

¿Es relevante para el tratamiento la clasificación del paciente como EspAax radiográfica o no radiográfica?

CLEMENTINA LÓPEZ MEDINA

H. Universitario Reina Sofía de Córdoba, IMIBIC

Universidad de Córdoba

Conflictos de interés

- Consultorías/ponencias: Eli Lilly, Novartis, UCB Pharma, Abbvie, Janssen y MSD.
- Becas investigación: Eli Lilly, UCB Pharma y Abbvie.
- Co-fundadora COBIOMIC BIOSCIENCE S.L.



**¿Cómo se definen EspAax
radiográfica y no radiográfica?**



ASAS Classification Criteria for Axial Spondyloarthritis (SpA)

In patients with ≥ 3 months back pain and age at onset < 45 years

Sacroiliitis on imaging*
plus
 ≥ 1 SpA feature

OR

HLA-B27
plus
 ≥ 2 other SpA features

- *Sacroiliitis on imaging
- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
 - definite radiographic sacroiliitis according to the modified New York criteria

SpA features:

- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

n=649 patients with back pain;

Overall

Sensitivity: 82.9%, Specificity: 84.4%

Imaging arm alone

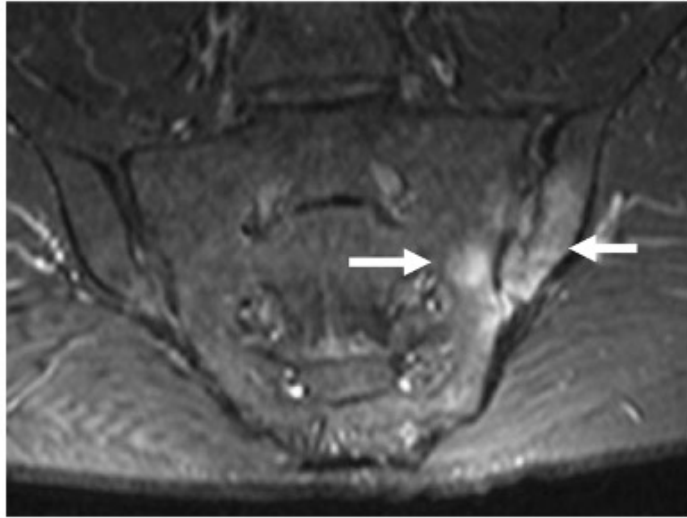
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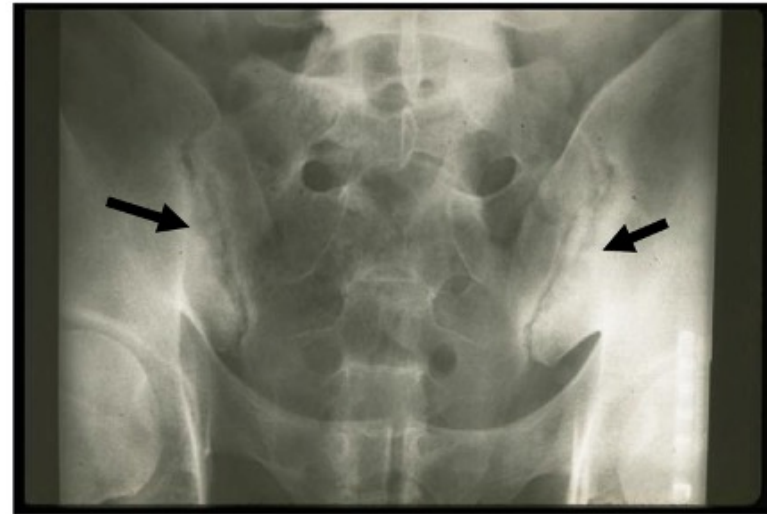
Sensitivity: 56.6%, Specificity: 83.3%



Sacroiliitis by MRI and X-ray in Patients with Axial Spondyloarthritis



Active inflammatory sacroiliitis
without bony changes

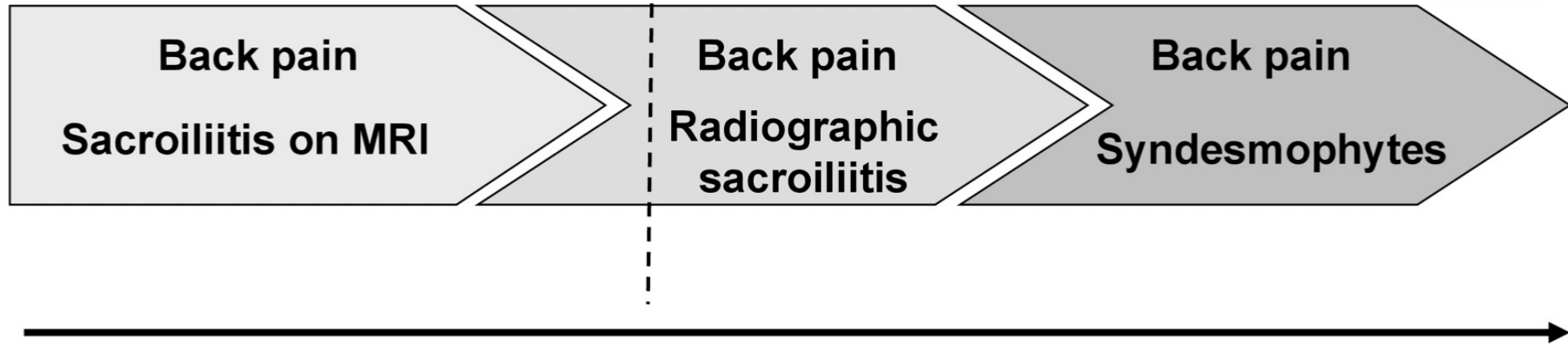


Sacroiliitis with bony
changes (grade II)

Non-radiographic stage

Radiographic stage

Modified New York Criteria 1984



Time (years)

Sacroiliitis Grade 2 Right, Grade 1 Left



		Central reader 1	
		Positive	Negative
Local reader 1	Positive	99	84
	Negative	55	450
	Agreement	58.8%	86.6%

Kappa: 0.46 (95%CI 0.38 – 0.53)

		Central reader 2	
		Positive	Negative
Central reader 1	Positive	96	58
	Negative	50	484
	Agreement	64%	90%

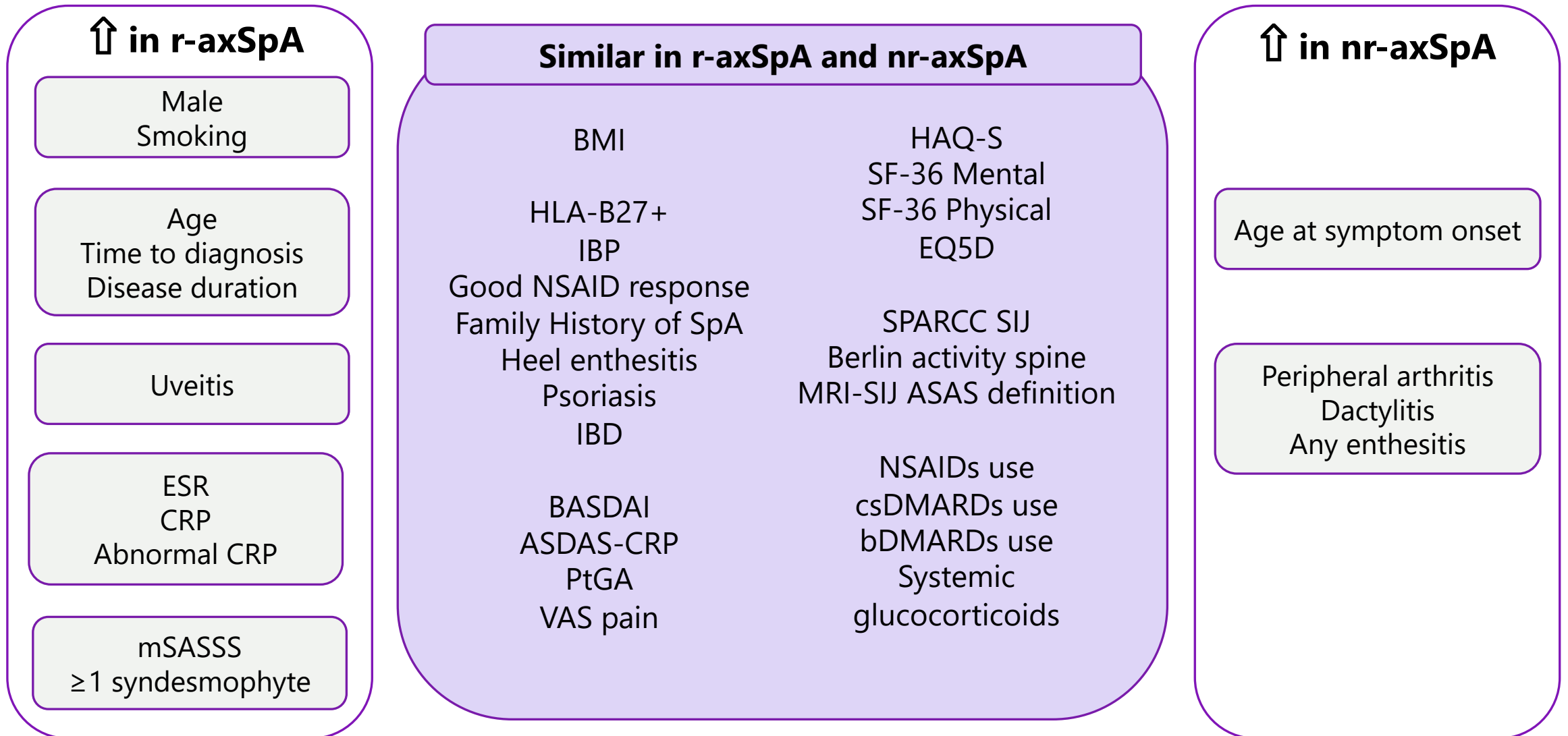
Kappa: 0.54 (95%CI 0.46 – 0.62)



**¿Es relevante su diferenciación
para el diagnóstico y pronóstico?**

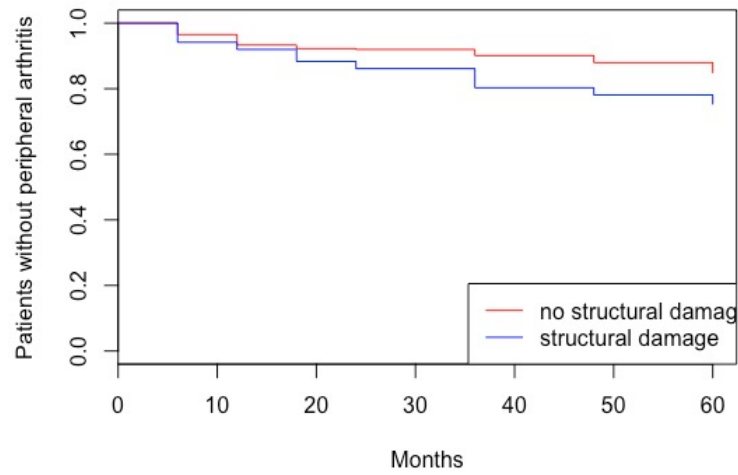


Similar characteristics and burden of r-axSpA and nr-axSpA

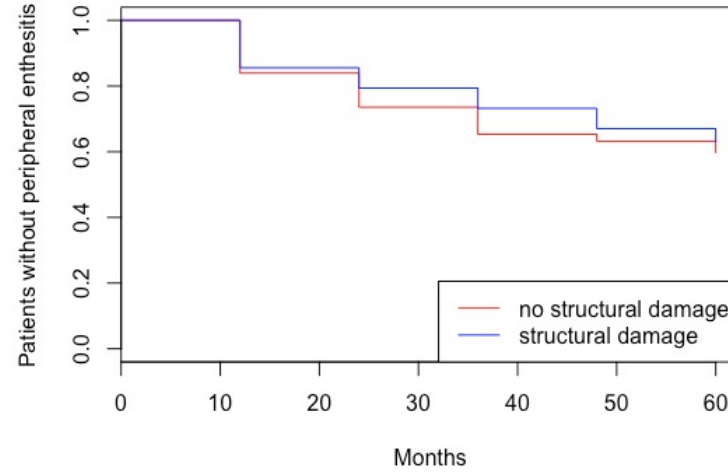


r-axSpA vs nr-axSpA over time

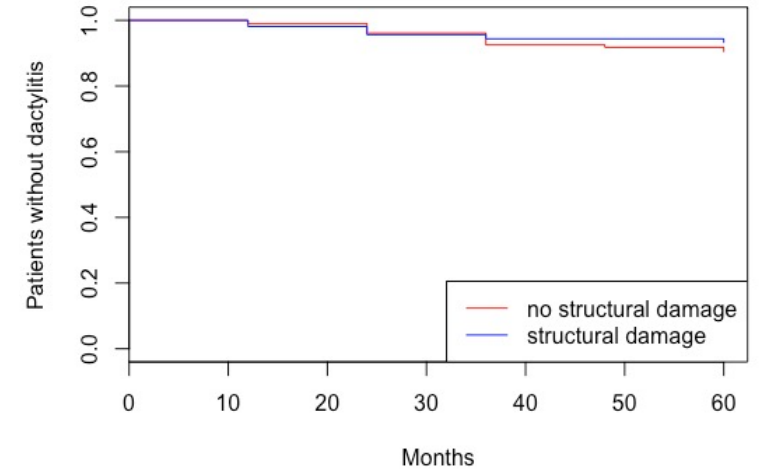
Incidence of peripheral arthritis



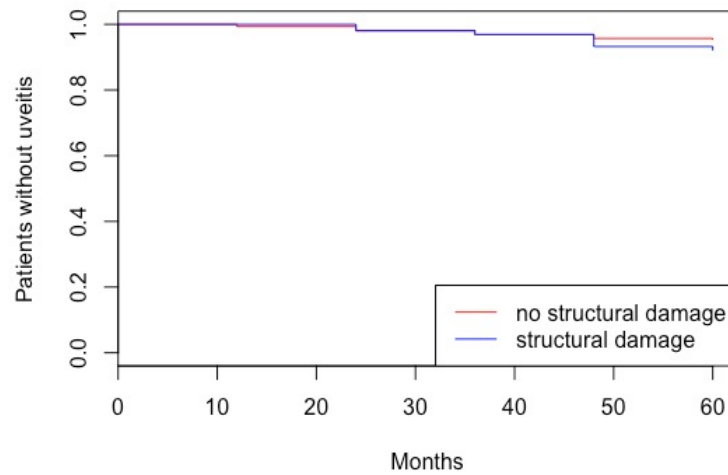
Incidence of peripheral enthesitis



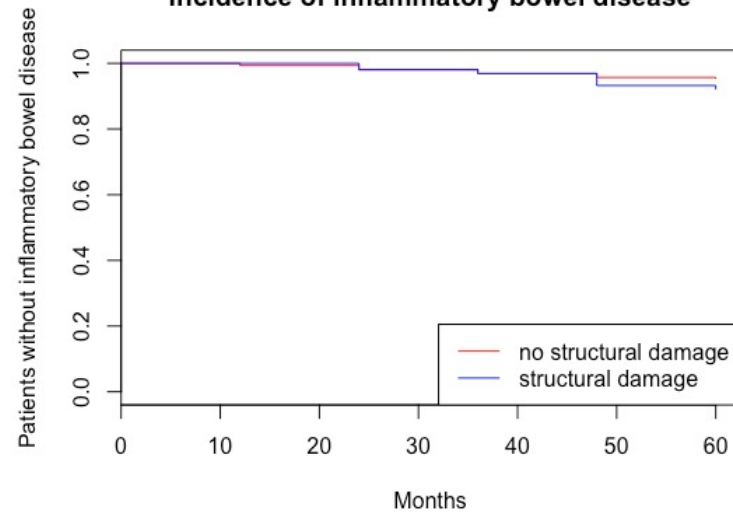
Incidence of dactylitis



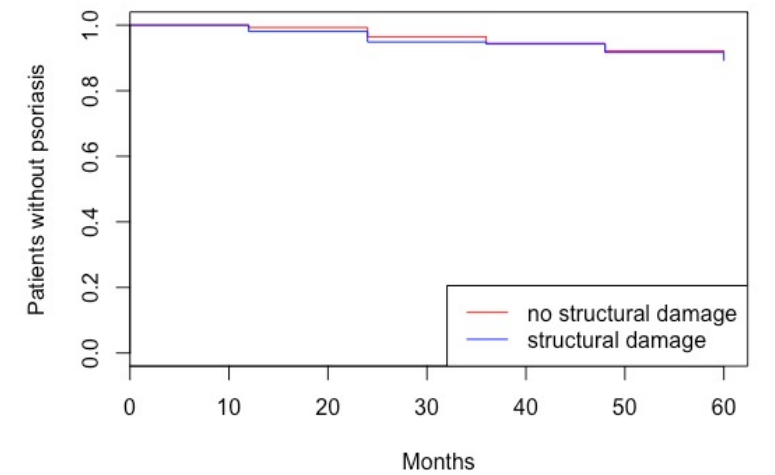
Incidence of uveitis



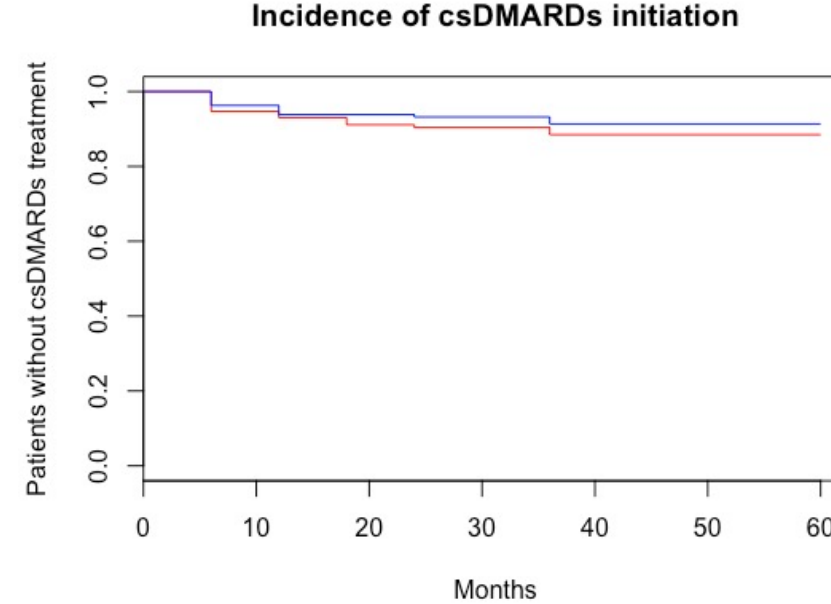
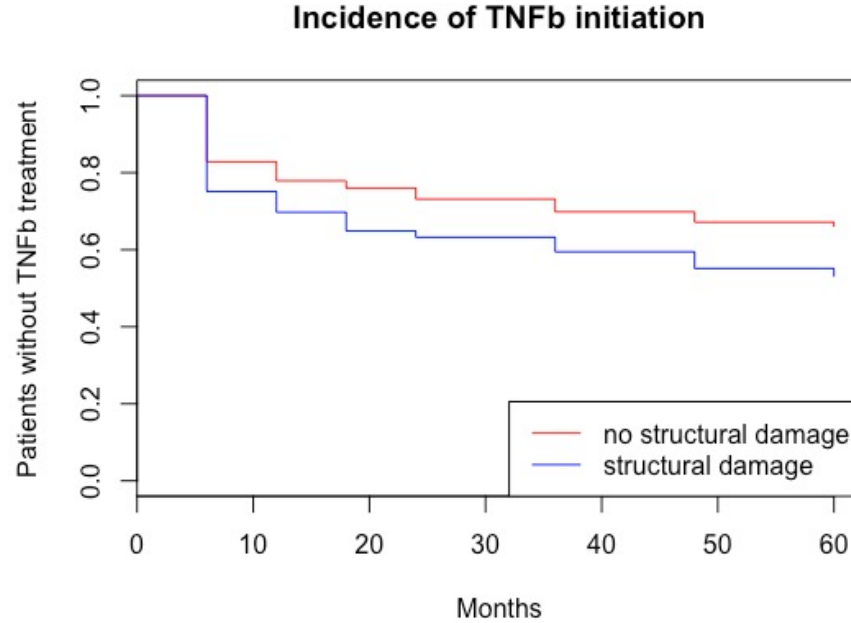
Incidence of inflammatory bowel disease



Incidence of psoriasis



r-axSpA vs nr-axSpA over time



	r-axSpA N = 185 Mean (SD)	nr-axSpA N = 484 Mean (SD)	Crude MM	MM adjusted by baseline value	MM adjusted by baseline value, age, sex and bDMARD
BASDAI	30.9 (20.9)	38.9 (21.5)	<0.001	<0.001	0.130
BASFI	20.7 (20.3)	26.1 (22.5)	0.002	0.004	0.236
SF-36 MCS	44.7 (11.2)	42.8 (11.3)	0.016	0.148	0.662
SF-36 PCS	44.1 (8.59)	41.5 (9.6)	<0.001	0.003	0.214
Days of sick leave	14.9 (45.5)	24.3 (65.9)	0.009	0.082	0.424

MM: Mixed model



**¿Es relevante su diferenciación
para el tratamiento?**



	axSpA	
	r-axSpA	nr-axSpA
Infliximab	Green	Red
Adalimumab	Green	Green
Etanercept	Green	Green
Golimumab	Green	Green
Certolizumab	Green	Green
Secukinumab	Green	Green
Ixekizumab	Green	Green
Upadacitinib	Green	Green
Tofacitinib	Green	Red

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Ixekizumab	Green	Green
Upadacitinib	Green	Green
Tofacitinib	Green	Red



“Making a diagnosis of axSpA implies pattern recognition by an expert rheumatologist rather than applying classification criteria for axSpA”

“The approval of TNF inhibitors for the indication of nr-axSpA according to the existing ASAS definition will lead to an uncontrollable explosion of TNF inhibitor usage in the US.”

“FM patients will too easily be classified as having nonradiographic axSpA”

Criteria de clasificación ≠ Criterios diagnósticos

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- family history for SpA
- HLA-B27
- elevated CRP

Sensibilidad: % verdaderos positivos
DIAGNÓSTICO

Especificidad: % verdaderos negativos
CLASIFICACIÓN

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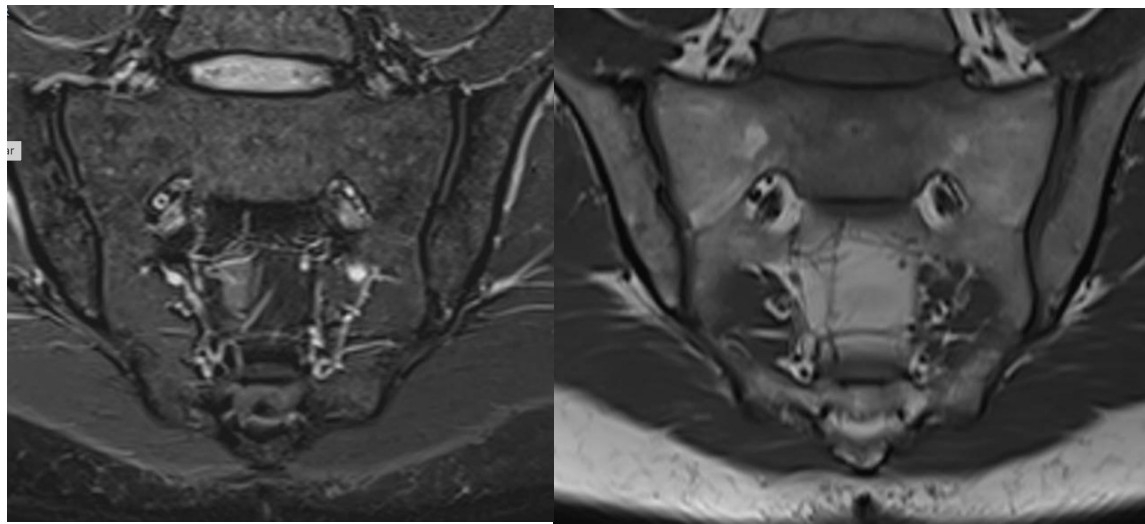
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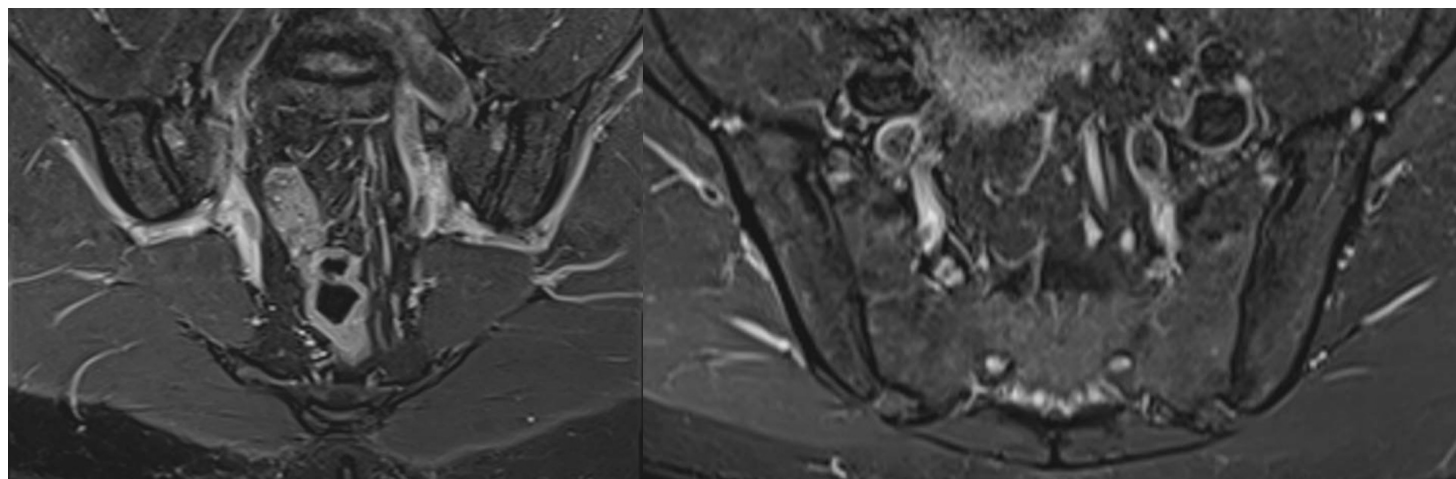
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“MRI findings are too often false-positive”



**Varón de 45 años.
Dolor en nalgas de ritmo mixto.
HLA-B27-, PCR <5 mg/L**



Imágenes del HU. Reina Sofía

Cohorte ASAS

Probabilidad pre-test de
axSpA = 60%



Consulta Reumatología

Probabilidad pre-test de
axSpA = 20%



Consulta A. Primaria

Probabilidad pre-test de
axSpA = 5%



1 lesión en 2 cortes consecutivos o ≥ 2 lesiones en 1 corte



Especificidad muy alta



Especificidad
media/alta



Especificidad muy
baja

*“clinical trial design in the US should focus primarily on selecting patients who **meet the imaging component** of the ASAS criteria, subgrouped into those with and those without elevated CRP levels, as well as an arm consisting of **patients with elevated CRP levels alone**.*

Positive MRI and/or elevated CRP

Etanercept vs. Sulfasalazine

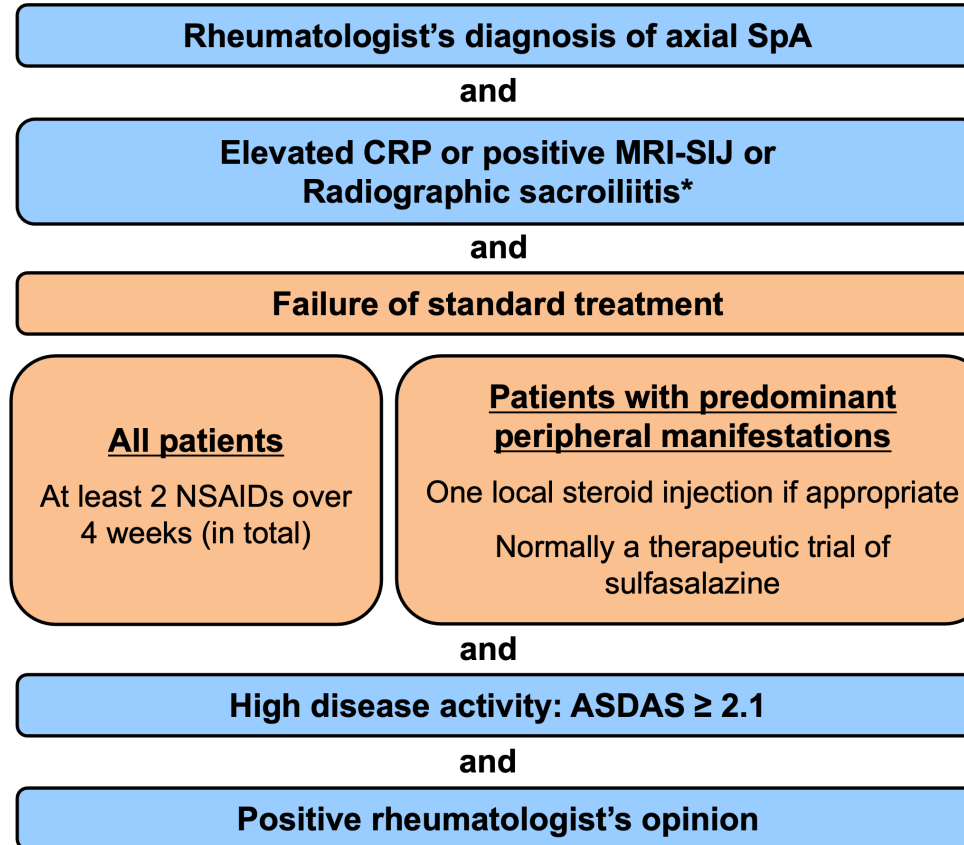
Follow-up	1 year Patients (n) = 40			3 years Patients (n) = 61		
	r-axSpA	nr-axSpA	p-value	r-axSpA	nr-axSpA	p-value
ASAS partial remission	40%	60%	n.s.	26%	33%	NA
ASDAS major improvement	30%	25%	n.s.	26%	37%	NA
ASDAS				1.6 (1.0)	1.5 (1.0)	n.s.
BASDAI				2.7 (2.5)	2.4 (2.3)	n.s.

Certolizumab vs. Placebo									
Follow-up	6 months Patients (n) = 325					2 years Patients (n) = 325		4 years Patients (n) = 218	
	200 mg Q2W		400mg Q2W			Any dose		Any dose	
	r-axSpA	nr-axSpA	r-axSpA	nr-axSpA	P-value	r-axSpA	nr-axSpa	r-axSpA	nr-axSpA
ASAS40	47.7%	56.6%	58.9%	45.1%	n.s.	50.4%	50.5%	68.0%	68.3%
ASDAS major improvement						51.2%	47.4%		
ASDAS inactive disease						30.6%	38.1%	28.8%	35.0%

		Secukinumab vs. Placebo		Ixekizumab vs. Placebo	
Follow-up	4 months		4 months		
	r-axSpA	nr-axSpA	r-axSpA	nr-axSpA	
ASAS40	40%	41%	52%	40%	

Upadacitinib vs. Placebo		
Follow-up	3 months	
	r-axSpA	nr-axSpA
ASAS20	65%	66.7%
ASAS40	52%	45%

ASAS-EULAR recommendations for the treatment of patients with axial SpA with b/tsDMARDs.



* Radiographic sacroiliitis is currently mandatory for infliximab and JAKi



Thank you

