Spondyloarthritis treatment

AB0750 BACK PAIN AND MORNING STIFFNESS AS MEDIATORS OF TOFACITINIB TREATMENT EFFECT ON FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A MEDIATION ANALYSIS

L. E. Kristensen 1, P. C. Taylor 2, V. Navarro-Compán 3, M. Magrey 4, J. C. Cappellini 5, A. G. Bushmakin 6, A. Yndestad 7, O. Dina 8,9,10,11,12
1Copenhagen University Hospital, Bispebjerg and Frederiksberg, The Parker Institute, Copenhagen, Denmark; 2University of Oxford, Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom; 3University Hospital La Paz, IDiPaz, Madrid, Spain; 4Case Western Reserve University, Division of Rheumatology, Cleveland, OH, United States of America; 5Pfizer Inc, Inflammation and Immunology, Groton, CT United States of America; 6Pfizer Inc, Inflammation and Immunology, Oslo, Norway; 7Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America

Background: Fatigue is a prevalent symptom of ankylosing spondylitis (AS) and can contribute to higher levels of disease, disability and poor health-related quality of life. Back pain and morning stiffness are also commonly reported symptoms. 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). 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) and Phase 3 (NCT03502016) studies of pts with active AS treated with tofacitinib 5mg 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. The initial model included: treatment as the independent binary variable (tobacitinib 5mg 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 ~44% 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:

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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

U. Kiltz 1, J. Brandt-Juergens 2, P. Klotzner 3, E. Riechers 4, D. Peterlik 5, C. Budden 6, H. P. Tony 7
1Rheumazentrum Ruhrgebiet, Herne and Ruhr-Universität Bochum, Herne, Germany; 2Rheumatologie, Schwerpunktpraxis, Berlin, Germany; 3Ambulantes Rheumazentrum, Medizinisches Versorgungszentrum, Erfurt, Germany; 4Medizinische Hochschule Hannover, Hannover, Germany; 5Novartis Pharma GmbH, Immunologie, Hepatologie & Dermatologie, Nürnberg, Germany; 6Novartis Pharma GmbH, Immunologie, Hepatologie & Dermatologie, Nürnberg, Germany; 7Novartis Pharma GmbH, Immunologie, Hepatologie & Dermatologie, Nürnberg, Germany.

Background: Obesity is a risk factor for worse overall health in people with ankylosing spondylitis (AS). 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, AASFI).

The mediation models were based on pooled data from Phase 2 (NCT01786668) and Phase 3 (NCT03502016) studies. Treatment is represented by a binary variable (tobacitinib 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.