Spondyloarthritis - treatment

AB0750

BACK PAIN AND MORNING STIFFNESS AS MEDIATORS OF TOFACITINIB TREATMENT EFFECT ON FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A MEDIATION ANALYSIS

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Background: Fatigue is a prevalent symptom of ankylosing spondylitis (AS)[1] and can contribute to higher levels of disease, disability and poor health-related quality of life.[2] Back pain and morning stiffness are also commonly reported symptoms.[3] Tofacitinib is an oral Janus kinase inhibitor for the treatment of adult patients (pts) with AS. In randomised studies, pts with active AS treated with tofacitinib experienced greater improvements in fatigue, back pain and morning stiffness at Week 12 and 16 of treatment compared with placebo (PBO).[4,5] Treatment of these symptoms is a priority for pts with AS and their healthcare providers, however, the mechanisms underlying the interrelationships between fatigue, back pain, morning stiffness and treatment are unclear.

Objectives: To describe the interrelationships between fatigue, back pain, morning stiffness and tofacitinib treatment in pts with AS, using mediation modelling.

Methods: Data from Phase 2 (NCT01786668)[4] and Phase 3 (NCT03502616)[5] studies of pts with active AS treated with tofacitinib 5 mg twice daily (BID) or PBO were used. Mediation modelling, a statistical method to assess the extent to which the effect of an independent variable on a dependent variable is indirect, via identified mediators, or direct, capturing all other (unmeasured) effects, was applied.[6,7] The initial model included: treatment as the independent binary variable (tofacitinib 5 mg BID vs PBO); fatigue (measured by Functional Assessment of Chronic Illness Therapy-Fatigue) as the dependent variable; mediators included back pain (measured by total back pain/nocturnal spinal pain [numerical rating scale, 0–10]) and morning stiffness (represented by the mean of Bath Ankylosing Spondylitis Disease Activity Index questions 5 and 6).

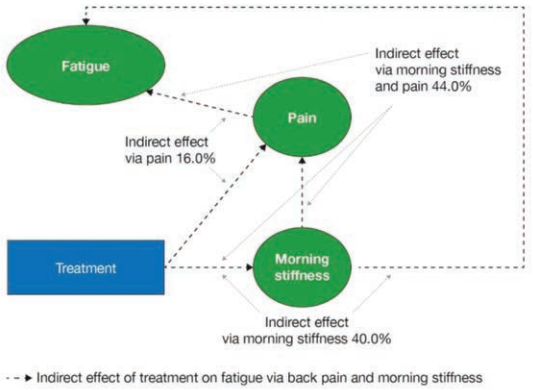
Results: Pooled data from 370 pts were included in the analysis. The initial model showed that 57.5% (p<0.001) of the tofacitinib treatment effect on fatigue was mediated via back pain and morning stiffness (indirect effect); mediation via morning stiffness alone was 49.7% (p<0.01), and 21.2% (p=0.02) via back pain alone. The effect of treatment attributable to factors other than back pain and morning stiffness (ie, direct effect) was not statistically significant (-28.4%; p=0.33). As a result, the initial model was re-specified to exclude the direct treatment effect on fatigue. In the re-specified model (Figure 1), 44.0% (p<0.0001) of the indirect effect of tofacitinib on fatigue was mediated via back pain and morning stiffness; mediation via morning stiffness alone was 40.0% (p<0.001), and 16.0% (p<0.01) via back pain alone. Analyses of the individual study data gave results generally consistent with those from the pooled data.

Conclusion: Overall, indirect pathways via morning stiffness accounted for ~84% of the effect of tofacitinib treatment on fatigue: (1) treatment affects morning stiffness, which impacts fatigue; and (2) treatment affects morning stiffness, which affects back pain and, ultimately, back pain affects fatigue. The indirect pathway via back pain alone accounted for ~16% of treatment effect on fatigue. These results suggest that in tofacitinib-treated pts with AS, improvements in fatigue are fully mediated through combined treatment effects on morning stiffness and back pain.

REFERENCES:

[1] Schneeberger EE et al. Clin Rheumatol 2015; 34: 497-501.
[2] Connolly D et al. Occup Ther Int 2019; 2019: 3027280.
[3] Braun J. Rheumatology (Oxford) 2018; 57: vi1-vi3.
[4] van der Heijde D et al. Ann Rheum Dis 2017; 76: 1340-1347.
[5] Deodhar A et al. Ann Rheum Dis 2021; 80: 1004-1013.
[6] Richiardi L et al. Int J Epidemiol 2013; 42: 1511-1519.
[7] Cappelleri JC et al. Boca Raton, FL: CRC Press, 2013.

Figure. Re-specified mediation model results



The mediation models were based on pooled data from Phase 2 (NCT01786668) and Phase 3 (NCT03502616) studies. Treatment is represented by a binary variable (tofacitinib 5 mg BID vs placebo). Pain is represented by total back pain due to AS on average during last week and pain at night due to AS on average during last week.
AS, ankylosing spondylitis; BID, twice daily

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AB0751

HOW DOES BODY MASS INDEX AFFECT SECUKINUMAB TREATMENT OUTCOMES AND SAFETY IN PATIENTS WITH ANKYLOSING SPONDYLITIS? – REAL WORLD DATA FROM THE GERMAN AQUILA STUDY

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Background: Obesity is a risk factor for worse overall health in people with ankylosing spondylitis (AS)[1]. The German non-interventional study AQUILA provides real-world data in AS on the influence of body mass index (BMI) on therapeutic effectiveness and safety under treatment with secukinumab, a fully human monoclonal antibody that selectively inhibits IL-17A.

Objectives: The aims of this interim analysis are to describe selected baseline (BL) demographics and to evaluate secukinumab treatment outcomes on disease activity and global functioning and health and to report safety profile depending on the BMI of AS patients (pts).

Methods: AQUILA is an ongoing, multi-center, non-interventional study including up to 3000 pts with active AS or psoriatic arthritis. Pts were observed from BL up to week (w) 52 according to clinical routine. Real-world data were assessed prospectively and analyzed as observed. Validated questionnaires were used to collect data on disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI) and global functioning and health (Assessment of SpondyloArthritis-Health Index,

ASAS-HI). For calculation of proportion of pts that experienced (serious) adverse events ((S)AEs), all AS pts were included that received at least one dose of secukinumab. This interim analysis focuses on BMI subgroups ≤*25* kg/m^2 (normal weight), >*25 to* ≤*30* kg/m^2 (overweight) and >*30* kg/m^2 (obese) in AS pts.

Results: At BL, BMI data were available for 667 AS pts: 33.6% (n=224) normal weight, 39.9% (n=266) overweight and 26.5% (n=177) obese AS pts (Table 1). In all BMI subgroups the proportion of men was higher, even doubled among overweight AS pts. As BMI increased, so did age and comorbidities/extraarticular manifestations (EAMs, Table 1).

Table 1. Overview of baseline characteristics in AS pts depending on BMI

Demographics	BMI ≤25 kg/m^2 (N=224)	BMI >25 to ≤30 kg/m^2 (N=266)	BMI >30 kg/m^2 (N=177)
Male*	123 (54.9)	178 (66.9)	94 (53.1)
Age, years**	43.3 (12.1)	47.5 (12.3)	49.2 (11.0)
BASDAI**	4.8 (2.0)	5.5 (1.8)	5.5 (2.0)
ASAS-HI**	7.4 (3.7)	7.7 (3.3)	8.1 (3.6)
Comorbidities/EAMs*			
Heart-related disease	4 (1.8)	12 (4.5)	12 (6.8)
Coronary heart disease	4 (1.8)	10 (3.8)	8 (4.5)
Stroke	1 (0.4)	0 (0.0)	2 (1.1)
Heart insufficiency	1 (0.4)	4 (1.5)	8 (4.5)
Uveitis	11 (4.9)	17 (6.4)	13 (7.3)
Depression	88 (55.3)	121 (58.2)	73 (54.9)

*variables are given as n (%); **variables given as mean (SD)

Mean BASDAI developed similarly over time with lowest scores for normal weight and highest scores for obese AS pts (Figure 1A). Mean improvement from BL to w52 was 1.3 (27.1%) for normal weight, 1.5 (27.2%) for overweight, and 1.2 (21.8%) for obese AS pts.

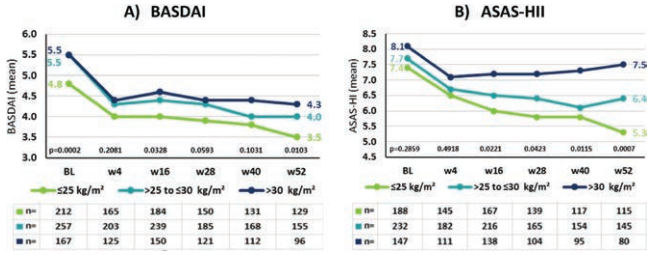

Figure 1. Disease activity and global functioning under secukinumab treatment in AS pts stratified by BMI

Mean ASAS-HI at BL was similar for all BMI subgroups (≤*25*: 7.4; >*25*-≤*30*: 7.7; >*30*: 8.1); the best improvement was observed in normal weight, the least in obese AS pts (Figure 1B). Mean improvement from BL to w52 was 2.1 (28.4%) for normal weight, 1.3 (16.9%) for overweight, and 0.6 (7.4%) for obese AS pts.

The occurrence of AEs/SAEs with or without suspected relationship to secukinumab increased with increasing BMI. For example, the percentage of SAEs in normal weight was 21%, in overweight 26.7% and in obese AS pts 30.9% (data not shown). There were no events with fatal outcome or unexpected safety signals in either subgroup.

Conclusion: In a real-world setting, secukinumab improved disease activity and global functioning and health in all BMI subgroups of AS pts; normal weight AS pts had numerically better ASAS-HI and BASDAI scores than obese AS pts. Altogether, real-world data of this interim analysis show that secukinumab is an effective treatment with a favorable safety profile up to 52 weeks in AS pts in all BMI subgroups.

REFERENCES:

[1] Chen, C.-H., *et al. International Journal of Rheumatic Diseases* **23**, 1165-1174 (2020).

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AB0752

HOW DOES TIME TO DIAGNOSIS AND GENDER AFFECT TREATMENT OUTCOMES IN PATIENTS WITH ANKYLOSING SPONDYLITIS OR PSORIATIC ARTHRITIS? – REAL WORLD DATA FROM THE GERMAN AQUILA STUDY WITH SECUKINUMAB

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Background: In both, ankylosing spondylitis (AS) and psoriatic arthritis (PsA), women typically have a longer delay in diagnosis.[1,2] There is scientific evidence that prognosis for AS and PsA improves when diagnosed early. The German non-interventional study AQUILA provides real-world data on the influence of time to diagnosis and gender on treatment outcomes under secukinumab, a fully human monoclonal antibody that selectively inhibits interleukin-17A.

Objectives: The aims of this interim analysis are to describe selected baseline (BL) demographics of AS and PsA patients (pts) and to evaluate the impact of time to diagnosis and gender on secukinumab treatment outcomes, such as disease activity and global functioning and health.

Methods: AQUILA is an ongoing, multi-center, non-interventional study including up to 3000 pts with AS or PsA. Pts were observed from BL up to week (w) 52 according to clinical routine. Real-world data were assessed prospectively and analyzed as observed. Validated questionnaires were used to collect data on disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI), global functioning and health (Assessment of SpondyloArthritis-Health Index, ASAS-HI) in AS, and skin and joint-related disease activity (Psoriasis Area and Severity Index, PASI; tender/swollen joint counts, TJC/SJC) and impact of disease (Psoriatic Arthritis Impact of Disease - 12 items, PsAID-12 score) in PsA pts. This interim analysis focused on the subgroups of male and female AS and PsA pts stratified by time to diagnosis after disease onset (˂1 year [y] and ≥1y for early and late diagnosis, respectively).

Results: At BL, 609 AS and 1145 PsA pts were included with information on time to diagnosis (Table 1); only 18.7% of AS and 25.8% of PsA pts were diagnosed within one year. Of interest, both female AS and PsA pts as well as male PsA pts with increased BMI tended to be diagnosed later (Table 1). Regarding BASDAI scores, male AS pts diagnosed late had increased disease activity at BL and throughout the study (Figure 1A); female AS pts diagnosed late showed reduced total treatment effect with increasing time to diagnosis (Figure 1B). Similarly, both male and female AS pts diagnosed late had slightly increased ASAS-HI at BL and throughout the study (Table 1). For PsA pts, there was no difference in skin- (PASI, Figure 1C/D) and joint-related (Figure 1E/F) disease activity with respect to time to diagnosis. Furthermore, there was no difference in PsAID scores (data not shown) between early- and late-diagnosed PsA pts.

Table 1. Overview of selected BL characteristics in AS and PsA pts stratified by time to diagnosis

	AS (N=609)			
	Time to diagnosis ˂1 year (n=114)		Time to diagnosis ≥1 year (n=495)	
	Male (n=63)	Female (n=51)	Male (n=301)	Female (n=194)
Age, years	43.1	46.3	45.9	47.7
BMI	27.7	25.9	27.3	27.8
BASDAI	4.7	5.0	5.3	5.2
ASAS-HI	6.7	8.0	7.4	8.2
	PsA (N=1145)			
	Time to diagnosis ˂1 year (n=295)		Time to diagnosis ≥1 year (n=850)	
	Male (n=126)	Female (n=169)	Male (n=363)	Female (n=487)
Age, years	50.1	51.8	52.3	53.1
BMI	28.7	29.4	29.3	28.8
PASI	6.5	6.2	7.0	7.2
PsAID	4.6	5.2	4.8	5.3
TJC/SJC	5.9/3.3	7.3/3.2	7.0/3.7	7.3/3.8

All variables given as mean