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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Summary

n=89

- Active axSpA
- High risk of AAU flares
- HLA-B27 positive

Loading dose:
CZP 400 mg at Weeks 0/2/4 → CZP 200 mg Q2W to Week 96

During 96 weeks' CZP treatment vs pre-baseline period:

82% reduction in AAU flare event rate

Substantial improvements in axSpA disease activity

No new safety signal

CZP is a suitable treatment option for patients with axSpA and a history of recurrent AAU

Objective

To report final 2-year outcomes from the C-VIEW study, which investigated the impact of certolizumab pegol (CZP) on the frequency of acute anterior uveitis (AAU) flares in patients with active radiographic or non-radiographic axial spondyloarthritis (r/nr-axSpA) and a recent history of AAU.

Background

- AAU, defined as a non-infectious, acute inflammation of the anterior uveal tract and adjacent structures, is the most common extra-musculoskeletal manifestation in axSpA, affecting up to 40% of patients and causing significant burden.[1,2]
- Common symptoms of AAU include blurred vision, photophobia and pain, with HLA-B27 positive patients at increased risk of developing recurrent AAU.[3,4]
- TNF inhibitors (TNFi) may reduce the incidence of AAU flares in patients with r-axSpA, but there remains a paucity of data for patients across the axSpA spectrum with recurrent AAU.[2,5–9]

Methods

Study Design

- C-VIEW (NCT03020992), a phase 4, prospective, open-label study, investigated the impact of CZP treatment on the frequency of AAU flares in HLA-B27 positive patients with active axSpA and recurrent AAU (Figure 1).

Key Patient Inclusion Criteria

- ≥18 years of age, adult-onset axSpA with ≥3 months' symptom duration
- Active axSpA: BASDAI score ≥4 and spinal pain ≥4
  - r-axSpA: sacroiliitis on X-ray meeting the mNY classification criteria
  - nr-axSpA: sacroiliitis on MRI and/or CRP level > upper limit of normal
- HLA-B27 positive
- Documented history of ≥2 AAU flares (≥1 in the last 12 months prior to baseline)
- Inadequate response or contraindication to ≥2 NSAIDs

Methods

- The primary efficacy analysis compared AAU event rate in the 2 years prior to CZP treatment with the 96 weeks of treatment using Poisson regression analysis, adjusting for the difference in duration of time in each period.
- Secondary efficacy variables to Week 96 included: Assessment of SpondyloArthritis international Society 20%/40% (ASAS20/40) response and Ankylosing Spondylitis Disease Activity Score (ASDAS).

Results

Patients

- Of 115 enrolled patients, 89 initiated CZP treatment; 83 completed Week 96.
- Baseline demographics and characteristics are shown in Table 1.

Number and Incidence of AAU Flares

- 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 2A).
- The primary analysis revealed an 82% reduction in AAU flare event rate during CZP treatment compared with pre-treatment (Figure 2B; rate ratio [95% CI]: 0.18 [0.12, 0.28], p<0.001).
- The AAU event rate per 100 patient-years decreased from 97.5 (95% CI: 83.2, 113.5) to 17.7 (95% CI: 11.7, 25.5) during 96 weeks of CZP treatment (Figure 2C).
- Subgroup analyses, investigating AAU flare event rates stratified by axSpA subpopulation, age and gender, were consistent with the primary analysis (Figure 3).

Secondary Outcomes

- There were substantial improvements in axSpA disease activity to Week 96 (Figure 4).
- No new safety signal was identified compared to previous reports.[10]

Figure 1 Study design

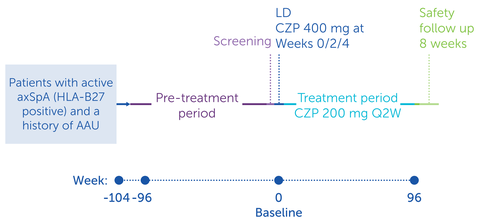


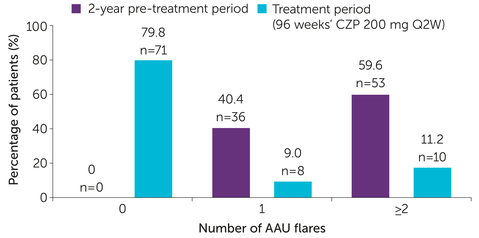
Table 1 Baseline demographics and patient characteristics

	CZP 200 mg Q2W (N=89)
Age (years), mean (SD)	46.5 (11.2)
Male, n (%)	56 (63)
Diagnosis, n (%)	
Radiographic axSpA	76 (85)
Non-radiographic axSpA	13 (15)
Time since axSpA diagnosis (years), mean (SD)	9.1 (8.6)
HLA-B27 positive, n (%)	89 (100)
Uveitis history, n (%)	89 (100)
Time since onset of first uveitis flare (years), mean (SD)	10.1 (9.2)
Patients with active flare at baseline, n (%)	5 (6)
Prior medication exposure, n (%)	
TNFi	5 (6)[a]
NSAIDs	85 (96)
Conventional DMARDs	22 (25)
Concomitant medication use at baseline, n (%)	
TNFi	0
NSAIDs	76 (85)
Conventional DMARDs	16 (18)
CRP, mg/L, mean (SD)	13.8 (27.2)
ASDAS, mean (SD)	3.5 (1.0)
BASDAI total score, mean (SD)	6.5 (1.5)
Total spinal pain score, mean (SD)	6.7 (2.0)
BASFI, mean (SD)	5.1 (2.4)
Patient's GADA, mean (SD)	6.7 (2.2)

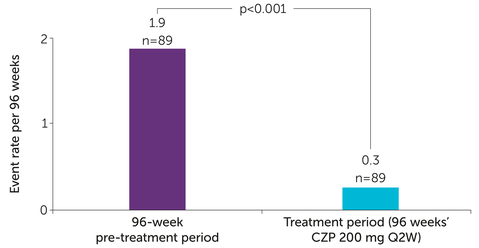
[a]Etanercept in four patients and investigational drug (etanercept vs placebo) for remaining patient. All patient-reported outcomes were assessed using a numerical rating scale (0–10), with higher numbers indicating poorer outcomes.

Figure 2 Summary of AAU flares (observed data)

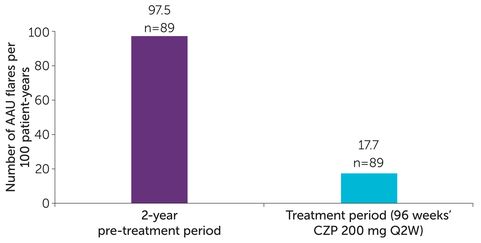
A) Percentage of patients experiencing 0, 1 or ≥2 AAU flares



B) AAU event rate per 96 weeks[a]

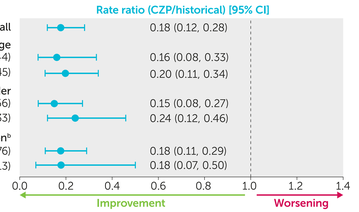


C) AAU event rate per 100 patient-years



Please refer to Figure 3 footnote for methodology.

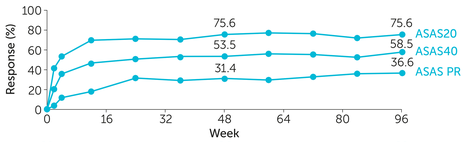
Figure 3 AAU flare event rate to Week 96 overall and by subgroups (observed data)[a]



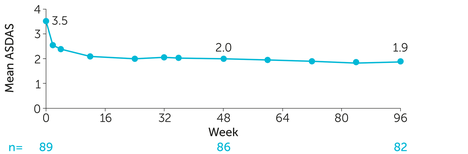
[a]Poisson regression analysis, with period (pre-/post-baseline) and axSpA disease duration as covariates and adjusting for the length of time in the pre- and post-baseline periods. [b]As determined by investigator. Treatment period: after start of study medication until Week 96 or discontinuation visit. Pre-treatment period: 24 months prior to treatment start. Flares on the same eye are combined and counted as one flare if the time interval between two subsequent flares is <3 months (90 days).

Figure 4 Changes in axSpA disease activity to Week 96 (observed data)

A) ASAS20/40 and ASAS PR



B) ASDAS



Conclusions

C-VIEW is the first clinical trial to prospectively assess the impact of TNFi on AAU in an axSpA population at high risk of recurrent AAU.

Results support the use of CZP for the treatment of patients across the full axSpA spectrum with a history of recurrent AAU.

AAU: acute anterior uveitis; ASAS20/40: Assessment of SpondyloArthritis international Society 20%/40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CI: confidence interval; CRP: C-reactive protein; CZP: certolizumab pegol; DMARD: disease-modifying antirheumatic drug; GADA: Global Assessment of Disease Activity; HLA-B27: human leukocyte antigen-B27; LD: loading dose; mNY: modified New York; MRI: magnetic resonance imaging; (n)r-axSpA: (non-) radiographic axial spondyloarthritis; NSAID: non-steroidal anti-inflammatory drug; PR: partial remission; Q2W: every two weeks; SD: standard deviation; TNFi, tumour necrosis factor inhibitor.

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