SAT0315 STRUCTURAL DAMAGE PROGRESSION OVER 4 YEARS OF SECUKINUMAB TREATMENT IN ANKYLOSING SPONDYLITIS: POST-HOC ANALYSIS OF MEASURE-1 TRIAL USING A LONGITUDINAL BAYESIAN MIXTURE MODEL

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Background: Ankylosing spondylitis (AS) is an inflammatory disease resulting in progressive disability due to structural damage in the spine. The identification of predictors of progression would allow treating physicians to personalize treatments but requires an approach accounting for a relatively short follow-up of clinical studies, large between-patient variability, and low sensitivity of X-ray images which generate intra-patient variability when repeated measurements are taken.
Objectives: 1) To identify patient characteristics predicting faster structural damage progression. 2) To quantify the progression over four years of secukinumab treatment, depending on dose/exposure.
Methods: Data came from the phase 3 randomized placebo-controlled trial MEASURE 1 (NCT01358175)[1] in which patients were treated with secukinumab (intravenous loading of 10 mg/kg at weeks 0, 2, and 4, followed by secukinumab subcutaneously at a dose of either 75 mg or 150 mg every 4 weeks) over 208 weeks. Only patients treated with secukinumab with at least two assessments of structural damage were included. We explored the effect of multiple baseline demographic traits, disease stage, severity, bone cartilage biomarkers as well as prior and current treatment on change in modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) using a longitudinal Bayesian mixture model with random effects, which accounted simultaneously for the probability of progression, magnitude of progression and inter-patient variability. Posterior predictive check was performed.
Results: Out of 249 patients randomized to secukinumab, 167 had their structural damage assessed at least twice. These patients contributed in total 409 assessments of change in structural damage between weeks 0, 52, 104 and 208.
Of the factors tested, a higher baseline BASMI score was associated with faster progression rate in a statistically significant way (+0.60 in mSASSS/year for each additional standard deviation of baseline BASMI (SD=1.74), 95% interval 0.03 to 1.14). Trends were also detected for association between faster mSASSS progression and younger age, prior exposure to TNFα inhibitor, HLA-B27 positivity, and higher osteocalcin levels. Increased exposure to secukinumab was associated with slower structural damage progression (-0.23 in mSASSS/year for each additional standard deviation in exposure, 95% interval -0.58 to 0.10). Model estimation suggested that secukinumab 150 mg was associated with a yearly progression of -0.2 (95% interval -1.2 to 0.8) in the first two years of treatment and 0.1 mSASSS (95% interval -0.8 to 1.0) in the third and fourth year of treatment. Analogously, secukinumab 75mg (currently not approved for clinical use) was associated with a progression of -0.2 mSASSS/year (95% interval -1.3 to 0.9) in the first two years of treatment and 0.5 mSASSS/year (95% interval -0.5 to 1.6) in the third and fourth year of treatment.
Conclusion: Potential predictors of structural progression suggested by the model were higher baseline BASMI, younger age, prior exposure to TNFα inhibitor, HLA-B27 positivity, and higher osteocalcin at baseline, although only baseline BASMI showed statistical significance. Further analyses using larger, deeper and real-world data are needed to confirm these findings and to estimate progression rates in AS patients in daily practice.

REFERENCE

[1] Baeten D, Sieper J, Braun J, et al. Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis. N Engl J Med. 2015;373(26):2534-2548.

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SAT0316 EARLY RECOGNITION OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS BY USING A PRACTICAL REFERRAL SYSTEM – EVALUATION OF THE RECENTLY PROPOSED 2-STEP STRATEGY

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Background: Early recognition of axial spondyloarthritis (axSpA) in primary care (PC) is difficult due to the high prevalence of low back pain resulting in a major delay for a diagnosis of axSpA. Recently we proposed a 2-step referral strategy (1) which concentrates on patients ≤45 years with chronic back pain who are to be referred to a rheumatologist if fulfilling 2 of 3 features: buttock pain, improvement by movement, psoriasis (Step 1), or, in case of ≤1 feature, positive testing for HLA-B27 (Step 2).
Objectives: To prospectively evaluate this 2-step referral strategy in PC.
Methods: Consecutive patients ≤45 years who presented in PC to general practitioners or orthopedic surgeons working in PC with back pain lasting ≥2 months who had not been diagnosed before received questionnaires (Q1) relevant for the referral process. Thereafter, the PC physician asked the same questions in a separate questionnaire (Q2), including the decision on HLA-B27 testing. All patients were then referred to two experienced rheumatologists in a tertiary center who performed a complete workup including clinical, laboratory and imaging with radiographs and magnetic resonance imaging (MRI) examinations before their final diagnosis of axSpA or non-SpA (Q3).
Results: A total of 320 patients (mean age 35.9±10.3 years) was recruited. The proposed referral strategy (prS) was fulfilled by 127 patients in Q1 (39.7%), 160 in Q2 (50%), 102 by both, Q1 and Q2 (31.9%), and 83 with either Q1 or Q2 (25.9%). Overall, 47 patients were diagnosed with axSpA by the rheumatologist at Q3 (14.7%), 66% of which were male, mean age 34.7±10.1 years, 70.2% HLA-B27 positive, mean CRP 0.8±1.4mg/dl, mean ASDAS 3.2±0.8, mean BASDAI 5.1±2.0. Of these, 37 patients had fulfilled the prS in Q1 or Q2 (78.7%), and 31 in both Q1 and Q2 (66%), respectively. In the latter, the HLA-B27 prevalence was significantly higher (27/31, 87.1%) as compared to patients diagnosed with axSpA at Q3 but who did not fulfill the prS in Q1 and Q2 (5/16, 31.3%) ($p<0.001$).
The sensitivity and specificity of the prS was 78.7% and 69.2% in Q1, 78.7% and 62.2% in Q2, and in both, Q1 and Q2, 66% and 74%, respectively.
AxSpA patients correctly identified by the prS in Q1 and Q2, were significantly more frequently positive for HLA-B27 and CRP and fulfilled more frequently the ASAS definition of inflammatory back pain in Q3.
Conclusion: This study confirms the feasibility a simple referral strategy using a combination of clinical features for identifying axSpA patients in PC without laboratory and imaging examinations. This strategy performed already well at the early patient and PC physician level just based on a symptom-based questionnaire.

REFERENCE

[1] Braun A et al, ARD 2011

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