Spondyloarthritis – treatment

POS0895

EFFECT OF TOFACITINIB ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM A PHASE 3 TRIAL

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Background: Ankylosing spondylitis (AS) can significantly impact quality of life. Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of adult patients (pts) with AS. The safety/efficacy (including pt-reported outcomes [PROs]) of tofacitinib in pts with AS was assessed in a Phase 3 trial (NCT03502616).¹

Objectives: To evaluate the effect of tofacitinib on pt-reported pain, fatigue, overall health and work productivity in pts with active AS enrolled in the Phase 3 trial.

Methods: Pts with an inadequate clinical response or intolerance to ≥ 2 oral NSAIDs were randomised in a double-blind fashion to tofacitinib 5 mg twice daily (BID) or placebo (PBO) for 16 weeks. At Week (W)16, all pts received open-label tofacitinib 5 mg BID up to W48. Least squares (LS) mean changes from baseline (Δ) up to W48 are reported for the following outcomes: pt assessment of nocturnal spinal pain, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Short Form-36 Health Survey version 2 (SF-36v2; W16 and W48 only), and Work Productivity and Activity Impairment Questionnaire (WPAI; W16 and W48 only).

Results: At W16, there were greater improvements from baseline in pain (total back pain [previously published¹] and nocturnal spinal pain) and fatigue (FACIT-F total score; experience and impact domain scores) with tofacitinib vs PBO ($p \leq 0.05$; Table 1); improvements were observed as early as W2. Also, improvements in SF-36v2 physical component summary (PCS) (Table 1), and physical functioning, role-physical, bodily pain, general health and social functioning domains (Figure 1) were greater with tofacitinib vs PBO at W16 ($p \leq 0.05$). Similarly, improvements in WPAI scores at W16 were greater with tofacitinib vs PBO ($p \leq 0.05$), except for % work time missed (Table 1). Improvements with tofacitinib

continued up to W48 (Table 1/Figure 1). Generally, pts receiving PBO who advanced to tofacitinib at W16 reported similar improvements after switching to tofacitinib (Table 1/Figure 1).

Figure. LS mean Δ SF-36v2 domain scores (norm-based) at W16 and W48

** $p < 0.01$, *** $p < 0.001$ for tofacitinib 5 mg BID vs PBO (analysis of covariance model)

Conclusion: In pts with active AS, improvements in spinal pain, fatigue, overall health and work productivity were greater with tofacitinib vs PBO at W16; improvements continued up to W48. These PRO findings support the primary efficacy results of this Phase 3 trial,¹ and add to the overall understanding of the benefit/risk profile of tofacitinib in patients with AS.

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Table 1. PROs at baseline and Δ at W16 and W48

	Baseline, mean (SD) [N1]		Δ , W16, LS mean (SE)		p value	Δ , W48, LS mean (SE)	
	Tofacitinib 5 mg BID (N=133)	PBO (N=136)	Tofacitinib 5 mg BID	PBO		Tofacitinib 5 mg BID	PBO→tofacitinib 5 mg BID
Nocturnal spinal pain ^a	6.8 (1.9)	6.8 (1.9)	-2.67 (0.20)	-0.84 (0.20)	<0.0001	-3.52 (0.23)	-3.01 (0.23)
FACIT-F	27.2 (10.7)	27.4 (9.3)	6.54 (0.80)	3.12 (0.79)	0.0008	9.54 (0.90)	7.35 (0.89)
total score ^{a,b}	8.9 (4.3)	8.7 (4.0)	2.85 (0.36)	1.29 (0.36)	0.0007	4.22 (0.40)	3.40 (0.40)
FACIT-F experience domain ^a	18.3 (6.9)	18.8 (5.9)	3.68 (0.49)	1.81 (0.49)	0.0028	5.32 (0.54)	3.95 (0.54)
FACIT-F impact domain ^a	33.5 (7.3)	33.1 (7.0)	6.69 (0.59)	3.14 (0.59)	<0.0001	8.81 (0.720)	7.39 (0.71)
SF-36v2 PCS ^{b,c}	39.4 (11.1)	39.8 (12.7)	3.45 (0.91)	2.13 (0.92)	0.2529	7.07 (0.93)	6.35 (0.92)
SF-36v2 MCS ^c	56.5 (23.4)	56.0 (21.4)	-19.03 (1.97)	-5.63 (1.97)	<0.0001	-27.37 (2.34)	-19.77 (2.31)
WPAI ^e	9.9 (22.4)	11.5 (24.6)	-3.65 (2.66)	0.88 (2.62)	0.1784	-8.10 (2.14)	-5.79 (2.05)
% activity impairment	48.4 (26.3)	49.6 (22.2)	-19.83 (2.27)	-6.94 (2.30)	<0.0001	-25.35 (2.77)	-23.00 (2.66)
% work time missed	50.8 (27.4)	53.5 (23.1)	-21.49 (2.51)	-7.64 (2.56)	<0.0001	-27.63 (3.01)	-23.22 (2.90)
% impairment while working							
% overall work impairment							

^aMMRM^bGlobal type I error-controlled endpoint^cAnalysis of covariance model for W16 and MMRM for W48MCS, mental component summary; MMRM, Mixed Model for Repeated Measures; N, number of pts in full analysis set; N1, number of pts included in the analysis (if different from N); SD, standard deviation; SE, standard error

POS0896

PREDICTORS OF RESPONSE IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS RECEIVING CERTOLIZUMAB PEGOL IN THE C-AXSPAND STUDY

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Background: Identification of predictive clinical factors of long-term treatment response in non-radiographic axial spondyloarthritis (nr-axSpA) may contribute to improved management of patients with this chronic disease. Certolizumab pegol (CZP) is currently the only FDA-approved tumour necrosis factor inhibitor (TNFi) for treatment of nr-axSpA.¹

Objectives: To identify whether any demographic or baseline characteristics of nr-axSpA patients from the C-axSpAnd study² are predictive of achieving a clinical response after 1 year of CZP treatment.

Methods: C-axSpAnd (NCT02552212) was a phase 3, interventional multi-centre study including a 52-week double-blind, placebo-controlled period. Full

study design is reported elsewhere.² Multivariate stepwise logistic regression analysis was used to identify predictors of response for the primary efficacy variable (Ankylosing Spondylitis Disease Activity Score – major improvement [ASDAS-MI] at Week 52) and the main secondary efficacy variable (Assessment of SpondyloArthritis international Society 40% [ASAS40] at Week 52) in patients randomised to CZP 200 mg every 2 weeks (Q2W). Predictive factors used in the model included demographic and baseline characteristics, and clinical outcomes at Week 12. A p value ≤ 0.05 was required for forward selection into the model and $p=0.1$ for backward elimination from the model. Non-responder imputation was used to account for missing data or values collected after switching to open-label treatment. A sensitivity analysis was conducted to account for patients who had changes in their non-biologic background medication during the 52-week placebo-controlled period.

Results: A total of 159/317 patients were randomised to CZP 200 mg Q2W and 158/317 to placebo. Predictive factors identified for Week 52 ASDAS-MI in the CZP-treated patients included being positive for both presence of sacroiliitis on MRI (MRI+) and human leukocyte antigen (HLA)-B27 (HLA-B27+), having a higher Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at baseline, and having a larger Week 12 improvement in ASDAS (Figure 1A). For ASAS40 response, MRI+/HLA-B27+ was also identified as a predictor of Week 52 response, along with a lower baseline Bath AS Metrology Index (BASMI) and larger Week 12 improvements in Patient Global Assessment of Disease Activity (PtGADA) and AS Quality of Life (ASQoL; Figure 1B). Sensitivity analysis identified the same predictors for ASDAS-MI and ASAS40, with the exception of change from baseline in PtGADA as a predictor of ASAS40. Sensitivity analysis also identified achievement of Week 12 ASAS40 as a predictor of Week 52 ASAS40. In placebo-treated patients, no meaningful predictors of response at Week 52 were identified.

Conclusion: Presence of sacroiliitis on MRI and HLA-B27 positivity were identified as consistent predictors of Week 52 response (ASDAS-MI and ASAS40) in nr-axSpA patients treated with CZP. To our knowledge, this is the first report from an interventional 52-week placebo-controlled study in nr-axSpA to identify objective clinical features, particularly the presence of sacroiliac joint inflammation, as being predictive of response.

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Figure. Predictive factors of Week 52 response in CZP-treated patients

[a] Included in the predictive model as continuous variables; for these factors, an odds ratio >1 indicates a higher probability of larger values being predictive of a response. For Week 12 change from baseline measures, a lower (negative) value is indicative of improvement, while larger (positive) values indicate worsening. ASAS40: Assessment of SpondyloArthritis international Society 40%; ASDAS-MI: Ankylosing Spondylitis Disease Activity Score – major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CI: confidence interval; HLA: human leukocyte antigen; MRI+/–: presence/absence of sacroiliitis on magnetic resonance imaging; PtGADA: Patient Global Assessment of Disease Activity; vs: versus.

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REDUCTION OF ANTERIOR UVEITIS FLARES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS DURING CERTOLIZUMAB PEGOL TREATMENT: 96-WEEK RESULTS FROM THE C-VIEW STUDY

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Background: Acute anterior uveitis (AAU) is the most common extra-articular manifestation in axial spondyloarthritis (axSpA), affecting up to 40% of patients and causing significant burden.¹ Previous studies have shown that tumour necrosis factor inhibitors (TNFi) can reduce the incidence of AAU flares in patients with radiographic axSpA (ankylosing spondylitis),^{2–4} but few have focused on patients across the full axSpA spectrum.¹

Objectives: To report 2-year outcomes from the phase 4, open-label C-VIEW study (NCT03020992), which investigated the impact of certolizumab pegol (CZP) treatment on AAU in patients with active axSpA and a recent history of AAU.

Methods: C-VIEW prospectively investigated patients with active axSpA who were HLA-B27 positive and had recurrent AAU, with a history of ≥ 1 AAU flare in the year prior to baseline (additional study criteria and study design are described elsewhere⁵). The primary efficacy variable was the incidence of AAU flares during 96 weeks of CZP treatment versus the 2-year pre-baseline period. AAU incidence was evaluated using Poisson regression adjusted for duration of time in each period, with period (pre- and post-baseline) and axSpA disease duration as covariates. Secondary efficacy variables were Assessment of SpondyloArthritis international Society 20%/40% (ASAS20/40) response rates, as well as mean Ankylosing Spondylitis Disease Activity Score (ASDAS) and mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) to Week 96.

Results: Of 115 enrolled patients, 89 initiated CZP treatment; 83 completed Week 96. The primary analysis revealed an 82% reduction in the incidence of AAU flares during CZP treatment compared with pre-baseline (Figure 1A; rate ratio [95% CI]: 0.18 [0.12, 0.28], $p<0.001$). The percentage of patients experiencing ≥ 1 and ≥ 2 AAU flares reduced from 100% and 59.6% pre-baseline to 20.2% and 11.2% during treatment (Figure 1B). There were also improvements in axSpA disease activity (Table 1): by Week 96, 75.6% and 58.5% of patients had achieved ASAS20 and ASAS40 responses, respectively. ASDAS and BASDAI also improved substantially over the 96-week treatment period. No new safety signal was identified, compared to previous reports.⁵

Conclusion: These data support the use of CZP for the treatment of patients with axSpA and a history of recurrent AAU. During 96 weeks' CZP treatment, there was a significant reduction of 82% in the AAU flare rate compared to pre-baseline. There were also substantial improvements in patients' axSpA disease activity.

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