Comparison of Established and New, Preliminarily Proposed ASAS Cut-Offs for Inflammatory MRI Lesions in the Sacroiliac Joints in Axial Spondyloarthritis and Implications for Recruitment in Clinical Studies

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Objective

To investigate the effect of applying a recently proposed Assessment of SpondyloArthritis international Society positive MRI definition on outcomes in patients with axial spondyloarthritis.

Background

- In an MRI scan of the sacroiliac joint (SIJ), inflammatory and structural lesions typical of axial spondyloarthritis (axSpA) are scored using 48 data point locations (**Figure 1**).
- The Assessment of SpondyloArthritis international Society (ASAS) has recently proposed a preliminary, more stringent, data-driven definition requiring the presence of bone marrow edema (BME) in either four or more quadrants in the same slice, or in the same quadrant in three consecutive slices (**Figure 1**).[1]

Methods

- C-OPTIMISE (NCT02505542) enrolled 736 patients with active axSpA who received 400 mg certolizumab pegol (CZP) at Weeks 0, 2, and 4, then 200 mg CZP every two weeks to Week 48.[2] Baseline MRI SIJ scans were scored by two central readers.
- We assessed clinical outcomes of patients receiving CZP in C-OPTIMISE who were MRI-positive (MRI+) or negative (MRI–) according to both the existing and newly proposed definitions, as well as those who were MRI+ by the existing definition but MRI– by the newly proposed definition (discordant group).
- Proportions of patients achieving ASAS ≥40% improvement (ASAS40) response are reported using non-responder imputation. BASDAI change from baseline and ASDAS disease states are reported using last observation carried forward.

Results

MRI Classification

- Baseline MRI data were available for 657/736 (89.3%) patients, 358/657 (54.5%) of whom had radiographic (r)-axSpA and 299/657 (45.5%) non-radiographic (nr)-axSpA.
- 386/657 patients (58.8%) were classified as MRI+ according to the existing definition compared with 333/657 patients (50.7%) using the newly proposed definition; the discordant group comprised 35/299 patients (11.7%) with nr-axSpA and 18/358 (5.0%) with r-axSpA (**Table 1**).

Clinical Outcomes

- A numerically higher proportion of patients fulfilling the newly proposed MRI+ definition achieved ASAS40 at Week 48 versus those fulfilling the existing MRI+ definition (**Figure 2**, **Table 2**).
- Similar results were observed for mean BASDAI, with patients in the discordant group responding similarly to those originally classified as MRI– (**Figure 2**, **Table 2**).
- At Week 48, a lower proportion of patients in the discordant group achieved ASDAS inactive disease versus those classified as MRI+ according to either the existing or newly proposed definitions; differences between subgroups were more notable among patients with nr-axSpA than with r-axSpA (**Figure 3**, **Table 2**).

Conclusions

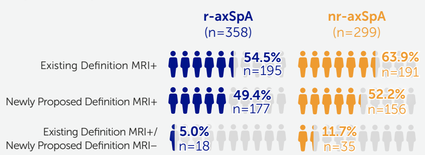
In this post hoc analysis of the C-OPTIMISE study, 11.7% fewer patients with nr-axSpA would have been classified as MRI+ at baseline using the preliminary proposed definition versus the existing definition.

Applying the preliminary definition could lead to fewer false-positive patients being recruited and improve the accuracy with which MRI+ patients are identified; the preliminary proposed definition should be applied in future studies to confirm this finding.

Summary

We applied both the existing and newly proposed ASAS definitions for MRI-positive axSpA to the dataset of the C-OPTIMISE trial

Proportion of patients classified as MRI+:



Proportion of patients achieving ASDAS low or inactive disease (ASDAS <2.1) at Week 48:

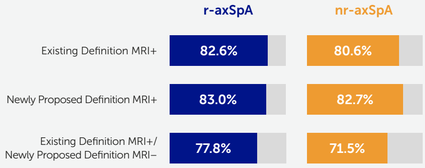
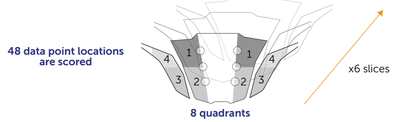


Figure 1 Quantitative component of ASAS definitions of a positive MRI for inflammatory and structural lesions typical of axSpA



Existing MRI+ Definition[3,4]

BME in either:
- At least **two** quadrants in the same slice

or
- The same quadrant in **two** consecutive slices

Newly Proposed MRI+ Definition[1]

BME in either:
- At least **four** quadrants in the same slice

or
- The same quadrant in **three** consecutive slices

An SIJ MRI comprises six slices, each with two sides containing four quadrants (1. upper sacrum; 2. lower sacrum; 3. lower ilium; 4. upper ilium) giving a total of 48 data point locations. Scoring for identifying active lesions is binary (0 or 1 depending on presence or absence of bone marrow oedema).

Table 1 Baseline demographics and disease characteristics

Baseline characteristic, mean (SD), unless otherwise stated	Existing Definition MRI+ n=386		Newly Proposed Definition MRI+ n=333		Discordant Group n=53		Existing Definition MRI– n=271		Newly Proposed Definition MRI– n=324	
	r-axSpA n=195	nr-axSpA n=191	r-axSpA n=177	nr-axSpA n=156	r-axSpA n=18	nr-axSpA n=35	r-axSpA n=163	nr-axSpA n=108	r-axSpA n=181	nr-axSpA n=143
Age, years, mean (SD)	32.7 (6.8)	31.9 (7.0)	32.7 (6.9)	31.1 (6.5)	32.4 (5.5)	35.4 (8.0)	34.6 (6.8)	32.7 (7.2)	34.4 (6.7)	33.3 (7.4)
Sex, male, n (%)	154 (79.0)	123 (64.4)	138 (78.0)	109 (69.9)	16 (88.9)	14 (40.0)	130 (79.8)	56 (51.9)	146 (80.7)	70 (49.0)
CRP, mg/L, mean (SD)	17.3 (17.7)	11.0 (18.5)	17.1 (17.1)	11.5 (19.0)	19.6 (23.3)	8.6 (15.9)	16.3 (20.3)	12.4 (17.3)	16.6 (20.6)	11.5 (17.0)
HLA-B27, positive, n (%)	169 (86.7)	148 (77.5)	153 (86.4)	127 (81.4)	16 (88.9)	21 (60.0)	147 (90.2)	83 (76.9)	163 (90.1)	104 (72.7)
Symptom duration, years, mean (SD)	3.5 (2.1)	2.9 (1.6)	3.6 (2.2)	2.9 (1.6)	3.2 (1.3)	3.2 (1.8)	3.7 (2.6)	3.0 (1.8)	3.7 (2.5)	3.0 (1.8)
BASDAI, mean (SD)	6.8 (1.4)	6.6 (1.4)	6.8 (1.4)	6.5 (1.4)	6.2 (1.7)	6.9 (1.4)	6.7 (1.4)	6.8 (1.3)	6.6 (1.4)	6.8 (1.3)
ASDAS disease state, n (%)										
ID	0	0	0	0	0	0	0	0	0	0
LDA	2 (1.0)	4 (2.1)	1 (0.6)	4 (2.6)	1 (5.6)	0	3 (1.8)	1 (0.9)	4 (2.2)	1 (0.7)
HDA	52 (26.7)	95 (49.7)	45 (25.4)	78 (50.0)	7 (38.9)	17 (48.6)	67 (41.1)	46 (42.6)	74 (40.9)	63 (44.1)
vHDA	141 (72.3)	92 (48.2)	131 (74.0)	74 (47.4)	10 (55.6)	18 (51.4)	93 (57.1)	61 (56.5)	103 (56.9)	79 (55.2)

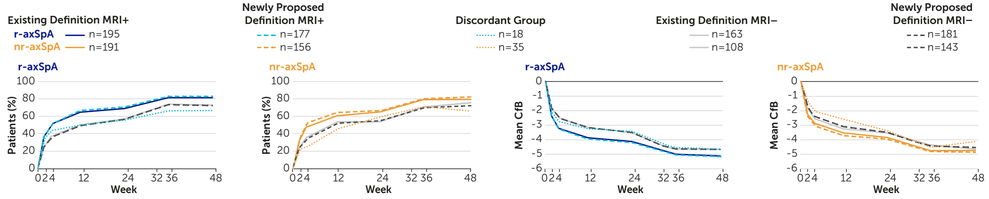
ID: ASDAS <1.3; LDA: ASDAS ≥1.3–<2.1; HDA: ASDAS ≥2.1–≤3.5; vHDA: ASDAS >3.5.

Table 2 Clinical outcomes at Week 48

	Existing Definition MRI+ n=386		Newly Proposed Definition MRI+ n=333		Discordant Group n=53		Existing Definition MRI– n=271		Newly Proposed Definition MRI– n=324	
	r-axSpA n=195	nr-axSpA n=191	r-axSpA n=177	nr-axSpA n=156	r-axSpA n=18	nr-axSpA n=35	r-axSpA n=163	nr-axSpA n=108	r-axSpA n=181	nr-axSpA n=143
ASAS40 [NRI], n (%)										
Responder	158 (81.0)	151 (79.1)	146 (82.5)	128 (82.1)	12 (66.7)	23 (65.7)	119 (73.0)	81 (75.0)	131 (72.4)	104 (72.7)
BASDAI CfB [LOCF], mean (SD)	−5.1 (2.3)	−4.7 (2.5)	−5.2 (2.2)	−4.9 (2.4)	−4.7 (2.8)	−4.2 (2.8)	−4.7 (2.5)	−4.7 (2.4)	−4.7 (2.5)	−4.5 (2.5)
ASDAS disease state [LOCF], n (%)										
ID	118 (60.5)	112 (58.6)	108 (61.0)	97 (62.2)	10 (55.6)	15 (42.9)	87 (53.4)	55 (50.9)	97 (53.6)	70 (49.0)
LDA	43 (22.1)	42 (22.0)	39 (22.0)	32 (20.5)	4 (22.2)	10 (28.6)	32 (19.6)	25 (23.1)	36 (19.9)	35 (24.5)
HDA	22 (11.3)	28 (14.7)	19 (10.7)	23 (14.7)	3 (16.7)	5 (14.3)	39 (23.9)	26 (24.1)	42 (23.2)	31 (21.7)
vHDA	12 (6.2)	9 (4.7)	11 (6.2)	4 (2.6)	1 (5.6)	5 (14.3)	5 (3.1)	2 (1.9)	6 (3.3)	7 (4.9)

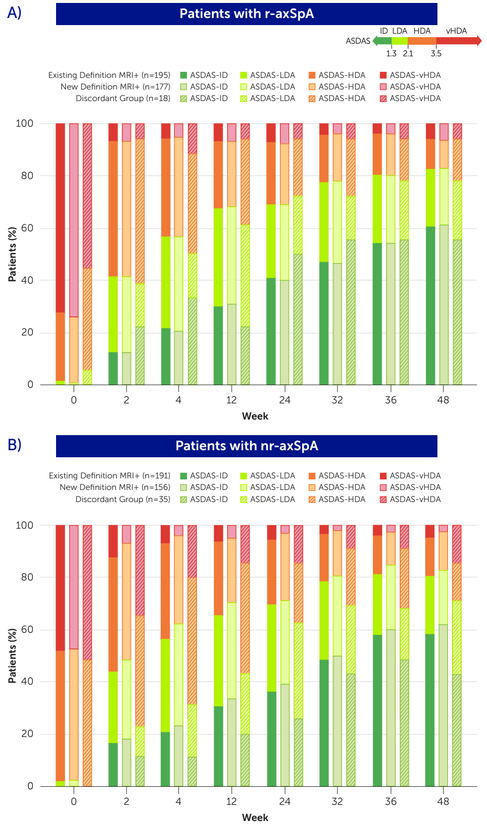
ID: ASDAS <1.3; LDA: ASDAS ≥1.3–<2.1; HDA: ASDAS ≥2.1–≤3.5; vHDA: ASDAS >3.5.

Figure 2 Clinical outcomes to Week 48 stratified by existing and newly proposed ASAS SIJ MRI definitions



Missing ASAS40 data imputed using NRI; BASDAI missing data imputed using LOCF. Week 48 values are reported in Table 2.

Figure 3 ASDAS disease states stratified by both existing, and newly proposed, ASAS SIJ MRI definitions



Missing data imputed using LOCF. Week 48 values are reported in Table 2.

ASAS: Assessment of SpondyloArthritis international Society; **ASAS40:** ASAS ≥40% improvement; **ASDAS:** Ankylosing Spondylitis Disease Activity Score; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BME:** bone marrow edema; **CfB:** change from baseline; **CRP:** C-reactive protein; **CZP:** certolizumab pegol; **HDA:** high disease activity; **HLA-B27:** human leukocyte antigen B27; **ID:** inactive disease; **LDA:** low disease activity; **LOCF:** last observation carried forward; **MRI:** magnetic resonance imaging; **NRI:** non-responder imputation; **nr-axSpA:** non-radiographic axial spondyloarthritis; **r-axSpA:** radiographic axial spondyloarthritis; **SD:** standard deviation; **SIJ:** sacroiliac joint; **vHDA:** very high disease activity.

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