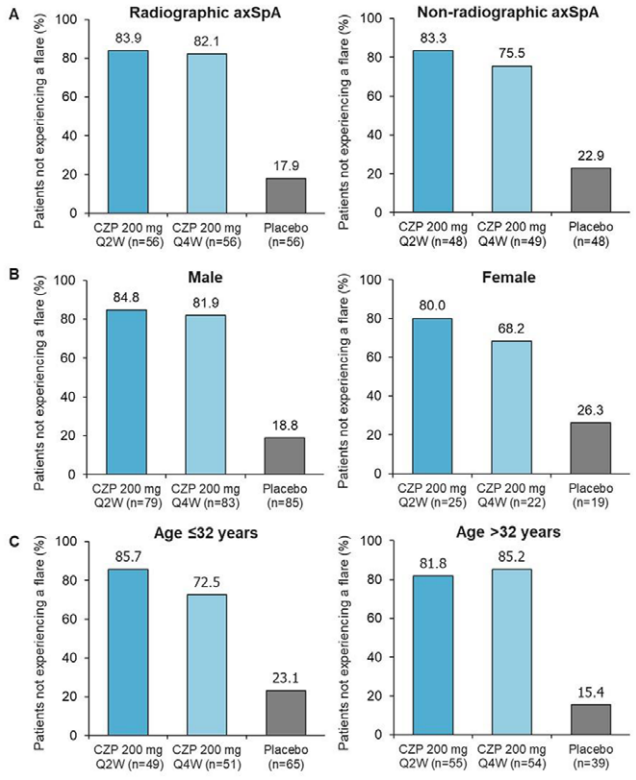
to axSpA subpopulation, gender and age ≤/> the median age of the randomised set (32 years).

Results: During the 48-wk induction period, 43.9% of patients (323/736) achieved sustained remission and 313 pts entered the 48-wk maintenance period (r/nr-axSpA: 168/145 pts; males/females: 247/66 pts; age ≤32/>32: 165/148 pts). During the maintenance period, responses in r- and nr-axSpA pts were comparable across all three randomised arms. 83.9% r-axSpA and 83.3% nr-axSpA pts receiving the full CZP maintenance dose did not experience a flare, and in the reduced maintenance dose arm 82.1% r-axSpA and 75.5% nr-axSpA pts did not experience a flare. In the PBO group this was reduced to 17.9% and 22.9%, respectively. Similar responses were seen in pts stratified by gender or age, with substantially higher percentages of pts randomised to CZP full or reduced maintenance dose remaining free of flares compared to PBO in all subgroups (Figure).

Conclusion: The results of C-OPTIMISE indicate that a reduced maintenance dose is suitable for pts with axSpA who achieve sustained remission following 1 year of CZP treatment, regardless of axSpA subpopulation, gender or age. Complete treatment withdrawal is not recommended due to the high risk of flare.

References: **[1]**Landewe R. Lancet 2018;392:134–44.

Figure. Patients not experiencing flares during the maintenance period of C-OPTIMISE, stratified by: A) disease subpopulation (radiographic vs non-radiographic axSpA); B) gender (male vs female); C) age (≤32 years vs >32 years)



axSpA: axial spondyloarthritis; CZP: certolizumab pegol; Q2W: every 2 weeks; Q4W: every 4 weeks.

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OP0104

THE IMPACT OF PERSISTENT INFLAMMATORY CHANGES ON PREVALENCE OF FATTY LESIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL: 4-YEAR MRI RESULTS FROM RAPID-AXSPA

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Background: Axial spondyloarthritis (axSpA) is a chronic disease characterised by inflammation in the sacroiliac joints and spine, causing severe back pain and stiffness. Emerging evidence suggests chronic spinal inflammation may be associated with osteoproliferation leading to syndesmophyte formation and spinal ankylosis, with subsequent worsening of patient mobility and function.[1] Fatty lesions (FLs) on magnetic resonance imaging (MRI) T1 sequences are considered to be post-inflammatory precursors to these changes. Certolizumab pegol (CZP), an Fc-free, PEGylated tumour necrosis factor inhibitor (TNFi), has proven efficacy in treating the signs and symptoms of axSpA.[2,3] CZP has also been shown to decrease spinal and sacroiliac joint MRI inflammation, and limit radiographic progression of the spine over 4 years of treatment.[4]

Objectives: To report the effect of early post-baseline (BL) inflammatory changes on fatty lesion prevalence over 4 years in a broad axSpA patient population treated with CZP.

Methods: RAPID-axSpA (NCT01087762) was a phase 3 trial which was double-blind and placebo (PBO)-controlled to Week (Wk) 24, dose-blind to Wk 48 and open-label to Wk 204. CZP-randomised axSpA patients (Wk 0 CZP: 200 mg every 2 wks [Q2W] or 400 mg Q4W) continued their assigned dose throughout; PBO-randomised axSpA patients (Wk 0 PBO) received CZP from Wk 24, or if non-responders, from Wk 16 onwards. Blinded spinal MRI scans at Wks 0, 12, 48, 96 and 204 were assessed by 2 central readers to evaluate FL and inflammatory lesions in vertebral edges (VEs). Changes in FL prevalence are reported as odds ratios (OR; FL+/FL-) between time points or inflammation states, with nominal 95% confidence intervals (CI), for Wk 0 CZP. ORs were estimated from a logistic regression model for VE level data with random effects for patient and VE (within patient). The fixed model effects included time point, inflammatory status of VEs at BL and Wk 12, FL status at BL, and interactions if appropriate.

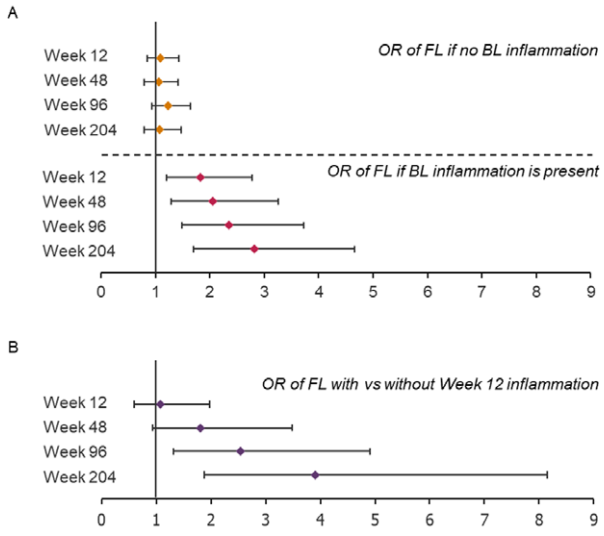
Results: Of 325 axSpA patients, 89 and 47 initially randomised to CZP or PBO, respectively, had a BL and ≥1 post-BL MRI and therefore were eligible for these analyses. In these patients, a total of 3,127 of VEs were assessed at BL; inflammation was observed in 21.6% and FL in 29.3% of VEs, equating to mean counts of 5.0 and 6.7 per patient; 10.5% of VEs had both inflammation and FL at BL. At BL, FLs were relatively more often observed in inflamed VEs vs non-inflamed VEs: OR (95% CI) of 3.30 (1.94, 5.61). This difference increased over time, as the OR of FL at Wk 204 vs BL was 2.82 (1.70, 4.66) in VEs that were inflamed at BL compared with 1.08 (0.79, 1.48) in VEs that were not inflamed at BL (Figure 1A). Resolution of inflammation by Wk 12 appeared to lower the risk of FL prevalence over 4 years. When adjusted for BL VE status with respect to inflammation and FL, if inflammation prevailed at Wk 12, the OR of FL vs no FL was 1.80 (0.93, 3.49) at Wk 48, 2.54 (1.32, 4.91) at Wk 96 and 3.91 (1.87, 8.15) at Wk 204 (Figure 1B).

Conclusion: This is the first report from a clinical interventional PBO-controlled study in a broad axSpA population showing that inflammation that prevailed after the start of TNFi treatment was associated with increased FL prevalence over 4 years. Reduction of inflammation by Wk 12 mitigated the risk of FL over the long-term, indicating the importance of early, effective and long-term treatment targeting inflammation. Similarly, a complete and persistent reduction of inflammation appears to be critical in these patients.

References:

[1] Maksymowych WP. Ann Rheum Dis 2013;72:23–8; **2.** Van der Heijde D. Rheumatology (Oxford) 2017;56:1498–509; **3.** Deodhar A. Arthritis Rheumatol 2019;71:1101–11; **4.** Van der Heijde D. Ann Rheum Dis 2018;77:699–705.

Figure 1. (A) OR for changes in FL prevalence vs presence or absence of inflammation at BL; (B) OR of FL for VEs with vs without inflammation at Week 12



A: An OR >1 represents an increase in FL from BL. A logistic regression with fixed effects for BL inflammation status by visit (including BL) and random effects for patient and VE (within patient). B: An OR >1 represents increased FL in VEs with vs without inflammation at Week 12, adjusted for BL VE status with respect to inflammation and FL. A logistic regression with fixed effects for Week 12 inflammation by visit (excluding BL) and BL inflammation by BL FL, and random effects for patient and VE (within patient). BL: baseline; FL: fatty lesion; OR: odds ratio; VE: vertebral edge.

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OP0105

EFFICACY AND SAFETY OF BIMEKIZUMAB IN ANKYLOSING SPONDYLITIS: 48-WEEK PATIENT-REPORTED OUTCOMES FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

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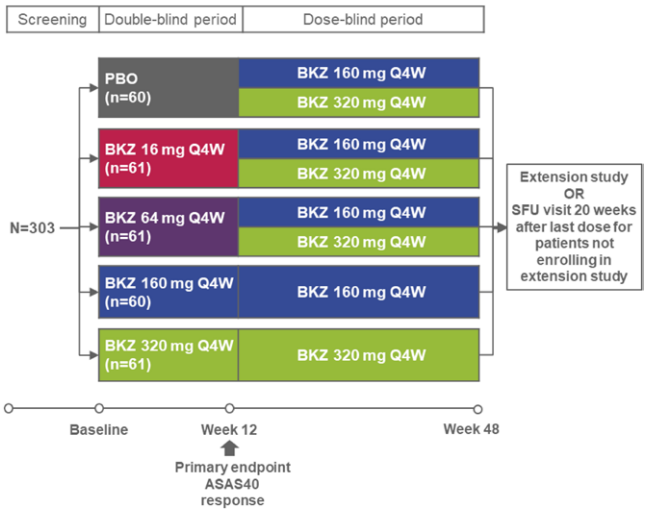
Background: Bimekizumab (BKZ), a monoclonal antibody that selectively neutralises interleukin (IL)-17A and IL-17F, is a potential therapeutic option in ankylosing spondylitis (AS).

Objectives: To report 48-week (wk) patient-reported outcomes (PROs) in patients (pts) with AS treated with BKZ in a phase 2b dose-ranging study (BE-AGILE; NCT02963506).

Methods: Pts with active AS (Bath AS Disease Activity Index [BASDAI] ≥4; spinal pain ≥4 [0–10]), fulfilling modified New York criteria (central reading), and inadequate response/intolerance to NSAIDs were randomised according to the study design (Figure 1). PROs included spinal pain, fatigue (BASDAI Q1), morning stiffness (mean of BASDAI Q5+6), Bath AS Functional Index (BASFI), Medical Outcomes Study (MOS) Sleep Problems Index II and AS Quality of Life questionnaire (ASQoL). Efficacy is reported for pts initially randomised to placebo (PBO) or BKZ 160/320 mg every 4 weeks (Q4W); treatment-emergent adverse events (TEAEs) are reported for pts who received ≥1 dose of study drug (Safety Set).

Results: Of 303 pts, 181 were randomised to PBO or BKZ 160/320 Q4W mg at Wk 0; 179/181 completed Wk 12 and 161/181 completed Wk 48. At Wk 12, improvements in pain, fatigue, morning stiffness, BASFI, sleep and ASQoL were greater in BKZ pts vs PBO pts. Responses were further improved or maintained to Wk 48, with no meaningful differences between BKZ 160 mg and 320 mg (Table 1). Serious TEAEs occurred in 13/303 (4.3%) pts (Table 2), which included 2 major adverse cardiac events considered not related to study drug. Oral candidiasis occurred in 16 (5.3%) pts.

Figure 1. Study design



ASAS40: Assessment of SpondyloArthritis international Society improvement of ≥40%; Q4W: every 4 weeks; SFU: safety follow-up.

Table 1. PRO efficacy endpoints to Week 48 (multiple imputation)

Mean (SD)	Wk	PBO – BKZ 160 mg (n=24)	PBO – BKZ 320 mg (n=36)	BKZ 160 mg (n=58)	BKZ 320 mg (n=61)
Spinal pain	0	6.9 (1.4)	7.0 (1.9)	6.6 (2.0)	7.3 (1.5)
CfB	12	-1.5 (1.6)	-0.7 (1.7)	-2.6 (2.2)	-3.6 (2.4)
	48	-3.7 (2.0)	-3.7 (2.6)	-3.8 (2.4)	-4.7 (2.1)
Fatigue	0	6.4 (1.7)	6.8 (1.6)	6.4 (1.7)	6.4 (1.9)
CfB	12	-0.7 (2.5)	-1.0 (1.7)	-2.1 (2.2)	-2.1 (2.5)
	48	-2.7 (2.2)	-2.8 (2.4)	-3.1 (2.1)	-3.3 (2.4)
Morning stiffness	0	6.9 (1.7)	6.7 (2.0)	6.5 (1.8)	6.6 (2.1)
CfB	12	-1.5 (1.7)	-1.1 (1.5)	-2.8 (2.0)	-3.4 (2.7)
	48	-3.9 (2.2)	-3.6 (2.4)	-3.9 (2.2)	-4.4 (2.4)
BASFI	0	5.8 (1.8)	5.5 (2.2)	5.5 (2.2)	5.9 (2.0)
CfB	12	-1.0 (2.1)	-0.3 (1.7)	-1.7 (1.8)	-2.2 (2.0)
	48	-2.9 (2.2)	-2.4 (2.2)	-2.5 (2.0)	-2.9 (2.2)
MOS Sleep Problems Index II	0	45.5 (8.1)	45.3 (7.9)	46.9 (7.5)	47.2 (9.4)
CfB	12	2.1 (8.3)	1.8 (6.8)	5.6 (6.7)	6.8 (7.5)
	48	7.6 (8.7)	8.0 (9.1)	6.5 (6.1)	8.0 (7.9)
ASQoL	0	8.4 (4.7)	9.2 (4.7)	8.4 (4.3)	8.7 (4.3)
CfB	12	-1.3 (5.5)	-1.3 (3.7)	-3.5 (4.3)	-4.6 (4.8)
	48	-4.2 (5.6)	-5.3 (5.6)	-4.9 (4.1)	-5.4 (4.8)

CfB: change from baseline

Conclusion: Pts with active AS demonstrated rapid and sustained improvements in PROs, sleep and quality of life over 48 wks of BKZ treatment. BKZ was generally well tolerated with no unexpected safety findings versus previous studies.

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