Certolizumab Pegol Efficacy in Patients with Non-Radiographic Axial Spondyloarthritis Stratified by Baseline MRI and C-Reactive Protein Status

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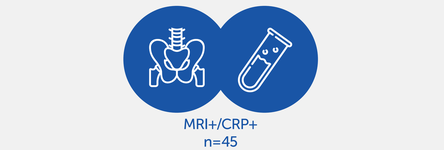
RheumNow Live 2021 | Forth Worth, TX | March 20–21, 2021

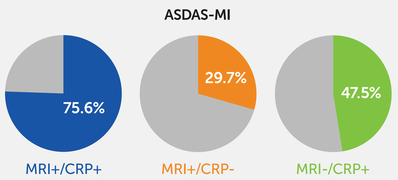
Summary

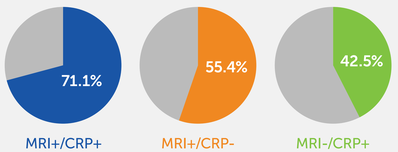
Does baseline MRI and C-reactive protein (CRP) status affect certolizumab pegol (CZP) response in patients with non-radiographic axial spondyloarthritis (nr-axSpA)?

CZP-treated patients were stratified by MRI/CRP status...



52 weeks' CZP treatment





Clinically relevant responses were observed in nr-axSpA patients treated with CZP with either MRI and/or CRP positivity.

Objective

This analysis from the phase 3 C-axSpAnd study aimed to evaluate whether the response to CZP, plus non-biologic background medication, in nr-axSpA is impacted by baseline MRI and CRP status.

Background

- nr-axSpA is distinguished from radiographic axSpA (ankylosing spondylitis) by the absence of detectable radiographic damage in the spine/sacroiliac joints. Patients with nr-axSpA present with objective signs of inflammation, such as sacroiliitis on MRI or elevated levels of CRP.[1]
- Herein we assess the impact of baseline MRI/CRP status on response to CZP, an Fc-free, PEGylated tumor necrosis factor inhibitor which has previously demonstrated efficacy and safety in patients with nr-axSpA.[2,3]

Methods

Study Design

- C-axSpAnd (NCT02552212) was a 3-year, phase 3, multicenter study including a 52-week double-blind, placebo (PBO)-controlled period; the full study design is reported elsewhere.[2]
- Eligible patients had a diagnosis of active nr-axSpA and objective signs of inflammation (defined as active sacroiliitis on MRI [MRI+] and/or CRP above the upper limit of normal (ULN; ≥10 mg/L [CRP+]).[2]
- Patients were randomized 1:1 to PBO or CZP (400 mg at Weeks 0, 2, and 4, then 200 mg every 2 weeks) for 52 weeks, which they received in addition to non-biologic background medication.[2]

Analysis

- Patients were stratified into prespecified subgroups based on MRI and CRP status. Responses evaluated: ASDAS-MI, ASAS40, and BASDAI.
- Comparisons between subgroups were descriptive only. P values for PBO vs CZP for subgroups were nominal. Missing values were imputed using non-responder imputation (ASDAS-MI and ASAS40) or double-blind last observation carried forward (BASDAI).

Results

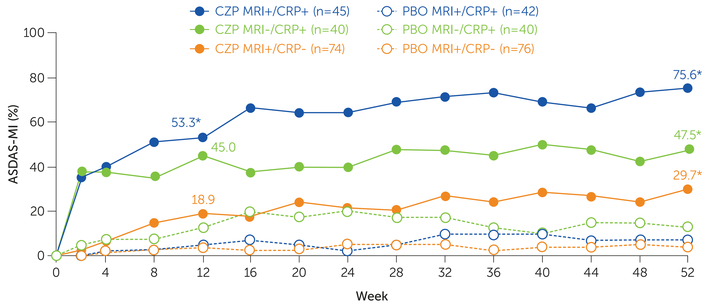
- 317 patients were randomized to CZP (n=159) or PBO (n=158) and stratified into subgroups (Table 1).
- At Weeks 12 and 52, ASDAS-MI was achieved by more CZP-treated patients compared to PBO-treated patients across all subgroups; responses were clinically relevant (Figure 1A).
- Response to ASDAS-MI was highest in the MRI+/CRP+ group and lowest in the MRI+/CRP- group (Figure 1A).
  - This was expected, given that patients in the MRI+/CRP- subgroup had a baseline CRP <ULN, and CRP is one of the main factors in derivation of the ASDAS.
- For ASAS40 and BASDAI, responses between MRI/CRP subgroups were comparable, although patients in the MRI+/CRP+ subgroup showed the greatest improvements (Figure 1B–C).

Table 1 Baseline characteristics by MRI/CRP subgroup

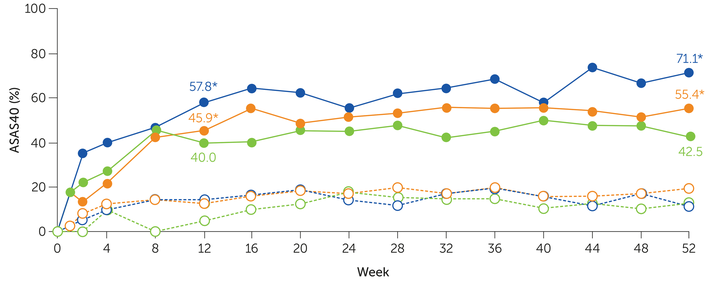
	MRI+/CRP+ (n=87)	MRI+/CRP- (n=150)	MRI-/CRP+ (n=80)
Age, years			
Mean (SD)	35.5 (9.7)	38.5 (11.2)	37.0 (10.3)
Range	18–67	18–73	18–61
Female, n (%)	31 (35.6)	77 (51.3)	55 (68.8)
Time since diagnosis, years			
Mean (SD)	3.1 (4.9)	4.5 (5.7)	3.2 (3.8)
Median (range)	1.7 (0.1–38.2)	2.2 (0.1–29.2)	1.7 (0.0–20.6)
Symptom duration, mean years (SD)	6.9 (7.3)	9.2 (8.2)	6.6 (6.4)
HLA-B27 positive, n (%)	74 (85.1)	110 (73.3)	77 (96.3)
ASDAS, mean (SD)	4.4 (0.7)	3.2 (0.5)	4.3 (0.7)
BASDAI total score, mean (SD)	7.1 (1.3)	6.6 (1.2)	7.0 (1.5)

Figure 1 Efficacy outcomes in patients stratified by baseline MRI/CRP status

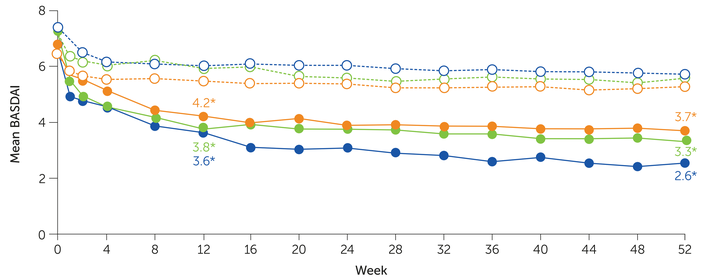
A) ASDAS-MI[a] (non-responder imputation)



B) ASAS40 (non-responder imputation)



C) BASDAI (double-blind last observation carried forward)



[a]ASDAS-MI indicates a ≥2.0-point decrease from the baseline score in the ASDAS and/or reaching the lowest possible ASDAS score of 0.6.[3] *p<0.001 for CZP vs PBO. Missing values, or values collected after switching to open-label treatment, were considered non-response (ASDAS-MI and ASAS40) or imputed using double-blind last observation carried forward (BASDAI).

Conclusions

Clinically relevant responses were observed in nr-axSpA patients treated with CZP with either MRI and/or CRP positivity. The highest response was seen in the MRI+/CRP+ subgroup.

ASAS40: Assessment of SpondyloArthritis international Society 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-MI: Ankylosing Spondylitis Disease Activity Score – Major Improvement; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; CZP: certolizumab pegol; HLA: human leukocyte antigen; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; SD: standard deviation.

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References: [1]Baraliakos X. Rheumatology 2017;56(7):1162–6; [2]Deodhar A. Arthritis Rheumatol 2019;71:1101–11; [3]van der Heijde D. Ann Rheum Dis. 2018;77:699–705. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **AD, LSG, SH, PCR, BH, LB, TK, WPM**; Drafting of the publication, or revising it critically for important intellectual content: **AD, LSG, SH, PCR, BH, LB, TK, WPM**; Final approval of the publication: **AD, LSG, SH, PCR, BH, LB, TK, WPM.** **Author Disclosures: AD**: Grant/research support, consultancy fees and speakers bureau from AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB Pharma. **LSG:** Grant/research support and/or consultancy fees from AbbVie, Eli Lilly, Gilead, GSK, Pfizer, Novartis, UCB Pharma. **PCR:** Speaking/consulting for AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, UCB Pharma; non-financial support from BMS and Roche; research grants from Janssen, Novartis, UCB Pharma. **SH:** Grant/research support from and/or consulting fees from AbbVie, Eli Lilly, Novartis, UCB Pharma. **BH, LB, TK:** Employees of UCB Pharma; own stock awards in UCB Pharma. **WPM:** Speakers bureau from AbbVie, Janssen, Novartis, Pfizer, UCB Pharma; consultant for AbbVie, BMS, Boehringer Ingelheim, Eli Lilly, Novartis, Pfizer, UCB Pharma; grant/research support from AbbVie, Novartis, Pfizer. **Acknowledgments:** This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Simone E. Auteri, MSc EMS PhD, UCB Pharma, Brussels, Belgium, for publication coordination, Olivia Wakeman, BSc, Costello Medical, Cambridge, UK, for medical writing and editorial assistance and the Costello Medical Design Team for design support. All costs associated with development of this poster were funded by UCB Pharma.

Previously presented at ACR Convergence 2020