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How to treat SpA? From physiotherapy to new IL-17 blocking drugs

OP0231

DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB WAS ASSOCIATED WITH IMPROVEMENTS IN PATIENT-REPORTED AND QUALITY-OF-LIFE OUTCOMES IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

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Background: Ankylosing spondylitis (AS) is a chronic immune-mediated inflammatory disease primarily affecting the sacroiliac joints and spine, causing pain, stiffness and loss of mobility and function. These manifestations can severely impair patients' quality of life (QoL).¹ Dual neutralisation of IL-17F in addition to IL-17A has been shown to reduce inflammation to a greater extent than inhibition of IL-17A alone in disease-relevant cell models.² Results previously reported from this Phase 2b study (NCT02963506) demonstrated that, during the 12-week double-blind treatment period, bimekizumab provided substantial clinical improvements in disease outcome measures, including Assessment of SpondyloArthritis international Society 40% (ASAS40), in patients with active AS.³

Objectives: To assess the impact of bimekizumab on patient-reported and QoL outcomes at Week 12 in patients with active AS.

Methods: In this 48-week Phase 2b study (double blind to Week 12 then dose blind to Week 48), 303 patients with active AS (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] ≥ 4 ; spinal pain ≥ 4 [0–10 numerical rating scale]), fulfilling the modified New York criteria, were randomised 1:1:1:1 to receive subcutaneous bimekizumab 16mg, 64mg, 160mg, 320mg or placebo Q4W for 12 weeks. Prior exposure to one anti-TNF therapy was permitted. Secondary and other endpoints included: BASDAI, $\geq 50\%$ improvement in BASDAI (BASDAI 50), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Quality of Life (ASQoL) and Patient's Global Assessment of Disease Activity (PGADA) at Week 12. Safety was also assessed.

Results: Overall, 297 (98.0%) patients completed the 12-week double-blind period. Baseline scores on patient-reported and QoL outcomes were similar across treatment groups (Table). At Week 12, BASDAI 50 was achieved by 23.7–47.5% of bimekizumab-treated patients versus 11.9% receiving placebo. All bimekizumab doses were associated with greater reductions in individual BASDAI components, including: fatigue (range: -1.6 to -2.5 vs -0.8); neck, back or hip pain (-2.0 to -3.3 vs -1.2); discomfort due to tenderness to touch or pressure (-1.6 to -3.0 vs -1.1); level of morning stiffness (-2.5 to -3.5 vs -1.2) and duration of morning stiffness (-1.7 to -3.3 vs -1.4) (Table). Compared with placebo, greater reductions from baseline were also achieved with bimekizumab for BASFI (-1.4 to -2.2 vs -0.6), ASQoL (-2.3 to -4.6 vs -1.3) and PGADA (-1.9 to -3.3 vs -1.0). The overall incidence of treatment-emergent adverse events was 89/243 (36.6%) for bimekizumab-treated patients versus 23/60 (38.3%) for placebo; the majority were of mild or moderate intensity. No unexpected safety findings were observed.

Measure (SD)	Placebo (n=60)	16mg (n=61)	64mg (n=61)	160mg (n=61)	320mg (n=60)
BASDAI: fatigue					
Baseline	6.7 (1.6)	7.1 (1.6)	6.8 (1.5)	6.5 (1.6)	6.4 (1.5)
Week 12	5.8 (2.3)	5.5 (2.2)	4.9 (2.2)	4.9 (2.3)	4.4 (2.4)
BASDAI: neck/back/hip pain					
Baseline	7.4 (1.8)	7.7 (1.2)	7.7 (1.2)	7.0 (1.7)	7.5 (1.5)
Week 12	6.3 (2.5)	5.8 (2.4)	4.9 (2.4)	4.4 (2.5)	4.2 (2.4)
BASDAI: discomfort due to tenderness to touch/pressure					
Baseline	5.9 (2.1)	6.2 (2.4)	6.2 (2.0)	5.8 (2.3)	6.2 (2.0)
Week 12	4.9 (2.8)	4.8 (2.5)	3.8 (2.4)	3.2 (2.5)	3.2 (2.5)
BASDAI: level of morning stiffness					
Baseline	7.3 (1.8)	7.3 (2.2)	7.3 (1.9)	6.9 (2.0)	7.1 (2.1)
Week 12	6.2 (2.4)	4.8 (2.5)	4.0 (2.5)	4.1 (2.4)	3.6 (2.4)
BASDAI: duration of morning stiffness					
Baseline	6.3 (2.4)	5.8 (2.3)	6.4 (2.0)	6.0 (2.3)	6.1 (2.0)
Week 12	5.0 (2.8)	4.1 (2.8)	3.4 (2.4)	3.3 (2.3)	2.8 (2.5)
BASFI: overall score					
Baseline	5.8 (2.0)	5.9 (1.7)	6.0 (1.8)	5.8 (2.2)	5.9 (2.0)
Week 12	5.3 (2.4)	4.5 (2.4)	4.1 (2.4)	3.8 (2.3)	3.7 (2.5)
ASQoL					
Baseline	8.9 (4.7)	8.9 (4.2)	8.8 (4.1)	8.5 (4.3)	8.7 (4.3)
Week 12	7.8 (5.2)	6.8 (5.0)	4.9 (5.3)	4.9 (4.5)	4.1 (4.1)
PGADA					
Baseline	7.0 (1.7)	7.1 (1.5)	7.0 (1.6)	6.5 (1.8)	7.1 (1.6)
Week 12	6.0 (2.4)	5.3 (2.3)	4.9 (2.2)	4.3 (2.2)	3.9 (2.2)

Conclusion: Dual neutralisation of IL-17A and IL-17F with bimekizumab was associated with improvements in patient-reported and QoL outcomes including pain, fatigue and tenderness in patients with active AS after 12 weeks of

treatment. No new safety findings were observed versus previous studies of bimekizumab.^{3,4}

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Disclosure of Interests:

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OP0232

NETAKIMAB REDUCES THE DISEASE ACTIVITY OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS. RESULTS OF ASTERA STUDY

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Background: Efficacy and safety of netakimab (NTK), a humanized anti-IL17A antibody, was established in phase 2 clinical trials in patients (pts) with radiographic axial spondyloarthritis (r-axSpA)¹ and psoriasis².

Objectives: The abstract presents 16-week data from ongoing ASTERA study (NCT03447704) in pts with active r-axSpA.

Methods: ASTERA is a phase 3 international double-blind placebo (PBO)-controlled study. 228 adult pts with r-axSpA, active (BASDAI ≥ 4) despite the standard NSAIDs, were randomly assigned (1:1) to receive 120 mg NTK or PBO SC at Week (Wk) 0, 1, 2 and then q2w through Wk 16. After Wk 16 all pts will start to receive NTK up to Wk 52. Primary endpoint was ASAS40 rate at Wk 16.

Results: The mean age at baseline was 39.14±9.9 years, the mean symptoms duration was 4.3±4.5 years. 76.8% of pts were naïve to biological treatment. At Wk 16 ASAS40 rate was higher in NTK arm compared to PBO: 40.35% versus (vs.) 2.63% pts (95% CI for the difference in ASAS40 rate was [27.37%; 48.07%] ($p<0.0001$, Figure 1). Efficacy of NTK was also proved by comparison of secondary endpoints (Figure 2); improvement in BASDAI, MASES, BASFI became significant from Wk 4 and remained during the study (no data presented). Most reported adverse events (AE) and treatment-related AEs (TRAE) were mild/moderate (Table 1). The most frequent AEs were anemia, neutropenia, ALT increase. One serious AE (SAE), not related to the treatment (bone fracture), was reported in NTK arm.

Conclusion: NTK at a dose 120 mg is well-tolerated drug with favorable safety profile that leads to decline in r-axSpA activity, function improvement and axial mobility in 16 Wks.

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Table 1. Safety data

% of patients with	NTK (n = 114)	PBO (n = 114)	p-value
AE/SAE	33.3% (38)	25.4% (29)	0.245
TRAE	17.5% (20)	14.0% (16)	0.586
SAE	0.9% (1)	0	1.0
Grade 3-4 AEs	2.6% (3)	3.5% (4)	1.0
Grade 3-4 TRAEs	1.8% (2)	1.8% (2)	1.0
Local reactions	1.8% (2)	0.9% (1)	1.0

Figure 1

Figure 2

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OP0233

THE IMPACT OF EXTRA-ARTICULAR MANIFESTATIONS ON THE CHOICE OF TNF INHIBITOR IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN THE BSRBR-AS REGISTER

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Background: Axial spondyloarthritis (axSpA) is associated with important extra-articular manifestations (EAMS), most notably acute anterior uveitis (AAU), inflammatory bowel disease (IBD) and psoriasis, which may influence the choice of biologic agent used to treat axSpA.

Objectives: To examine the factors associated with choice of 1st TNF inhibitor (TNFi) for the treatment of axSpA.

Methods: Clinical and patients-reported outcomes of 2420 patients with axSpA from 83 rheumatology centres in the United Kingdom were collected as part of the British Society for Rheumatology Biologics Register in Ankylosing Spondylitis (BSRBR-AS). History of pre-treatment AAU, IBD and psoriasis were analysed to explore their association with the choice of 1st TNFi. This preference was also examined in relation to other demographic and background factors. These associations were analysed using univariable and multivariable logistic regression models, considering necessary interaction terms.

Results: First-line biologic data was available for 441 patients, comprising of 284 (64.4%) adalimumab (ADA), 109 (24.7%) etanercept (ETA) and 48 (10.9%) certolizumab (CZP). Pre-treatment EAMS in the entire cohort were 568 cases of AAU, 247 IBD and 264 psoriasis.

Prior diagnosis of AAU was associated with a choice of ADA over the other TNFi (ETA and CZP) [OR=3.13, 95% CI: 1.78 – 5.52]. Conversely, a diagnosis of AAU was associated with less preference for ETA (OR=0.16, 95% CI: 0.07 – 0.37) compared with ADA and CZP.

The choice of a particular TNFi was not associated with HLA-B27, age, gender, axSpA disease duration, BASDAI or BASFI scores.

When IBD and psoriasis, and interactions with AAU, were considered in multivariable models (Table), a diagnosis of either AAU or IBD was associated with more preference of ADA versus other TNFi. In contrast, diagnosis of either AAU or IBD was associated with significantly less preference of ETA over other TNFi. The preference of CZP was not associated with presence any pre-treatment extra-articular manifestations.

Table 1. Pre-treatment extra-articular manifestations and the choice of 1st TNFi

		Wald	p value	OR	95% CI for OR
ADA vs. others	Acute Anterior Uveitis (AAU)	19.91	<0.001	3.79	2.11 - 6.80
	Inflammatory Bowel Diseases (IBD)	11.93	0.001	5.50	2.09 - 14.46
	Psoriasis	0.17	0.684	1.15	0.58 - 2.28
	Constant	3.08	0.079	1.23	
ETA vs. others	AAU	20.41	<0.001	0.14	0.06 - 0.33
	IBD	8.34	0.004	0.17	0.05 - 0.57
	Psoriasis	1.02	0.313	0.67	0.30 - 1.47
	Constant	27.38	<0.001	0.52	
CZP vs. others	AAU	0.01	0.959	1.02	0.48 - 2.16
	IBD	1.50	0.221	0.40	0.09 - 1.74
	Psoriasis	0.65	0.420	1.47	0.58 - 3.73
	Constant	126.09	<0.001	0.12	

Conclusion: EAMS appear to play an important role in the choice of TNFi in axSpA. Patients with previous AAU and IBD are more likely to be prescribed ADA