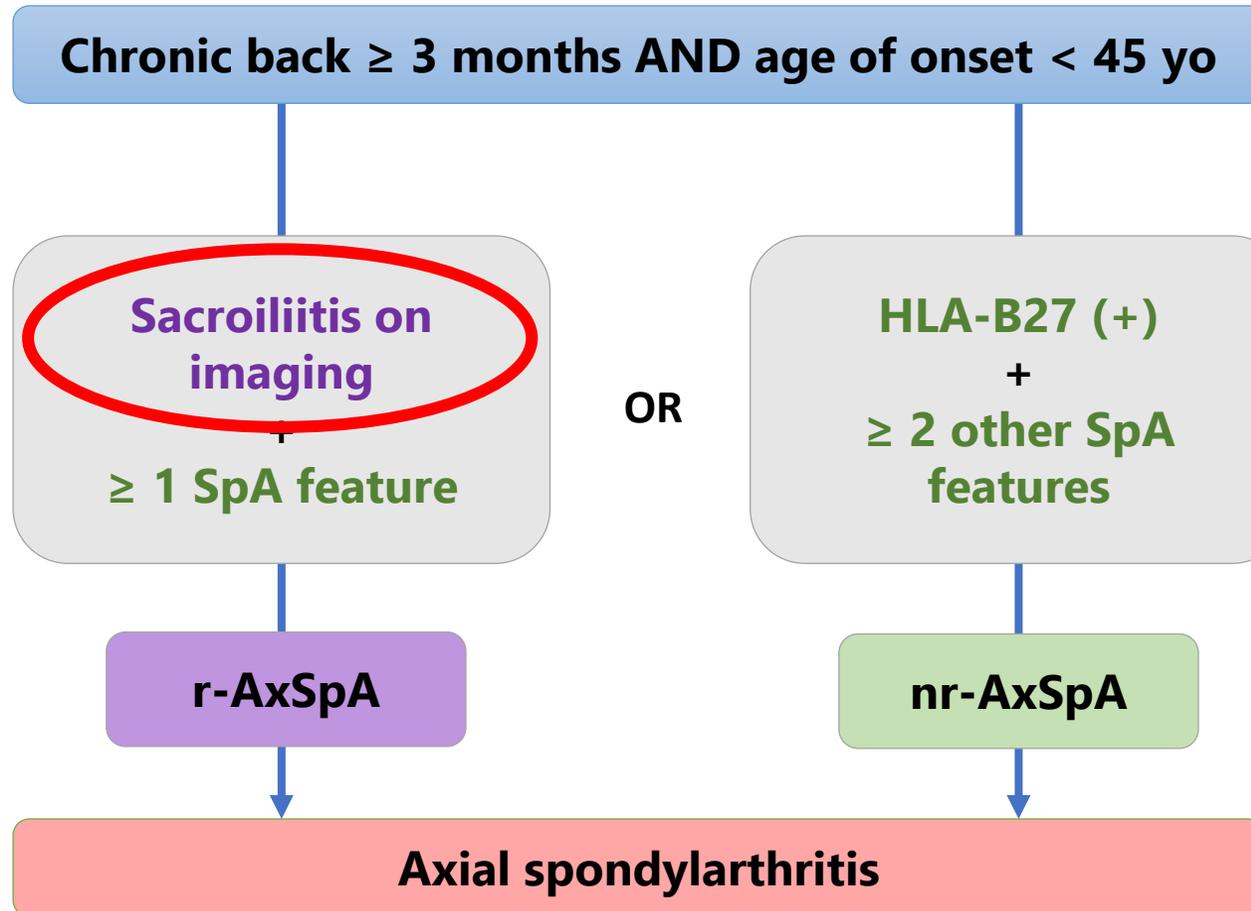


# Case presentation

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# ASAS classification criteria for AxSpA



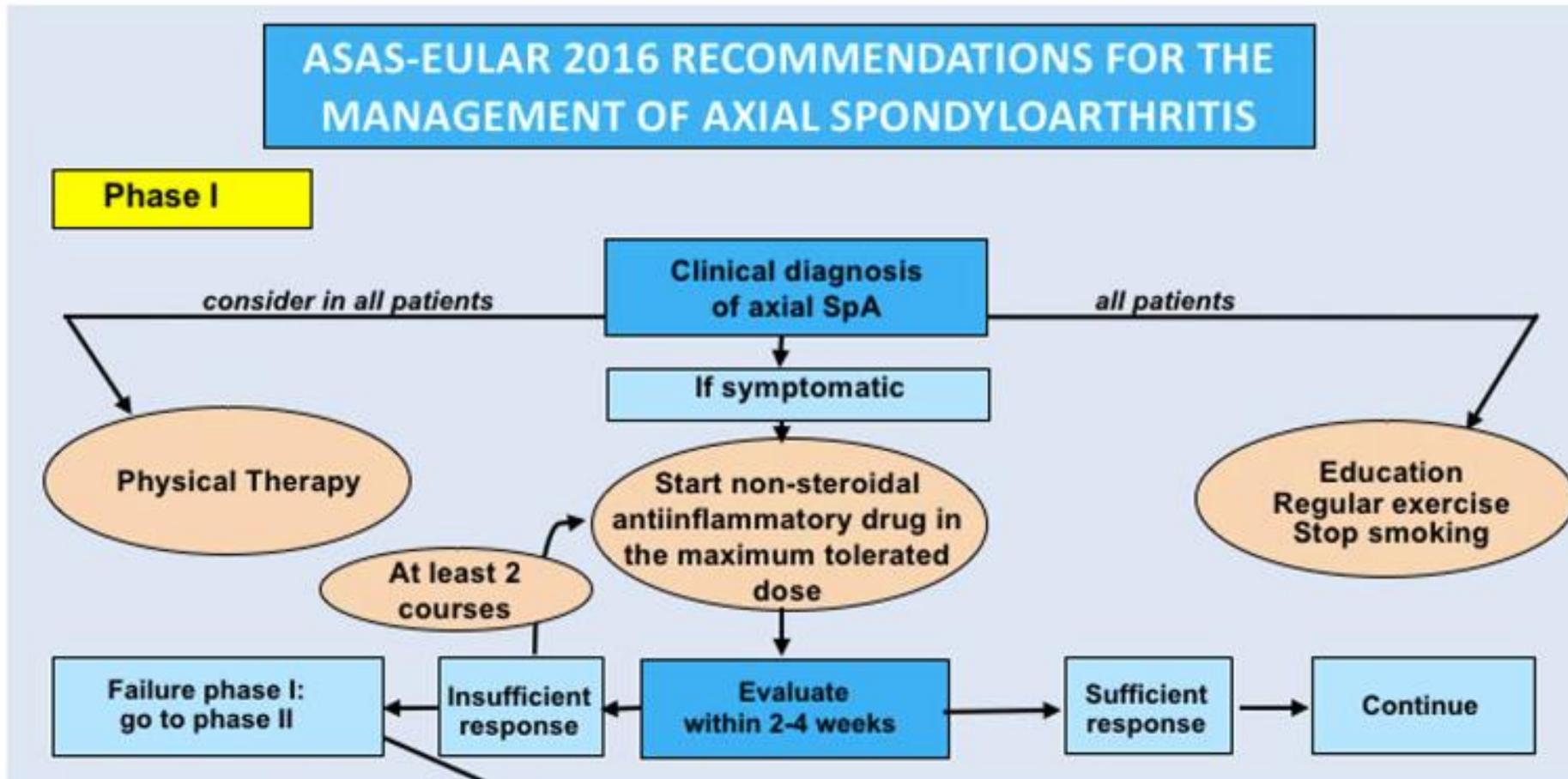
## Sacroiliitis on imaging

- Definite radiographic sacroiliitis according to mNY criteria
- Active inflammation on MRI highly suggestive of sacroiliitis

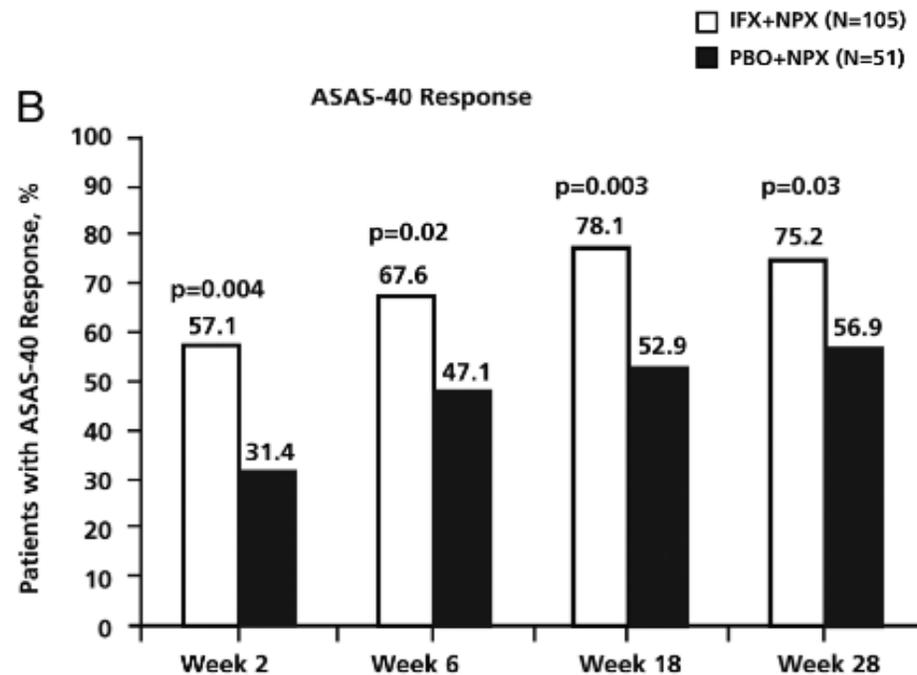
## SpA features

- IBP
- Arthritis
- Enthesitis
- Uveitis
- Dactylitis
- Psoriasis
- Crohn's/colitis
- Good response to NSAIDs
- Family history of SpA
- HLA-B27
- Elevated CRP

# Treatment choices in AxSpA: before the prism

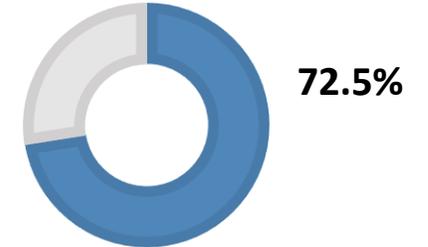


# How many patients will respond to NSAIDs?

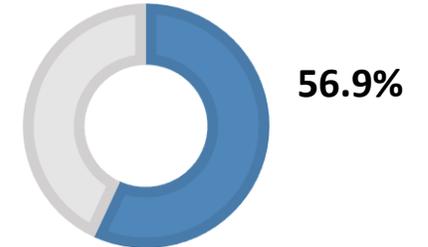


INFAST trial

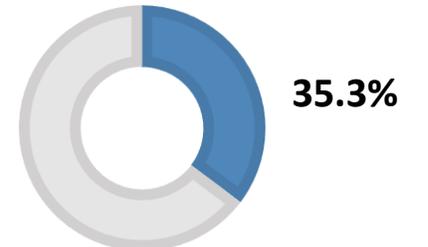
ASAS 20 response



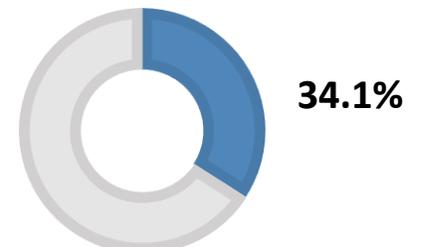
ASAS 40 response



ASAS partial remission

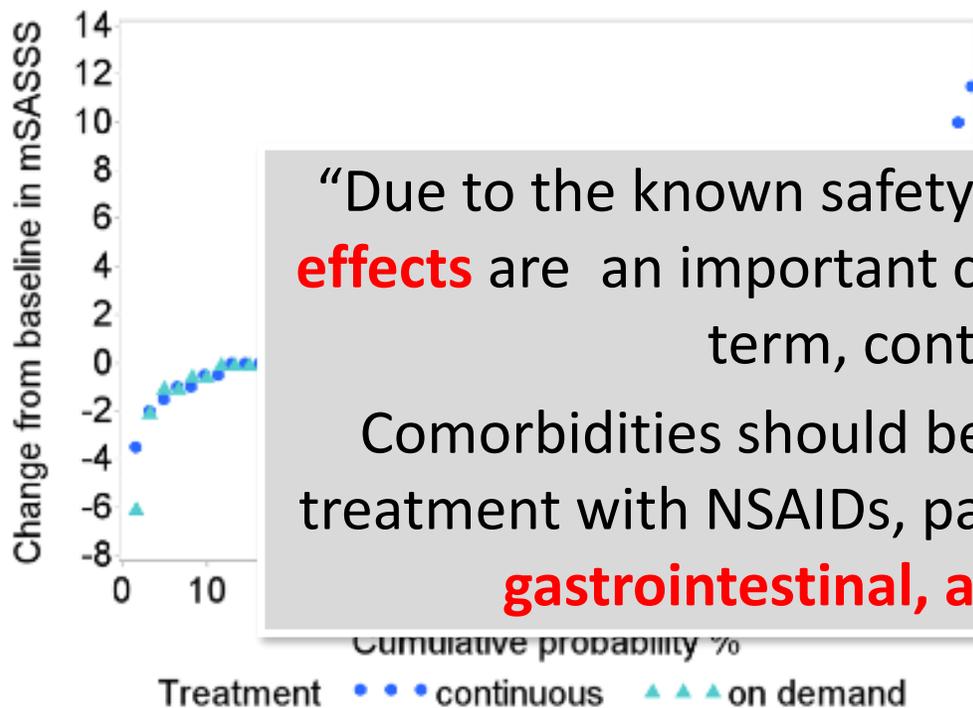


ASAS major improvement



# Can patients continue to take NSAIDs long term?

## ENRADAS trial



“Due to the known safety profile of NSAIDs, **potential side effects** are an important consideration for prescribing long-term, continuous treatment

Comorbidities should be considered before continuous treatment with NSAIDs, particularly **cardiovascular disease, gastrointestinal, and kidney** comorbidities”

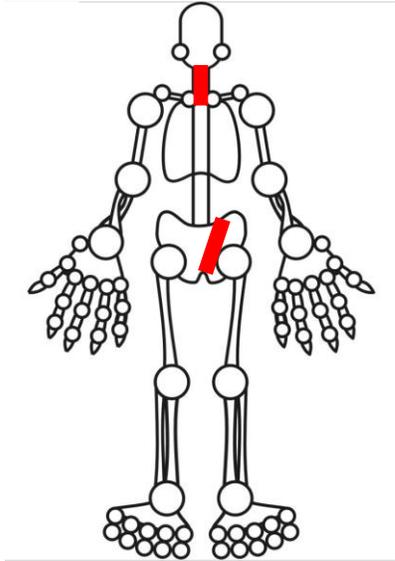
**Table 3** Number of serious adverse events (SAE) and SAE/100 patient years (pyrs) by treatment group (95% CIs are given in parenthesis)

	Continuous treatment group		On-demand treatment group	
	SAE	SAE/100 pyrs	SAE	SAE/100 pyrs
Cardiovascular disorders (total)	3	2.3 (0.5 to 6.6)	2	1.5 (0.2 to 5.4)
				0.8 (0 to 4.2)
				0.8 (0 to 4.2)
				5.3 (2.1 to 10.8)
				0.8 (0 to 4.2)
				1.5 (0.2 to 5.4)
				0.8 (0 to 4.2)
				0.8 (0 to 4.2)
				0.8 (0 to 4.2)
				0.8 (0 to 4.2)
Renal and urinary disorders (total)	1	0.8 (0 to 4.2)	2	1.5 (0.2 to 5.4)
Calculus ureteric	1	0.8 (0 to 4.2)		
Nephrolithiasis			2	1.5 (0.2 to 5.4)
Other SAE	14	10.6 (5.8 to 17.8)	10	7.5 (3.6 to 13.8)
SAE total	19	14.4 (8.7 to 22.5)	21	15.8 (9.8 to 24.1)

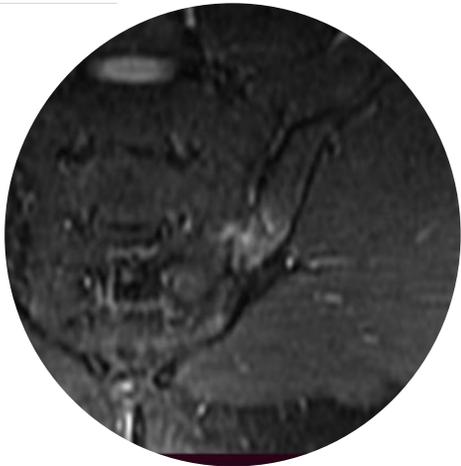
**Figure 3** Cumulative probability plot of radiographic progression; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

# Case presentation: metrics

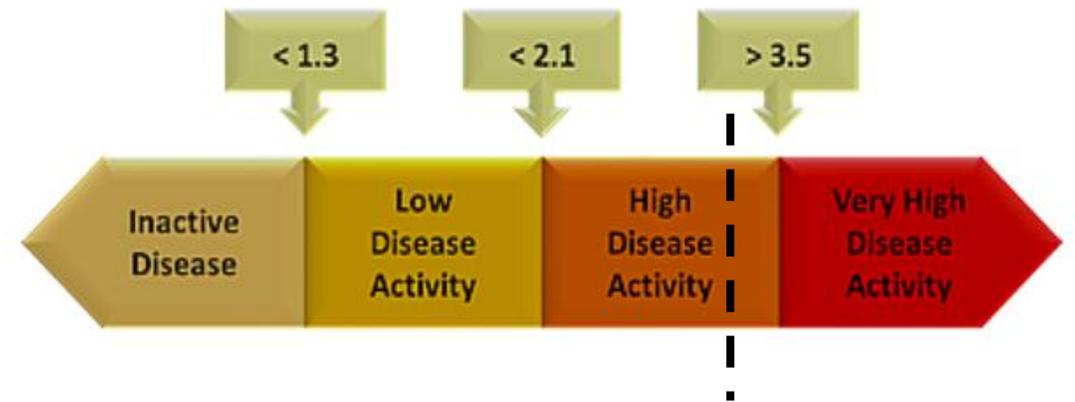
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**BASDAI: 5.2**  
**BASFI: 4.8**  
**ASDAS-CRP: 3.1**

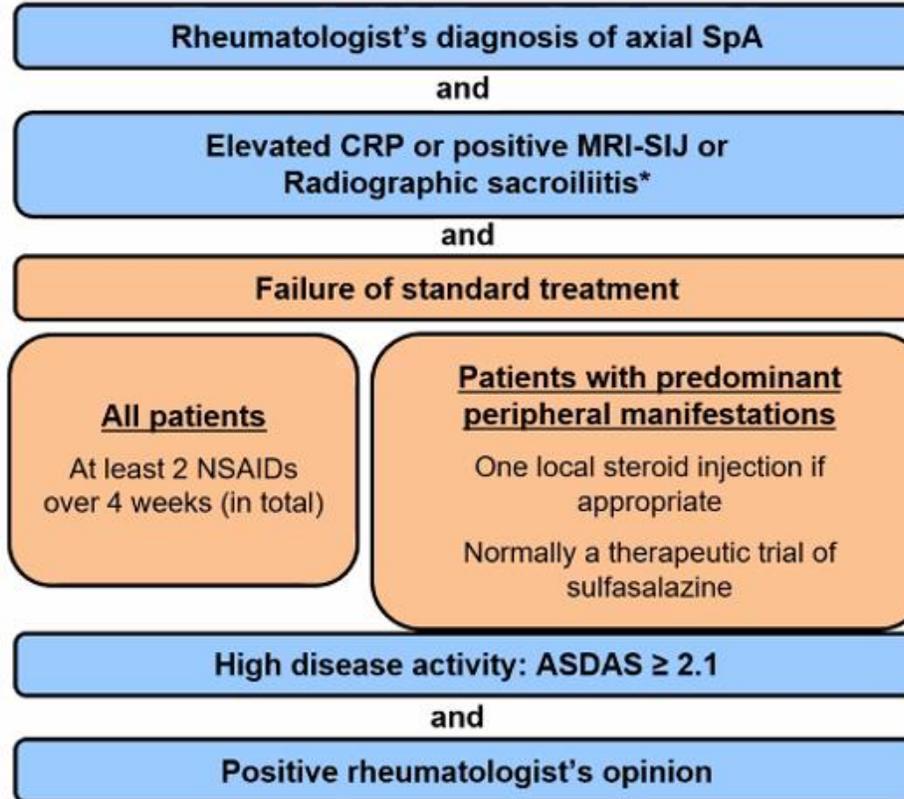


ASDAS disease activity states



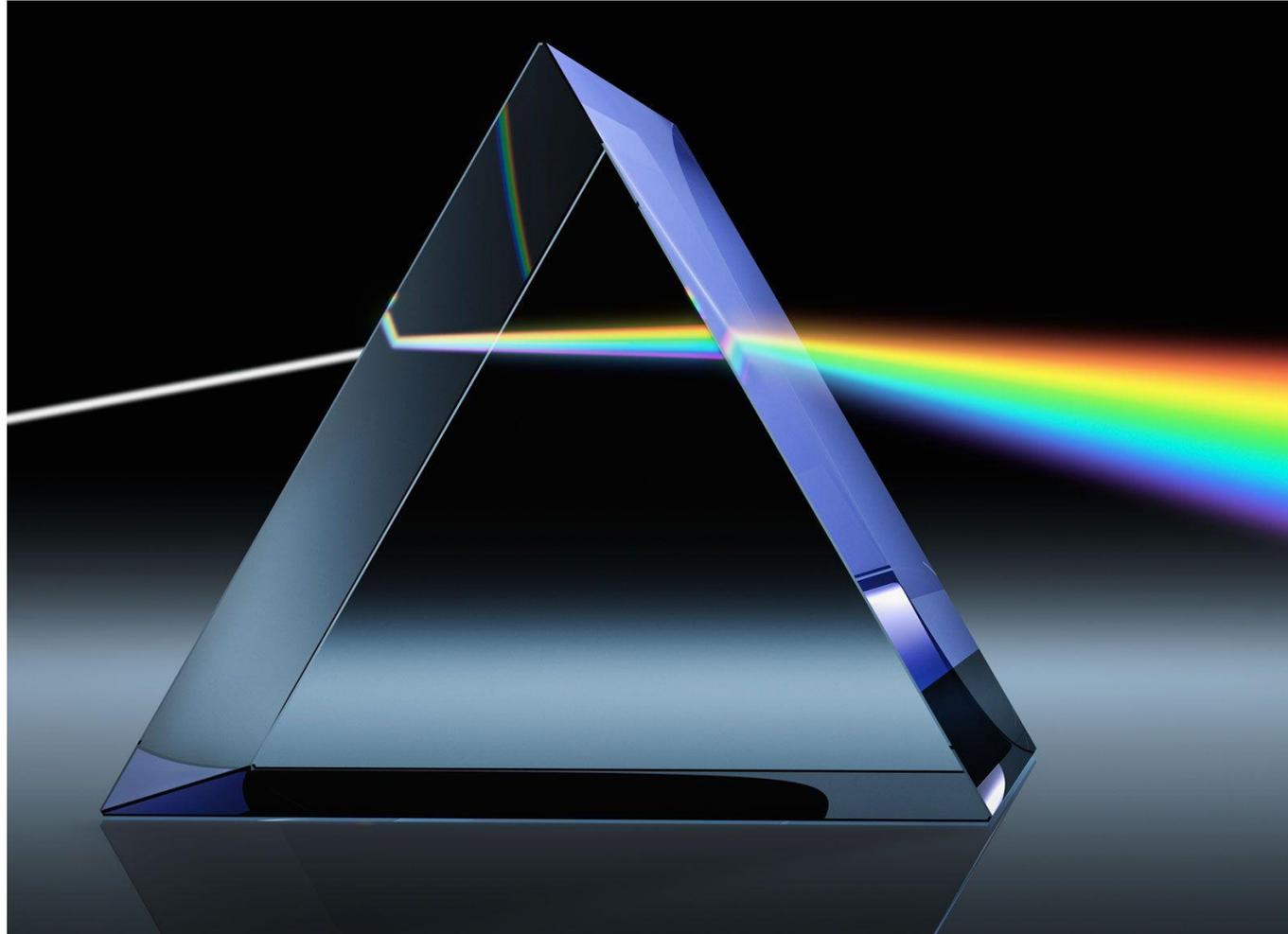
# AxSpA: advanced therapy

## ASAS-EULAR Recommendations for the treatment of patients with axSpA with b/tsDMARDs

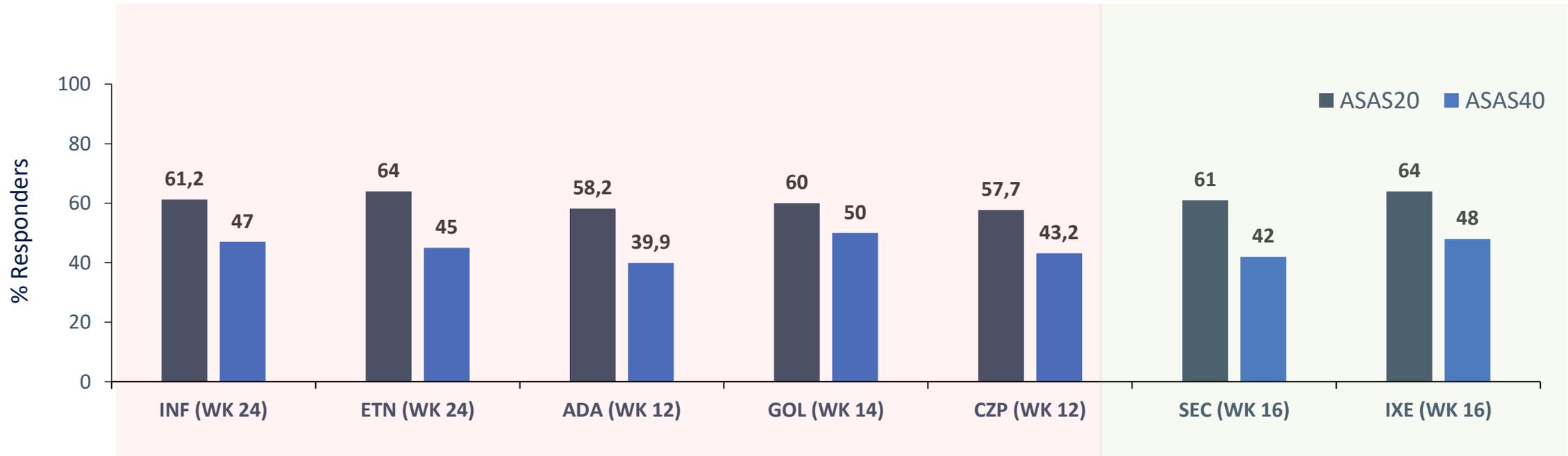


# AxSpA treatment choices in 2022: the prism of advanced therapy

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# Treatment choices in AxSpA: biologics



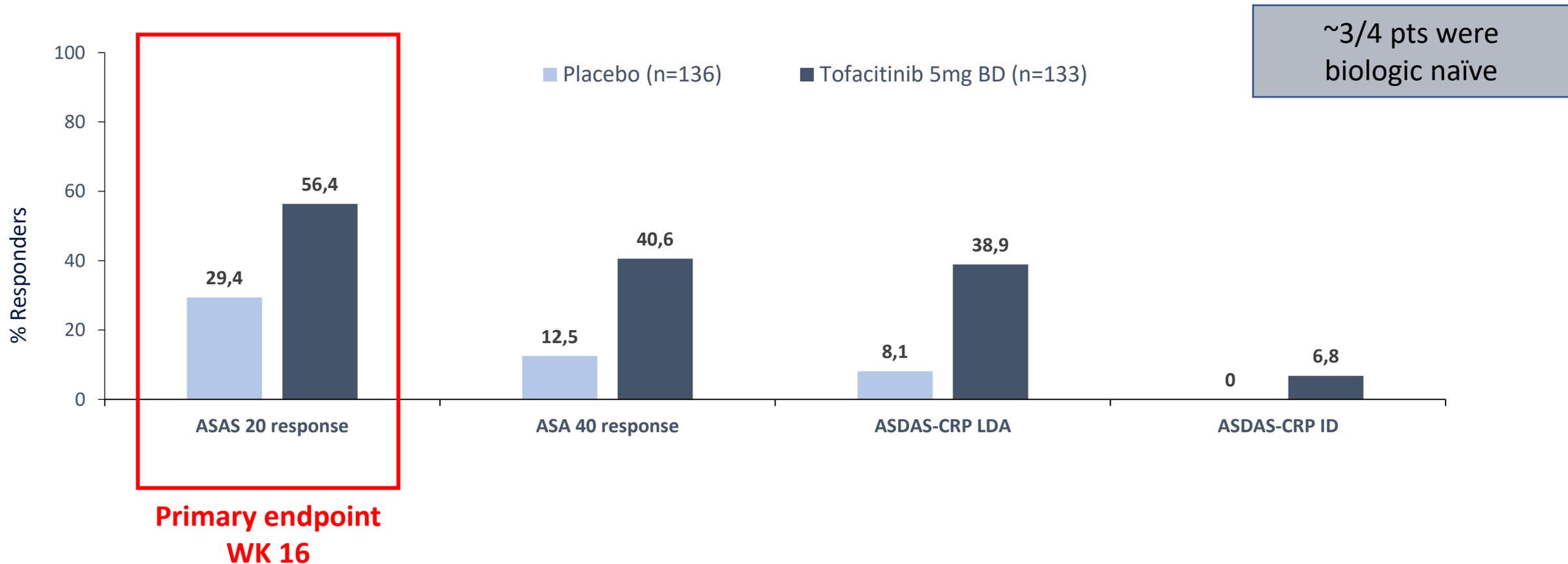
Proportions of patients receiving initial treatment achieving ASAS20 or ASAS40 response<sup>1-7</sup>

(Data not based on head-to-head trials. The data cannot be directly compared)

1. van der Heijde et al. Arthritis Rheum 2005; 2. Davis et al. ARD 2005; 3. van der Heijde et al. Arthritis Rheum 2006; 4. Inman et al. Arthritis Rheum 2008; 5. Sieper et al. ARD 2014; 6. Baeten et al. NEJM 2015.7. Dougados et al. ARD 2019

# Treatment choices in AxSpA: JAK inhibitors

## Tofacitinib in r-AxSpA

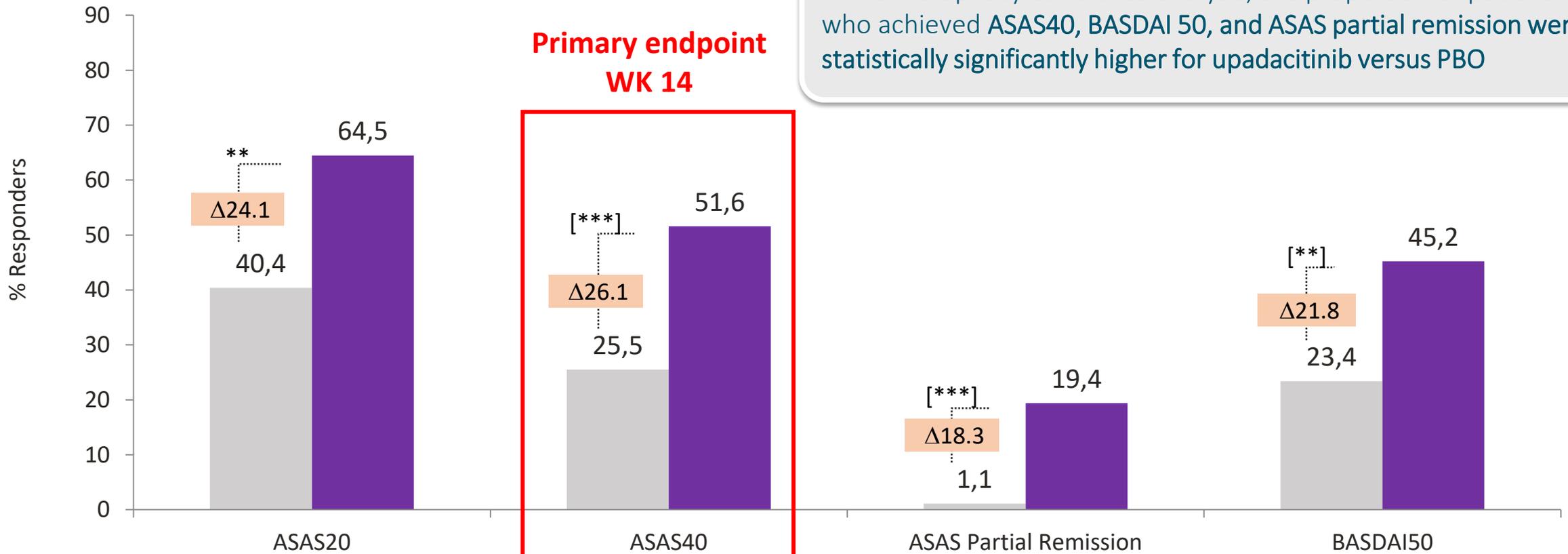


# Treatment choices in AxSpA: JAK inhibitors

## Upadacitinib in r-AxSpA

■ Placebo (N=94) ■ UPA 15 mg QD (N=93)

In the multiplicity-controlled analysis, the proportion of patients who achieved ASAS40, BASDAI 50, and ASAS partial remission were statistically significantly higher for upadacitinib versus PBO

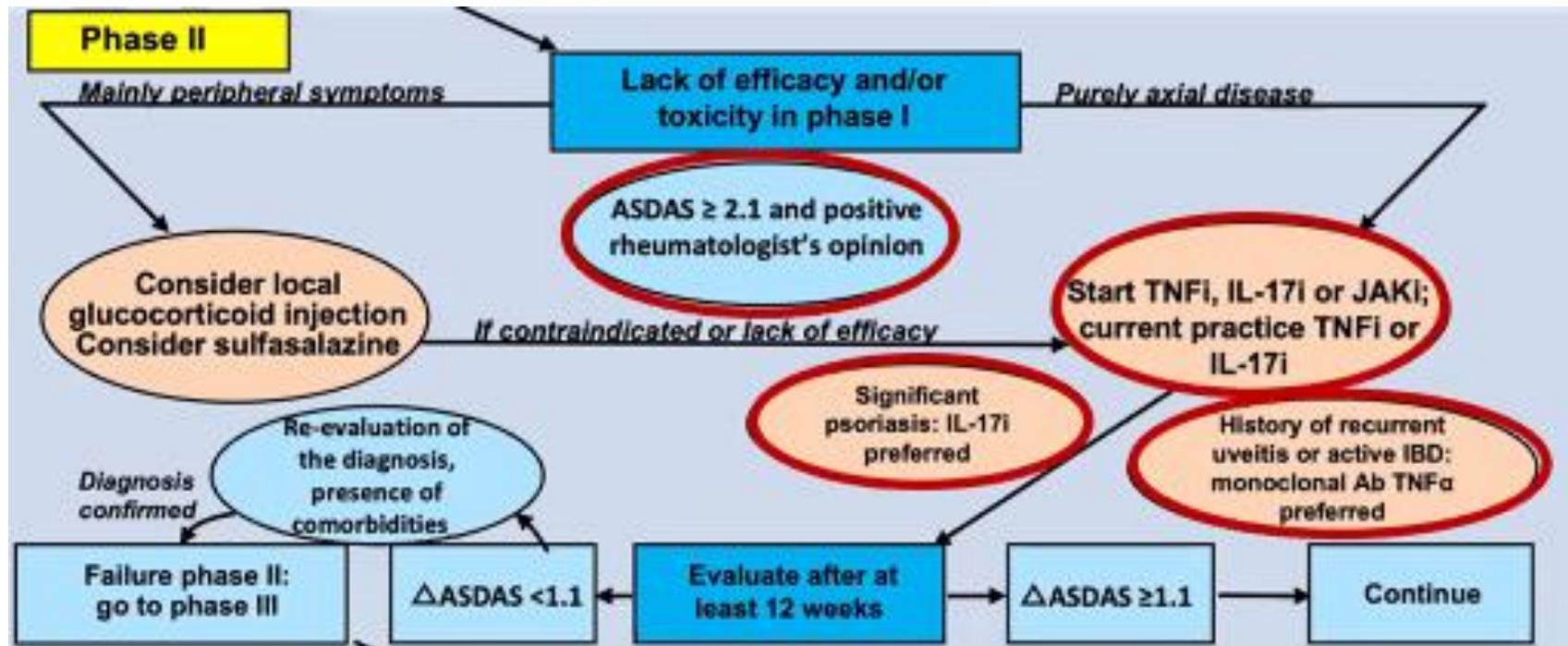


# Treatment choices in AxSpA: JAK inhibitors

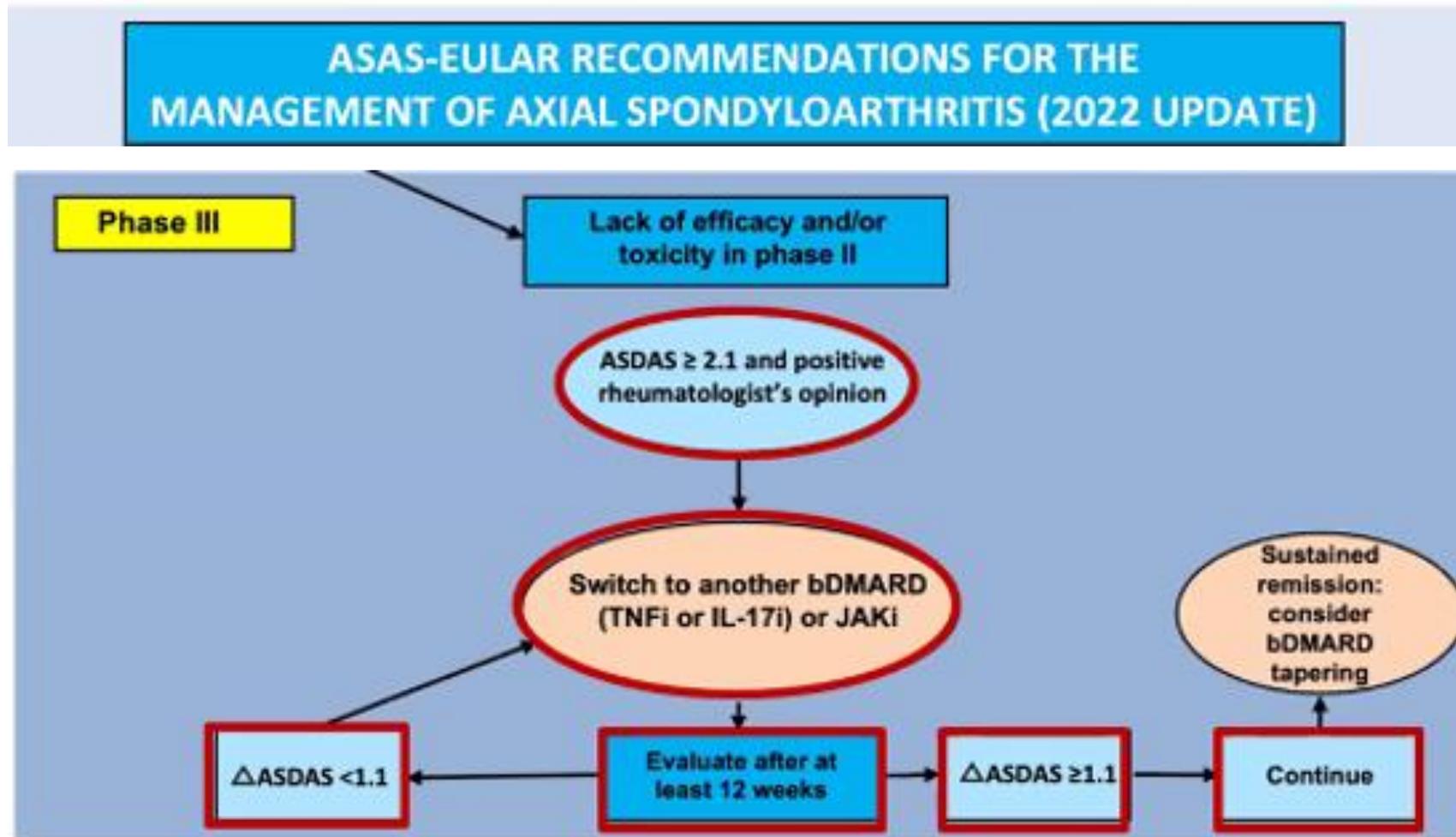
	r-AxSpA			nr-AxSpA
	TOFA study Tofacitinib Phase III	SELECT-AXIS 1 Upadacitinib Phase II/III	SELECT-AXIS 2 Upadacitinib Phase III	SELECT-AXIS 2 Upadacitinib Phase III
Patients	Majority bDMARD-naïve ~1/5 TNF-IR	bDMARD-naïve	bDMARD-IR	Majority bDMARD-naïve ~1/3 bDMARD-IR
Treatment arms	<ul style="list-style-type: none"> <li>TOFA 5mg BD for 48wks</li> <li>PBO for 16wks followed by TOFA 5mg BD for 32wks</li> </ul>	<ul style="list-style-type: none"> <li>UPA 15mg OD for 104wks</li> <li>PBO for 14wks followed by UPA 15mg OD for 90wks</li> </ul>	<ul style="list-style-type: none"> <li>UPA 15mg OD for 104wks</li> <li>PBO for 14wks followed by UPA 15mg OD for 90wks</li> </ul>	<ul style="list-style-type: none"> <li>UPA 15mg OD for 104wks</li> <li>PBO for 52wks followed by UPA 15mg OD for 52wks</li> </ul>
Sample size	269	187	420	314
Primary endpoint	ASAS 20 at week 16	ASAS 40 at week 14	ASAS 40 at week 14	ASAS 40 at week 14

# ASAS-EULAR recommendations for the management of AxSpA

## ASAS-EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF AXIAL SPONDYLOARTHRITIS (2022 UPDATE)

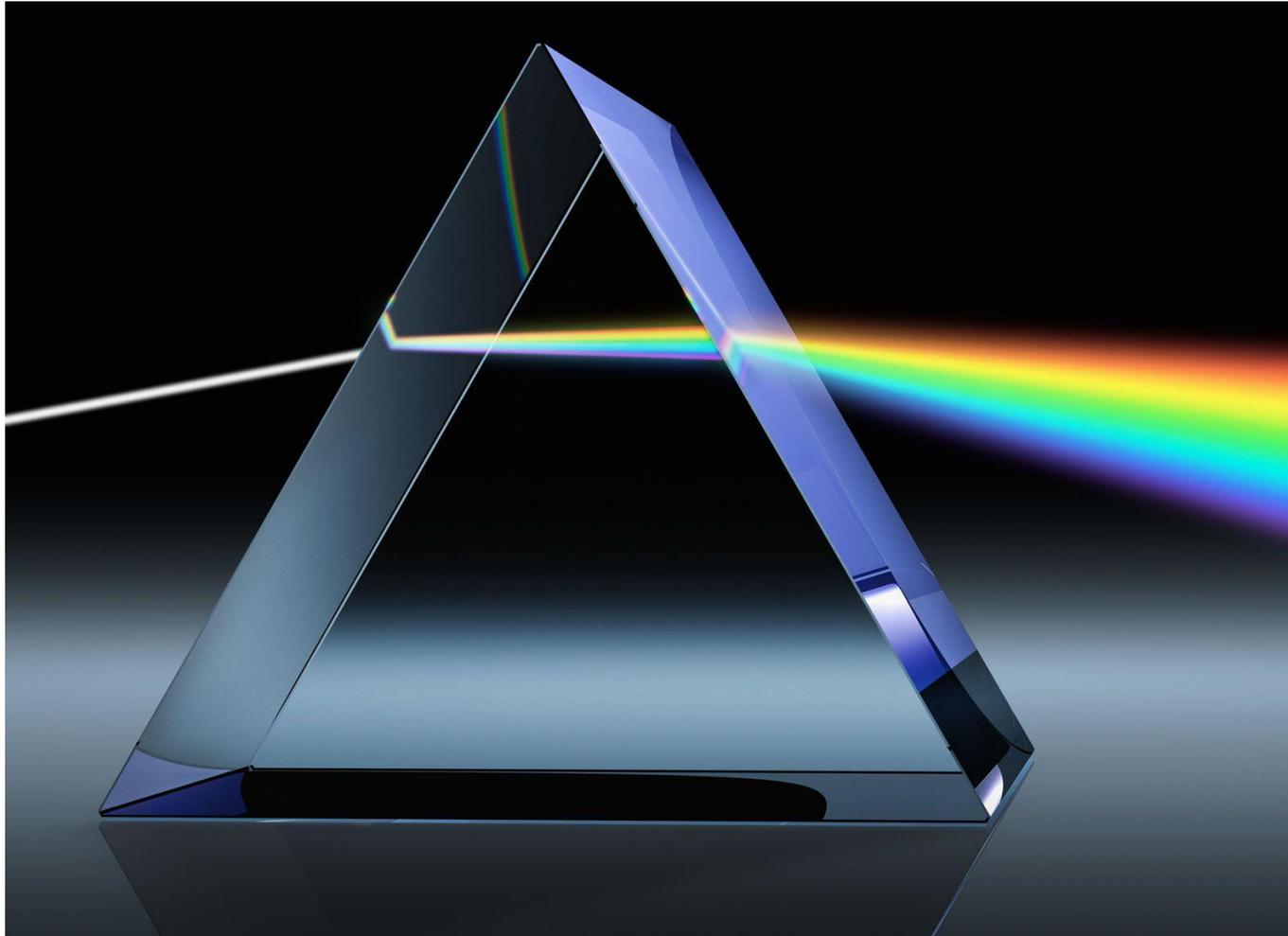


# ASAS-EULAR recommendations for the management of AxSpA

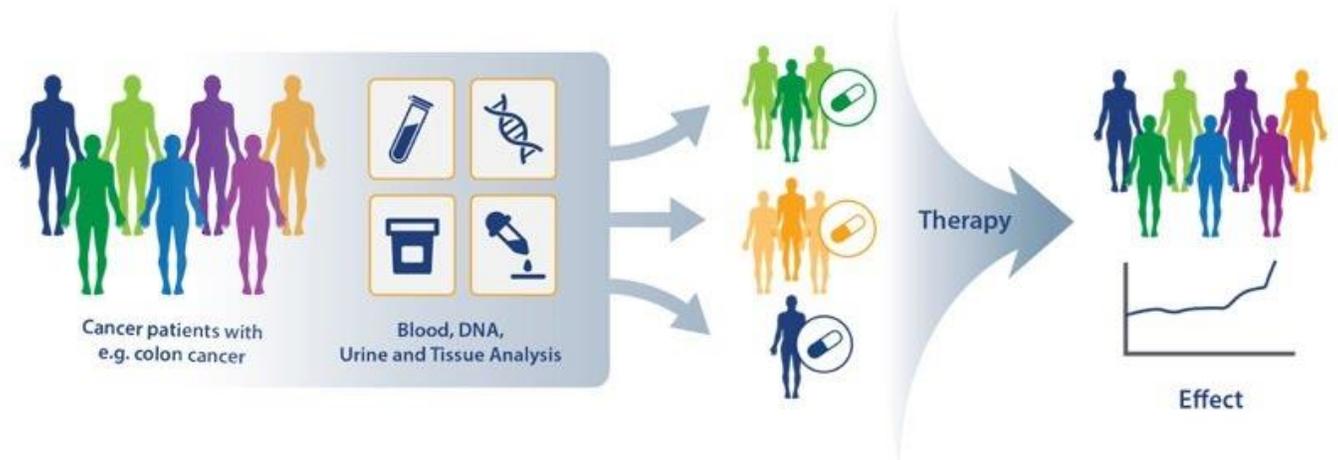
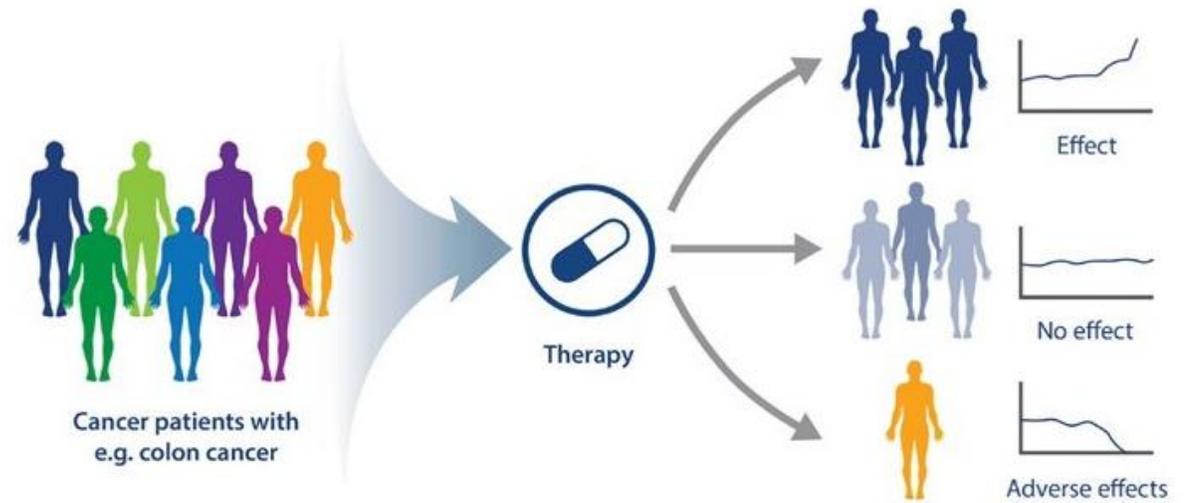
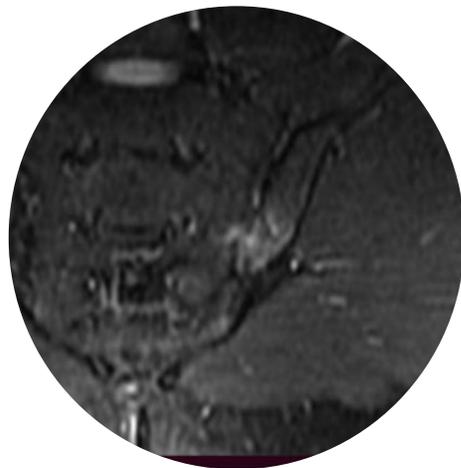
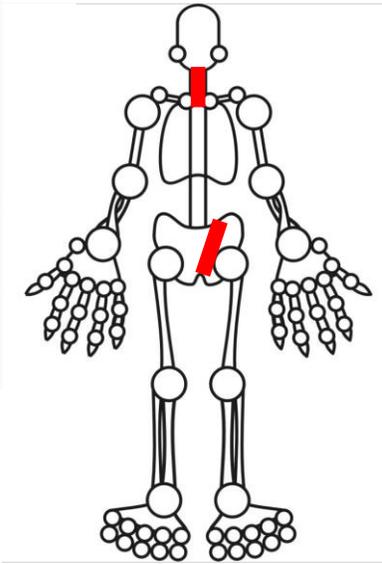


# AxSpA treatment choices in 2022: the prism of advanced therapy

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# Which drug to choose in real life practice?



# Which drug to choose in real life practice?

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## Previous treatment

- What if there is:
- Lack of response
  - Intolerance to therapy
  - Secondary treatment failure



## Presence of Extra-articular manifestations

- What if there is:
- Uveitis
  - Psoriasis
  - Inflammatory bowel disease



## Patient Preferences

- Consider:
- Medication characteristics (route, dose interval, monitoring)
  - Efficacy
  - Safety
  - Cost



## **Presence of Extra Articular Manifestations (EAMs)**



# Presence of Extra-articular manifestations

	Drug class		
	TNFi	IL-17i	JAKi
<b>AxSpA</b>	++	++	++
<b>Uveitis</b>	++	?	?
<b>IBD</b>	++	--	UC++ / CD (+)
<b>Psoriasis</b>	++	+++	+ / ++
<b>Hidradenitis suppurativa</b>	++	(+)	?

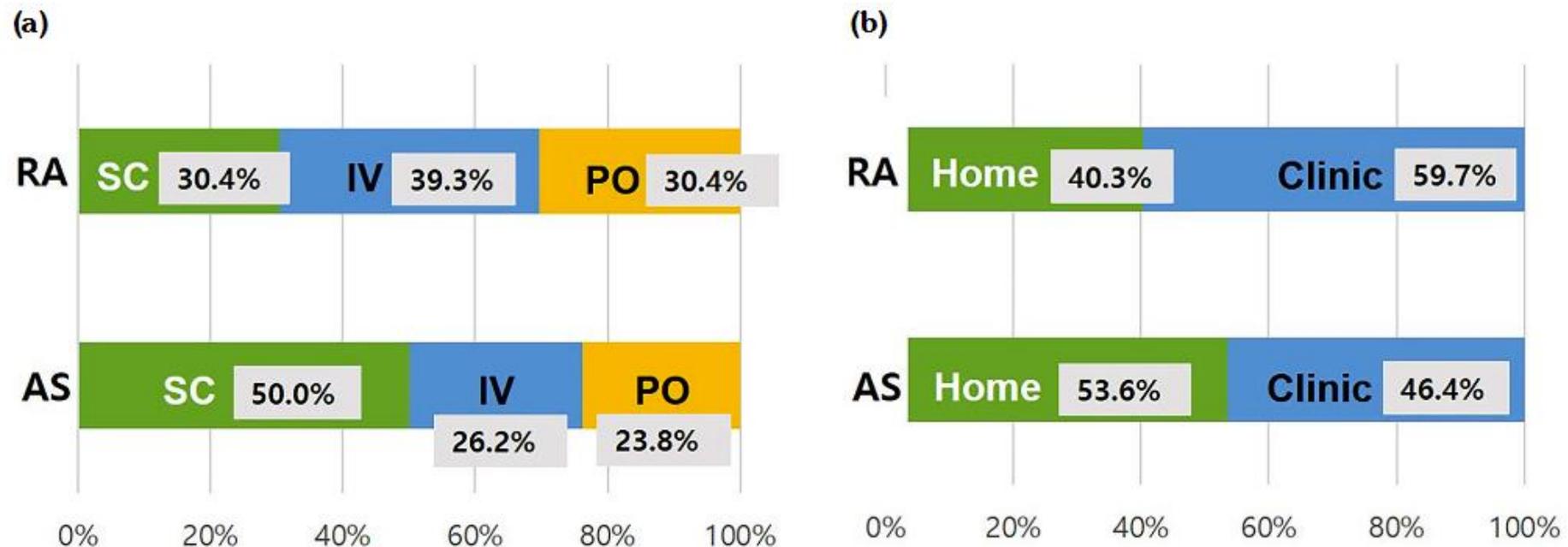


## **Patient Preferences**



# Patient preference: Route of administration

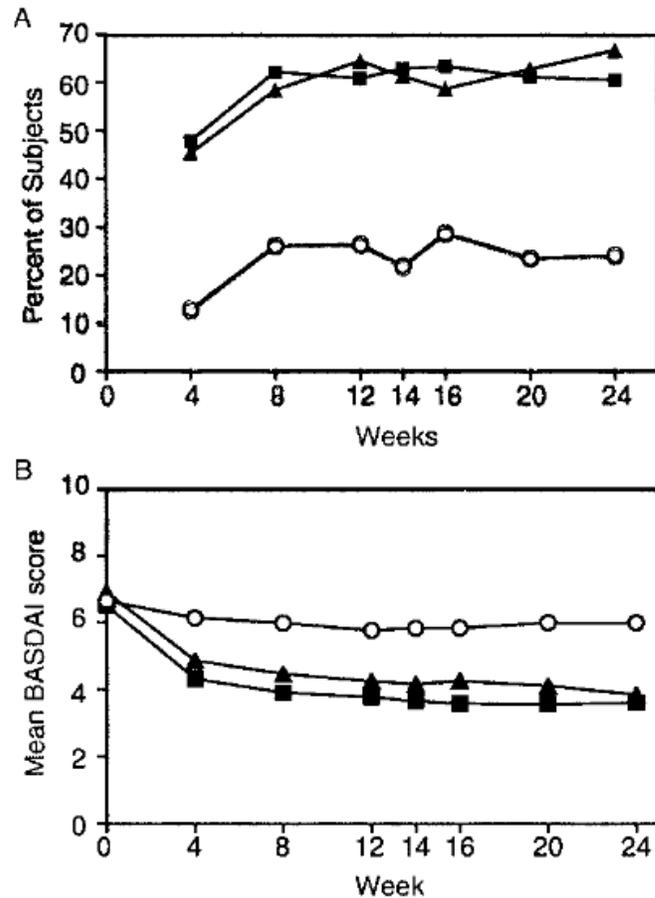
Patient perspectives on biological treatments for inflammatory arthritis: A multi-center study in Korea



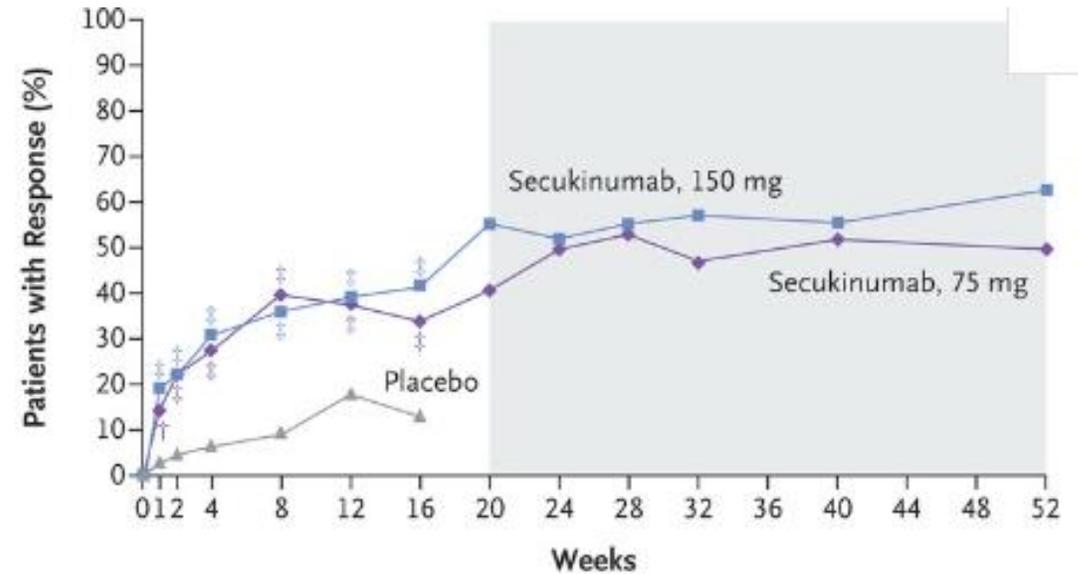


# Patient preference: Speed of action

## GO-RAISE



## MEASURE-1



### No. of Patients

Secukinumab, 150 mg	125	125	125	125	125	120	113	110	116	111	103
Secukinumab, 75 mg	124	124	124	124	124	116	113	111	112	112	108
Placebo	122	122	122	122	122						

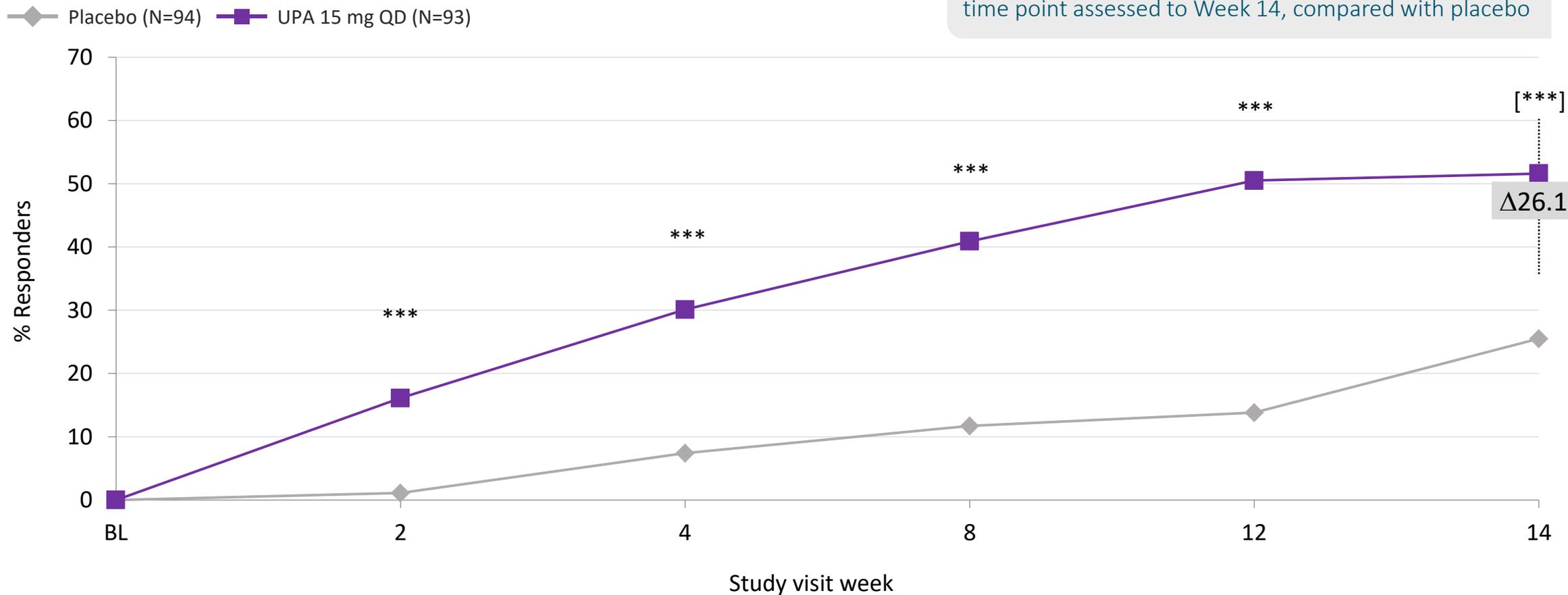


# Upadacitinib in AxSpA: speed of action



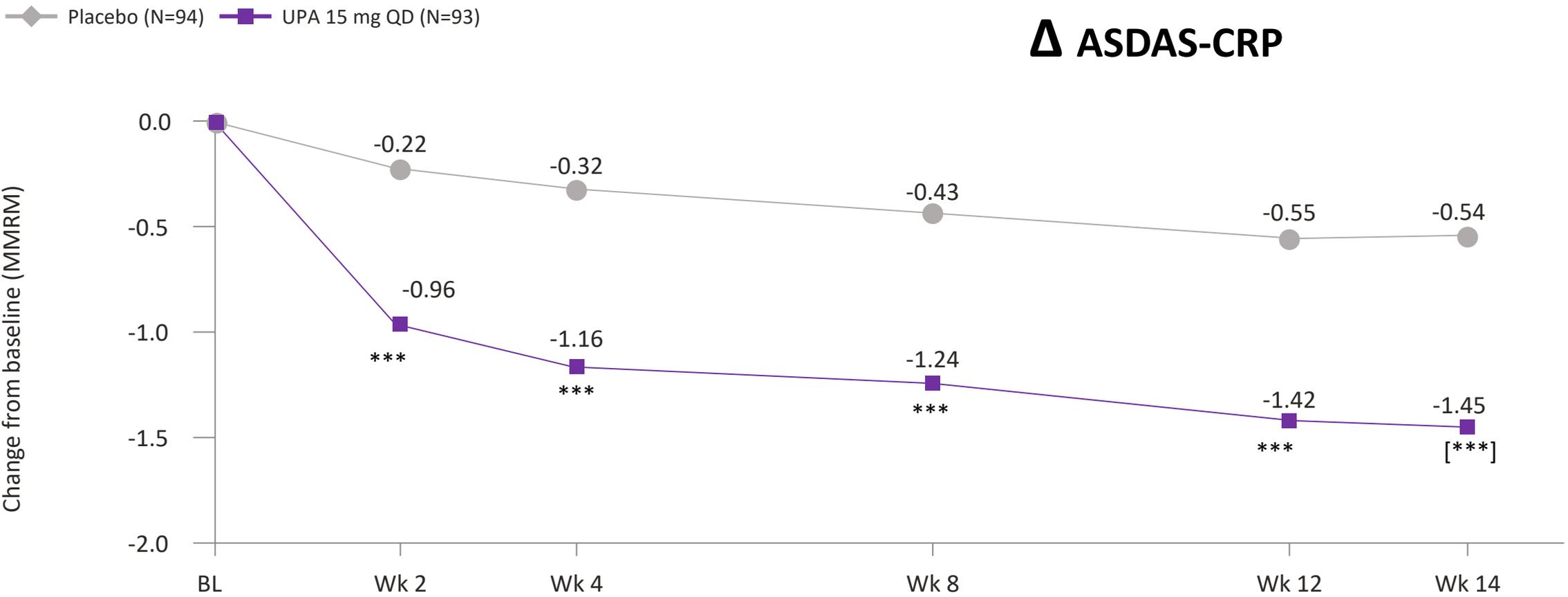
## ASAS 40 response

A greater proportion of patients in the upadacitinib arm achieved ASAS40 from Week 2 onwards, and at every time point assessed to Week 14, compared with placebo





# Upadacitinib in AxSpA: speed of action



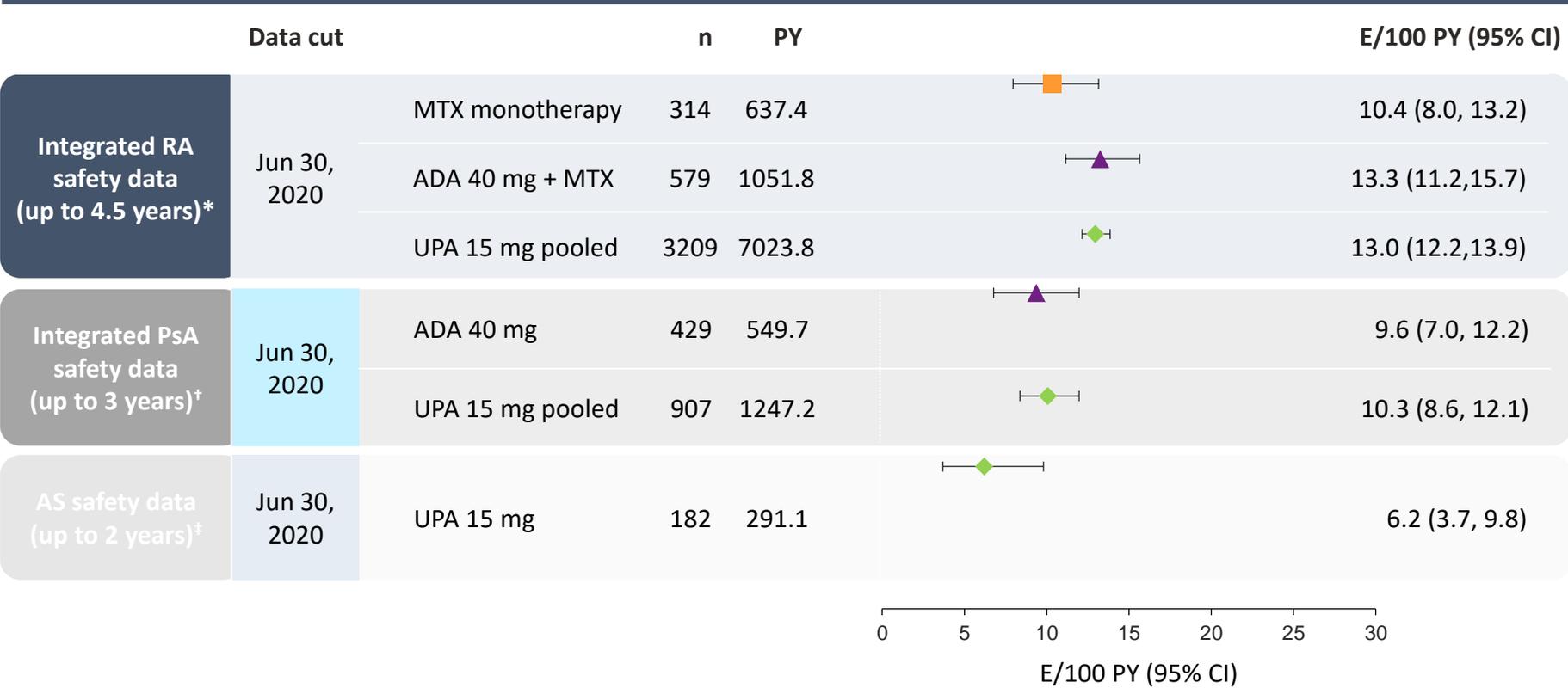
• From Week 2 onwards, a greater improvement in ASDAS was observed for upadacitinib vs PBO for all time points assessed



# Safety



## EAERs of serious AEs



Rates of serious AEs observed with UPA 15 mg were similar to those observed with MTX monotherapy or ADA for patients with RA and PsA

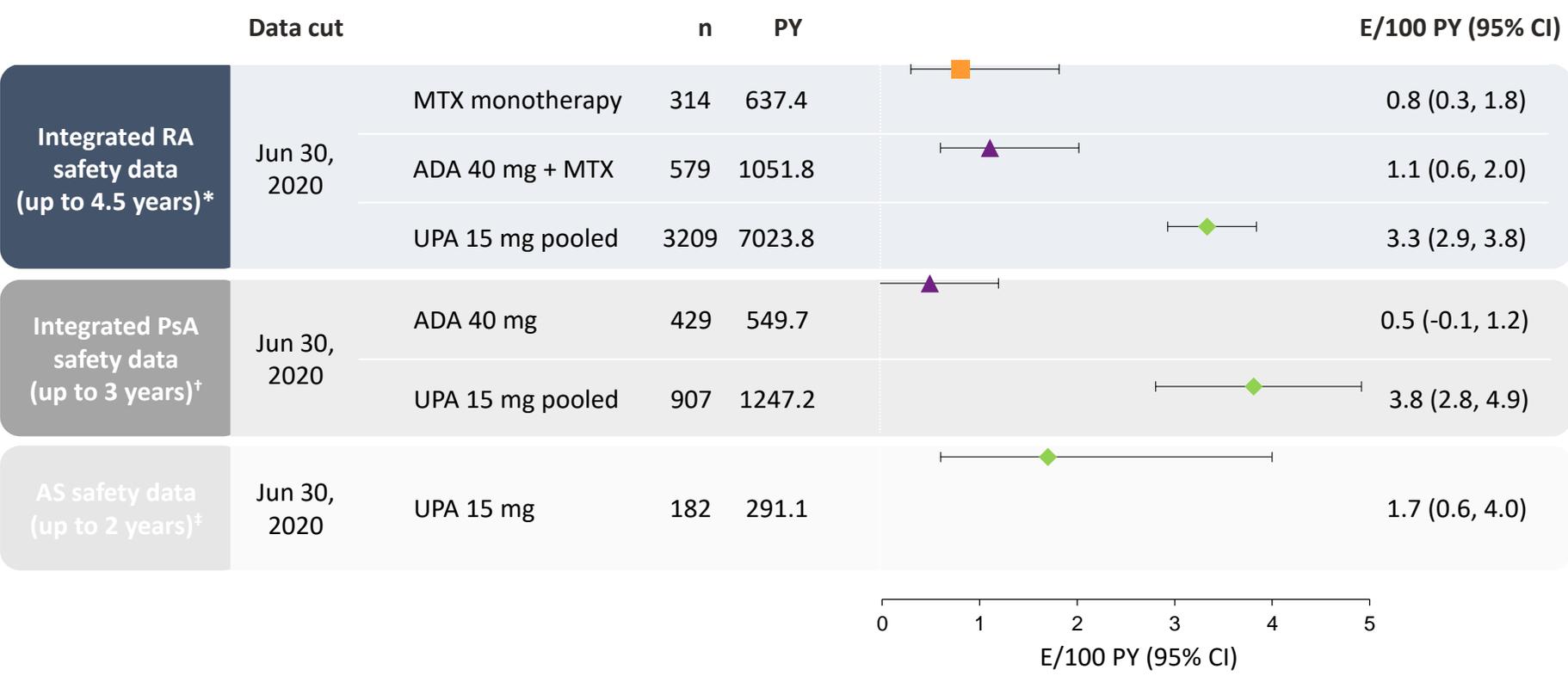
The rate of serious AEs in the SELECT-AXIS 1 trial was low



# Safety



## EAERs of HZ



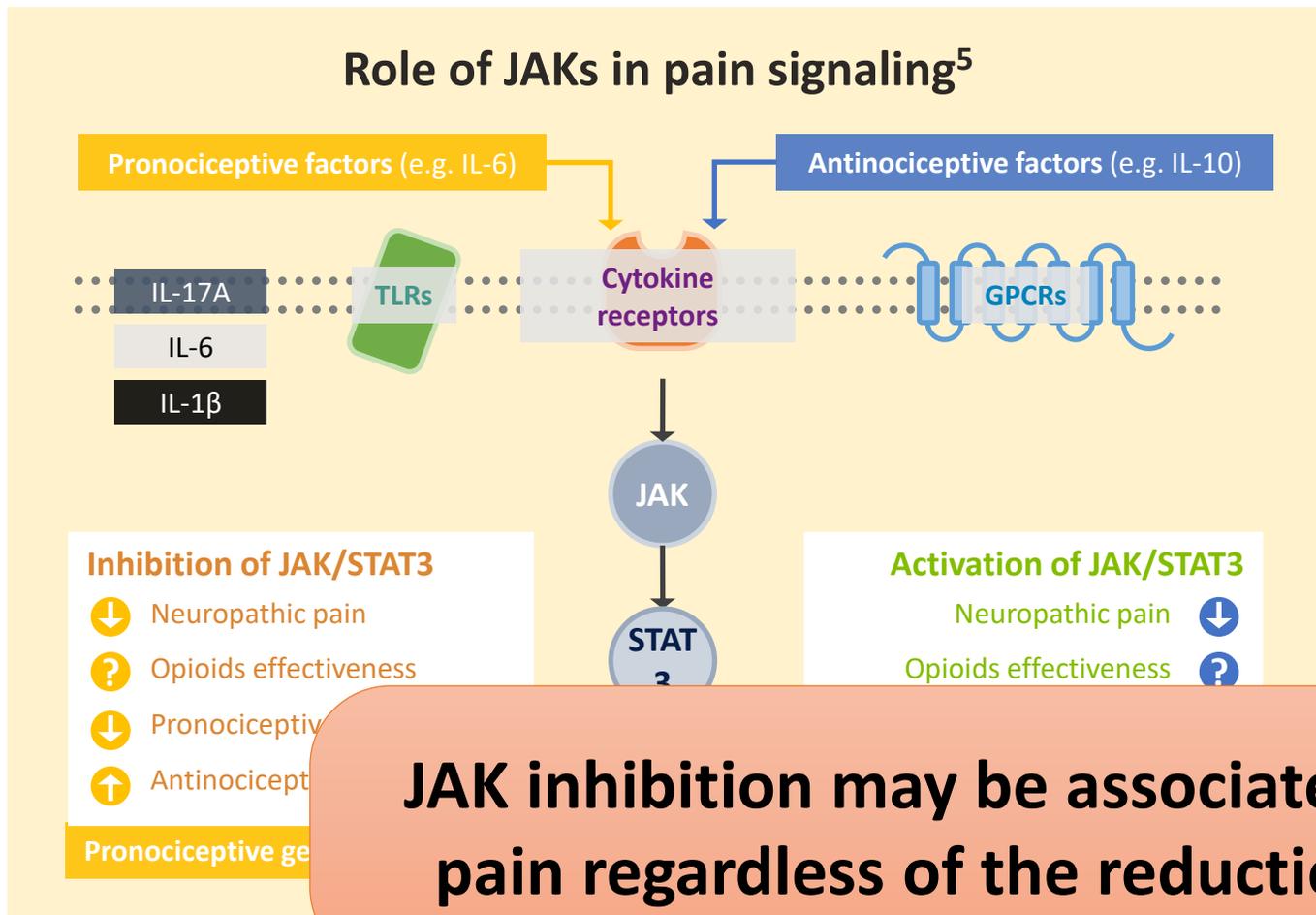
HZ was reported more often with UPA compared to ADA or MTX in RA and PsA

Most HZ events with UPA were non-serious and involved a single dermatome

Ophthalmic involvement with UPA was reported in RA (13 cases) and PsA (1 case), but no cases were reported in AS



# Effect of JAKi on pain



- In rodent models, inhibiting JAK-STAT3 activity reduced expression of IL-6 family cytokines and NF $\kappa$ B, reducing inflammation, allodynia, and joint destruction<sup>1,2</sup>

- JAKis block signaling through multiple cytokines, including IL-6 signaling via JAK1 inhibition<sup>3</sup>

- Rapid pain relief may be reported after JAKi therapy, suggesting a direct effect on pain mechanisms in addition to the reduction in inflammation

# Back to our case

## Θωμάς

- Χωρίς εξωαρθρικές εκδηλώσεις
- Επιθυμεί μια θεραπεία με γρήγορο αποτέλεσμα
- Λόγω επαγγέλματος, είναι δύσκολο να έχει μαζί του ενέσιμες θεραπείες

- Έναρξη **Upadacitinib 15mg OD**

- Τηλέφωνο μία εβδομάδα μετά:  
«Σημαντική βελτίωση»  
BASDAI: 3.4  
BASFI: 2.9

- Κλινικοεργαστηριακός έλεγχος σε ένα μήνα  
BASDAI: 2.9  
BASFI: 2.7  
ASDAS-CRP: 1.8



# Back to our case

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Hb: 13.2 g/dl, MCV: 95 fL, WBC: 5670 (Π 63%, Λ 21%), PLT: 388000

Cr: 0.9 mg/dl UR: 33mg/dL, Glu: 89 mg/dl

AST/ALT: 18/9 U/L (<34/<55), CK: 189 mg/dL

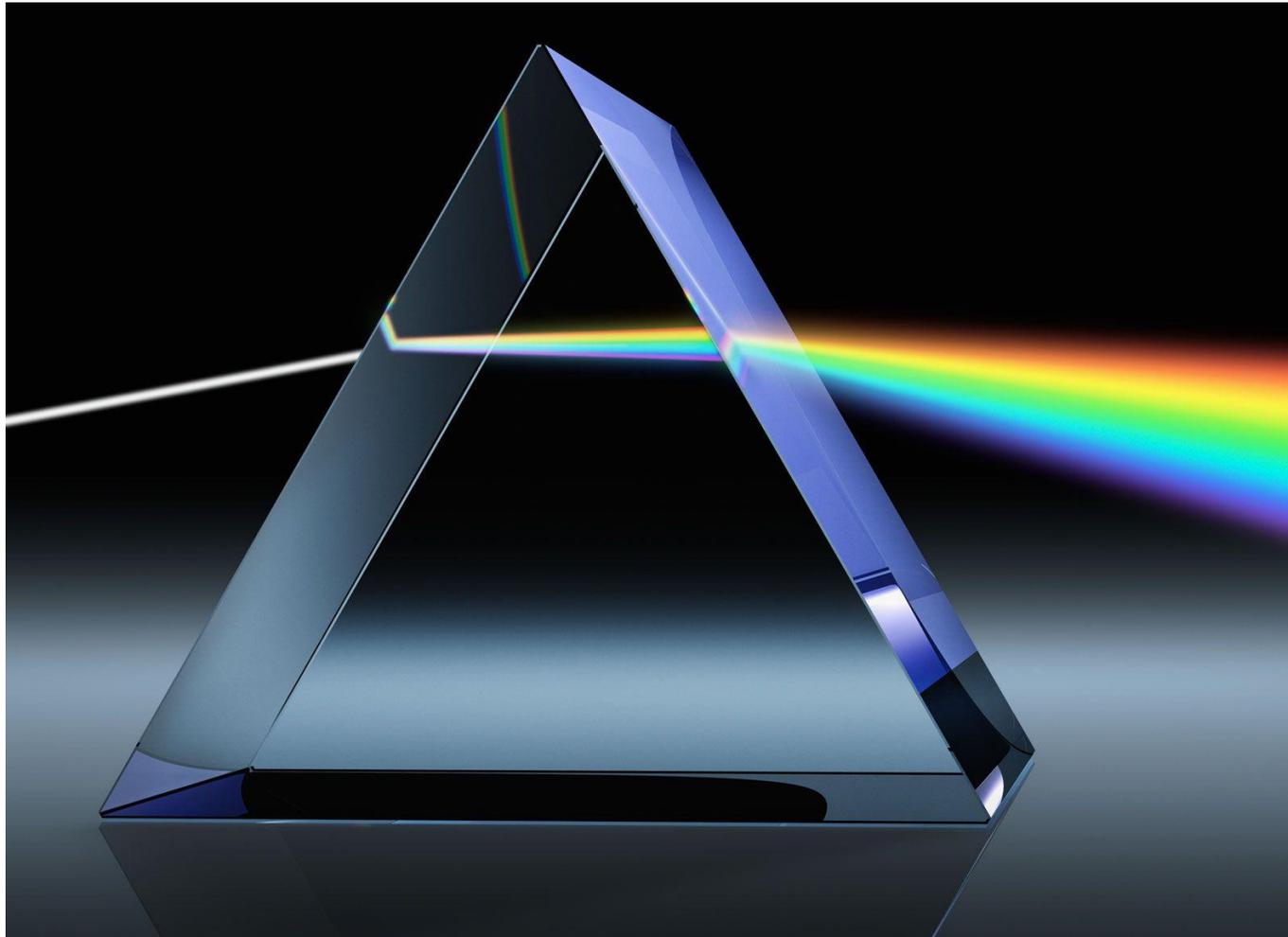
TChol: 201 mg/dL, HDL: 43mg/dL, LDL: 118 mg/dL, TGs: 95mg/dL

CRP: 4.3 (<5 mg/dl), TKE 28 mm/h



# Back to our case

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# Take home messages

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- ✓ **AxSpA: spectrum of diseases with significant but preventable effects over time**
  - ✓ **Treatment in 2022: many different choices**
  - ✓ **Choose based on clinical judgement and patient preference**
  - ✓ **JAK inhibitors: viable solution which can be of help in several cases and different treatment lines**
-

# Thank you for your attention

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