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FRI0396

CHARACTERIZATION OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN THE ANKYLOSING SPONDYLITIS COHORT PRIOR AND DURING ADALIMUMAB TREATMENT: DATA FROM A LARGE GERMAN NON-INTERVENTIONAL STUDY

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Background: Spondylarthritides (SpA) are characterized by different disease manifestations such as arthritis, enthesitis, dactylitis and associated to concomitant diseases like Inflammatory bowel diseases (IBD) including ulcerative colitis (UC) and Crohn's disease (CD). IBD might have a specific role to SpA due to common pathophysiological pathways. Characteristics of the rheumatic disease and response to treatment may differ within the phenotypic manifestation and with and without associated diseases. Adalimumab (ADA) is a monoclonal antibody inhibiting TNF alpha which has demonstrated efficacy in both, nraxSpA and ankylosing spondylitis (AS) as well as for UC and CD.

Objectives: To evaluate patient baseline characteristics prior to and treatment response on different disease manifestations in a cohort of AS patients with IBD compared to an AS without IBD during ADA treatment.

Methods: Data from a large German multicenter prospective observational non-interventional study (n=3.756) of patients with active AS who initiated ADA therapy during routine clinical care were analyzed with focus on specific patient groups: (1) patients with AS and IBD at baseline (n=166) and (2) patients with AS without IBD at baseline (n= 3.590). Patient characteristics and data of efficacy on different disease manifestations and prevalence of concomitant IBD over 24 months were analyzed.

Results: Of 3.756 patients in the main analysis set, 166 (4.4%) were identified to suffer from concomitant IBD at baseline. Baseline characteristics showed differences in gender distribution, proportion of patients with enthesitis, psoriasis and uveitis showing a higher proportion of each for the IBD group (Table). After 24 months of ADA treatment, both groups had similar decreases for BASDAI, BASMI, BASFI and dactylitis improvement. The IBD group had a fast decrease in BASDAI at M6 to its maximum improvement (delta of 1.9) which was kept stable until M24. For clearance of enthesitis, ADA had its largest therapeutic effect at M6 in the IBD group (clearance in 15.3% of the patients) while the AS without IBD group had the largest decrease of 10.2% at month 24. Resolving of uveitis with ADA therapy was more often seen in the IBD group compared to the AS without IBD (delta of 6% at M12 compared to delta of 2.6% at M12, respectively). The prevalence of IBD in AS in patients treated with ADA changed from 4.4% at baseline to 1.9% at M24.

Conclusion: Within the cohort of AS, patients' characteristics of manifestations are associated to different treatment responses: Patients identified to have IBD at baseline respond better for resolving of enthesitis and show a faster response in BASDAI compared to the group without IBD. Overall a significant reduction in the prevalence of clinically relevant IBD was seen earliest at month 3 after ADA initiation.

Table. Baseline characteristics of patients with IBD within the documented AS cohort treated with ADA

	All patients (n=3756)	
	AS with IBD (n=166)	AS without IBD (n=3590)
Gender (male)	88 (53.0%)	3012 (83.9%)
Age (mean) (years)	49	49
IBD (n=166)	166	0
UC (n=166)	166	0
CD (n=166)	166	0
Uveitis (n=166)	166	0
Enthesitis (n=166)	166	0
Psoriasis (n=166)	166	0
Dactylitis (n=166)	166	0

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FRI0397

EFFICACY AND SAFETY OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL: RESULTS FROM THE 48-WEEK RUN-IN PART OF C-OPTIMISE

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Background: C-OPTIMISE is the first trial to evaluate whether certolizumab pegol (CZP) can be reduced/discontinued in patients with radiographic(r)-axSpA/ankylosing spondylitis (AS) and non-radiographic(nr)-axSpA achieving sustained remission after 48 weeks' (wks') treatment.

Objectives: Here, we report interim efficacy and safety data for both sub-populations from the ongoing trial.

Methods: Up to Wk48, C-OPTIMISE (NCT02505542) was open-label (Part A), followed by 48-wk parallel-group, double-blind, placebo-controlled treatment (full dose and half dose) to Wk96 (Part B). Patients with adult-onset axSpA of <5 years' duration, fulfilling Assessment of SpondyloArthritis international Society (ASAS) classification criteria, were recruited. Part A: patients received CZP 400mg at Wks0/2/4, then 200mg every 2 weeks [Q2W]; patients achieving sustained remission (Ankylosing Spondylitis Disease Activity Score [ASDAS]<1.3 at Wk32 and <2.1 at Wk36 [or vice versa], and <1.3 at Wk48) were eligible for Part B (secondary outcome). Primary outcome (not reported): percentage of patients in Part B not experiencing a flare. Missing values were imputed using non-responder imputation (NRI) and last observation carried forward (LOCF).

Results: Part A: Of 736 patients (Table A), 43.9% achieved sustained remission (r-axSpA/AS: 42.8%; nr-axSpA: 45.3%; NRI). At baseline, 98.5% patients had high/very high disease activity (ASDAS≥2.1); at Wk48,

52.7% (r-axSpA/AS: 52.6%; nr-axSpA: 52.9%) had inactive disease (ASDAS<1.3; LOCF; **Table B**). The treatment-emergent adverse event (TEAE) rate/100 patient-years' exposure was 224.2; 3.9% patients discontinued CZP due to TEAEs. No new safety signal was identified. **Conclusion:** The run-in phase of C-OPTIMISE shows that similar and substantial proportions of patients with r-axSpA/AS and nr-axSpA achieved sustained remission during 48 wks' CZP treatment. No new safety signal was identified.

Table: A) Baseline Characteristics

	axSpA (N=736) [a]	r-axSpA/AS (n=407) [b]	nr-axSpA (n=329) [b]
Age (years), mean (SD)	52.9 (7.0)	53.7 (6.8)	52.1 (7.1)
Male, n (%)	513 (69.7)	318 (78.1)	195 (59.3)
Symptom duration (years), mean (SD) [c]	2.2 (1.7)	2.5 (1.8)	1.8 (1.6)
HLA-B27 positive, n (%)	597 (81.1)	354 (87.0)	243 (73.9)
Sacroiliitis on imaging, n (%) [d]	691 (93.9)	401 (98.5)	290 (88.1)
Prior anti-TNF treatment, n (%)	31 (4.2)	20 (4.9)	11 (3.3)

B) Clinical Outcomes

	axSpA (N=736)		r-axSpA/AS (n=407)		nr-axSpA (n=329)	
%	BL	Wk48 (NRI)	BL	Wk48 (NRI)	BL	Wk48 (NRI)
ASAS20	—	79.6	—	79.9	—	79.3
ASAS40	—	72.0	—	71.3	—	72.9
ASAS-PR	—	57.3	—	55.8	—	59.3
BASDAI50	—	71.7	—	71.3	—	72.3
Mean [e]	BL	Wk48 (LOCF [e])	BL	Wk48 (LOCF [e])	BL	Wk48 (LOCF [e])
ASDAS	3.7	1.6	3.8	1.6	3.6	1.5
HDA/VHDA, %	98.5	24.7†	98.5	25.8	98.5	23.2†
ID, %	—	52.7†	—	52.6	—	52.9†
CII, % [f]	—	76.5	—	78.6	—	73.9
MI, % [f]	—	56.3	—	58.7	—	53.2
BASFI	6.7	2.1	6.7	2.1	6.7	2.2
BASFI	5.3	1.7	5.4	1.7	5.1	1.6
BASMI	3.1	2.3	3.5	2.6	2.7	1.9
Nocturnal back pain	6.9	1.8	7.0	1.8	6.8	1.8
Fatigue	7.1	2.6	7.1	2.5	7.1	2.6
CRP (mg/L), median [g]	7.8	2.0	10.7	2.0	4.5	2.0

[a] Patients with prior exposure to >1 anti-TNF excluded. [b] Central reading of patients' sacroiliac joint x-rays was used to stratify patients into r-axSpA/AS and nr-axSpA subpopulations. [c] Time since diagnosis of disease. [d] MRI or x-ray. [e] Unless stated otherwise, [f] NRI. [g] Values below the limit of quantification were set to half of the limit. 1m-734, 1m-327: AS: ankylosing spondylitis; ASAS20/40: ≥20%/≥40% improvement in Assessment of SpondyloArthritis International Society response criteria; ASAS PR: ASAS Partial Remission; ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASDAI 50: ≥50% improvement in BASDAI; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BL: baseline; CII: ASAS Clinically Important Improvement (RFB 2.1.1); CRP: C-reactive protein; CZP: certolizumab pegol; HDA/VHDA: ASDAS High/Very High Disease Activity (ASDAS≥2.1); ID: ASDAS Inactive Disease (ASDAS<1.3); LOCF: last observation carried forward; MI: ASDAS Major Improvement (RFB 2.2.0); MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axSpA; NRI: non-responder imputation; r-axSpA: radiographic axSpA; RFB: reduction from baseline; Wk: week.

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FRI0398

IXEKIZUMAB IS EFFECTIVE IN THE TREATMENT OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS REGARDLESS OF THE LEVEL OF C-REACTIVE PROTEIN OR MAGNETIC RESONANCE IMAGING SCORES: 16-WEEK DATA FROM COAST-V AND COAST-W

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Background: Radiographic axial spondyloarthritis (r-axSpA) is a chronic inflammatory disease of the axial skeleton, and interleukin (IL)-17 plays an important role in the pathogenesis. Elevated C-reactive protein (CRP) levels in serum predict response to tumor necrosis factor inhibitors (TNFi)¹⁻⁴ but not to secukinumab.⁵ The role of baseline spine magnetic resonance imaging (MRI) as a predictor of response has not been investigated for IL-17 inhibitors.

Objectives: To evaluate response rates at week (wk) 16 with ixekizumab (IXE), an IL-17A antagonist, in patients with ankylosing spondylitis (AS)/r-axSpA and elevated or normal/low inflammation as measured by CRP or spinal MRI.

Methods: Two Phase 3, randomized, double-blind, placebo (PBO)-controlled trials (COAST-V, NCT02696785; COAST-W, NCT02696798) enrolled patients who were biologic-naïve or TNFi-experienced, respectively, with active disease (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] ≥4 and spinal pain ≥4 on a numeric rating scale) and an established diagnosis of r-axSpA and fulfilling Assessment of SpondyloArthritis international Society (ASAS) criteria (sacroiliitis on radiograph by modified New York [mNY] criteria and ≥1 spondyloarthritis feature). All patients fulfilling ASAS criteria also fulfilled mNY criteria for AS. Patients were treated with IXE (80 mg every 2 or 4 wks [Q2W, Q4W]) or PBO; adalimumab (40 mg Q2W) was an active reference arm in COAST-V. We examined ASAS 40% (ASAS40) response rates at wk 16 for the intent-to-treat population by CRP (≤5 or >5 mg/L) or MRI spine inflammation (Spondyloarthritis Research Consortium of Canada [SPARCC] spine score, <2 or ≥2). Baseline spine MRI was available in 96% of patients in COAST-V and 51% of patients in COAST-W; scoring was done by central readers. Higher scores reflect greater baseline disease activity. Sacroiliac joint MRIs were not assessed. Missing data for ASAS40 were imputed by nonresponder imputation.

Results: In the COAST-V/W integrated dataset that combined biologic-naïve and TNFi-experienced populations, significantly more patients treated with IXE achieved ASAS40 response at wk 16 than with PBO in the elevated (>5 mg/L) baseline CRP group (39.3%, 42.5%, and 16.7% for IXE Q4W, IXE Q2W and PBO, respectively; p<.001 for IXE Q4W, IXE Q2W vs PBO) and in the normal (≤5 mg/L) baseline CRP group (27.4%, 35.2%, and 12.3% for IXE Q4W, IXE Q2W and PBO, respectively; p<.05 for IXE Q4W, p<.01 for IXE Q2W vs PBO, Fig 1), and the magnitude of response with IXE between elevated vs normal CRP groups was not statistically significant. Notably, a significantly higher proportion of patients achieved ASAS40 at wk 16 with IXE than with PBO, regardless of whether MRI spine SPARCC scores were <2 (40%, 51.7%, and 15.5% for IXE Q4W, IXE Q2W and PBO, respectively; p<.01 for IXE Q4W, p<.001 for IXE Q2W vs PBO) or ≥2 (44.3%, 46.6%, and 18.7% for IXE Q4W, IXE Q2W and PBO, respectively; p<.001 for IXE Q4W, IXE Q2W vs PBO, Fig 1).

Figure 1 COAST-V/W Integrated Dataset, ITT ASAS40 Response at Week 16, NRI

*p<.05, **p<.01, ***p<.001 versus placebo. ASAS40=Assessment in SpondyloArthritis International Society 40% response rate; CRP=C-reactive protein; ITT=Intention-to-treat; IXE=ixekizumab; n=number of patients in the specified category; n/N=number of patients in the analysis population; NRI=nonresponder imputation; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SPARCC=Spondyloarthritis Research Consortium of Canada