for: Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, Speakers bureau: Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, J. Sieper Grant/research support from: AbbVie, Merck, Pfizer, and UCB, Consultant for: AbbVie, Merck, Pfizer, and UCB, Speakers bureau: AbbVie, Merck, Pfizer, and UCB, R. Inman Grant/research support from: AbbVie, Amgen, Janssen, Lilly, and Novartis, A. Pangan Employee of: AbbVie, X. Wang Employee of: AbbVie, J. Anderson Employee of: AbbVie

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THU0389 IS THERE ANY ROLE OF IMMUNOGENICITY ON THE RESPONSE TO THE ANTI-TUMOR NECROSIS FACTOR ALPHA THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: THE FIRST RESULTS OF A PROSPECTIVE COHORT STUDY

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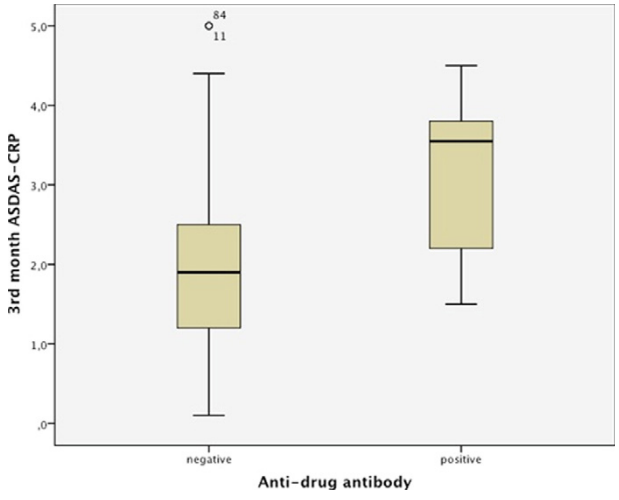
Background: Although anti-tumour necrosis factor agents (anti-TNFs) are very effective in most patients with ankylosing spondylitis (AS) significant proportion of patients quit the treatment due to non-response or adverse events. The development of anti-drug antibodies (ADAs) and low serum drug levels might have a mechanistic role in loss of efficacy of or the development of adverse events in patients treated with anti-TNFs. There is limited data regarding the immunogenicity of anti-TNFs in patients with AS.
Objectives: Therefore the aim of this study was to evaluatethe relationship between the formation of ADAs, serum through drug levels and clinical response to anti-TNFs in patients with AS.
Methods: In total 350 AS patients with a new anti-TNF agent prescription in the last two weeks period were planned to include this multi-center prospective observational cohort study. Herein we are presenting the data of first 102 patients who had >3months follow-up. Clinical data and serum samples were collected at baseline and at every three months of treatment. Serum drug levels and ADAs were measured by ELISA in one center to avoid inter-assay variability.
Results: 102 biologic naïve AS patients (75 [74%] male, mean (±SD) age; 37.2±10.7 years) who started anti-TNF agents (14 infliximab [13.7%], 27 adalimumab [26.5%], 33 etanercept [32.4%] and 28 golimumab [27.5%]) were included in the present analysis. In comparison to baseline values BASDAI, ASDAS-CRP and CRP values were significantly decreased in third months of follow-up ($P<0.001$) (table). At 12 weeks of follow-up 9 patients (9%; 2 on infliximab and 7 adalimumab) had ADAs and 20 (20%; 10 on adalimumab, 4 infliximab, 4 golimumab and 2 etanercept) had no detectable drug levels.The presence of ADAs were significantly correlated with serum drug levels ($P<0.001$). Up to 12 months of follow-up none of patients treated etanercept developed ADAs. Third month BASDAI and ASDAS-CRP values were significantly higher in patients with ADAs (BASDAI values were 5.2±1.4 vs 3.0±1.8; $P<0.001$ and ASDAS-CRP values were 3.1±1.0 vs 1.9±1.1; $P<0.001$) (figure) and patients with no detectable drug levels BASDAI values were 4.1±1.8 vs 2.9±1.8; $P=0.012$ and ASDAS-CRP values were 2.7±1.3 vs 1.9±1.0; $P=0.015$).
Conclusions: ADAs against anti-TNF agents might develop as early as 12 weeks of treatment. Our results confirm that ADA development may hinder the anticipated response to anti-TNF agents in patients with AS.

Table 1. Baseline and third month's follow-up indicators of activity and response in AS patients treated with anti-TNF agents

	Baseline	Third month
BASDAI	6.8±5.2	3.2±1.9
ASDAS-CRP	4.1±2.5	2.0±1.1
CRP	23.8±32.8	7.9±13.9



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THU0390 EFFECT OF REHABILITATION ON THE CHEST EXPANSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis that leads to pain, stiffness, progressive spinal deformity, and spinal fusion, limitation of the spine, rib cage motion and severe functional impairment. Pulmonary function is altered in AS owing mainly to the limited chest expansion.
Objectives: The purpose of this study was to investigate the effect of rehabilitation on the limited chest expansion measured by respiratory index and relationship between duration of the rehabilitation and age, disease onset, disease duration and respiratory index in patients with AS during physical treatment and rehabilitation.
Methods: The study was designed as a retrospective study that included 47 consecutive AS patients (33 male and 14 female), average age of 52.53±11.58 years that were hospitalized and treated in rehabilitation center. Average duration of the rehabilitation was 17.77±5.92 days. Respiratory index was measured for all AS patients at the beginning and at the end of rehabilitation with a centimeter ribbon. Student's t-test and Pearson's test of correlation were used for statistically analysis.
Results: Average disease duration was 13.35±8.74 years, disease onset was at 39.64±12.87 years. Respiratory index was 1.98±1.34 cm at beginning of rehabilitation and 3.01±1.75 cm at the end of rehabilitation. The difference was statistically significant (t=8.025, $p<0.001$). Pearson's test of correlation was shown statistically significant correlation between value of respiratory index at beginning and at the end of rehabilitation (r=0.872, $p<0.001$). Duration of the rehabilitation (hospital days) statistically significant correlate with value of respiratory index at beginning rehabilitation (r=-0.289, $p<0.05$), but not with age, disease duration and disease onset ($p>0.05$).
Conclusions: The physical therapy and rehabilitation has led to the improvement the respiratory index in patients with AS, which confirms its effectiveness. The value of respiratory index at beginning rehabilitation is associated with duration of the rehabilitation. Significant limitation in respiratory index indicates longer hospital stay. These results could be having importance in planning of rehabilitation of patients with AS.

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THU0391 FEMALE GENDER IS ASSOCIATED WITH A POORER RESPONSE TO TNF INHIBITORS IN ANKYLOSING SPONDYLITIS

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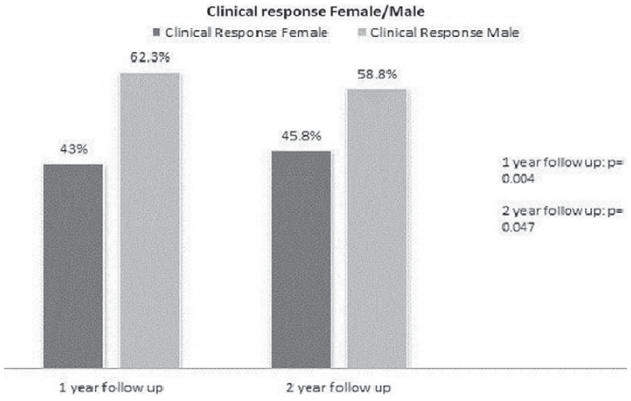
Background: Limited data are available on the influence of gender and lifestyle factors, such as smoking, alcohol consumption and Body Mass Index (BMI) on disease activity and response to TNF inhibitors (TNFi) in ankylosing spondylitis (AS).
Objectives: This study aimed to determine whether these factors influence age at diagnosis, disease activity and response to TNFi.
Methods: In a prospective study, clinical data (age, gender, C-reactive protein, Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Score (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI), smoking, alcohol consumption and BMI) were collected in AS patients from a observational cohort, who started or switched treatment with TNFi. Data were collected at baseline and after 6, 12 and 24 months. Independent T-tests and linear regression analyses were performed to assess the influence of gender and lifestyle factors on age at diagnosis and disease activity.

Results: In total, 312 consecutive AS patients, 34% female, were included with a mean follow-up of 18.9 months. Most patients (172, 55%) showed significant improvement after start of TNFi of whom 86 patients (28%) had a clinically important (ASDAS decrease >1.1) and 86 (26.9%) a major clinical improvement (ASDAS decrease >2.2). BMI was significantly correlated with age at diagnosis (p=0.016; 95% CI: 0.07 – 0.65): an increase of BMI with three points delayed the AS diagnosis with one year. At baseline, smoking and gender were not correlated with the ASDAS, but BASDAI and BASMI were both inversely related to BMI. Male gender was significantly associated with a higher chance at clinical response (improvement of the BASDAI with 50% or a 2 point decrease) to TNFi (p=0.041). At one year follow-up the clinical improvement of males versus females was respectively 62% vs. 43% and at two year follow-up 59% vs. 46%. Males also showed a significantly higher ASDAS improvement after one year of follow-up compared to females (p=0.015).



Conclusions: Significantly less females had a clinical response compared to males after one and two years of TNFi treatment. A higher BMI not only prolonged the time to AS diagnosis up to one year, but also negatively influenced the BASDAI and BASMI scores. Female gender and high body weight should be taken into consideration when the efficacy of TNFi is assessed, by stratifying for these factors in the analysis.

Disclosure of Interest: None declared

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THU0392 DO WE REALLY NEED DMARDS ADDITION TO ANKYLOSISNG SPONDYLITIS PATIENTS TREATED WITH TUMOR NECROSIS FACTOR ALPHA INHIBITORS?

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Background: The management of systemic inflammatory diseases, such as Rheumatoid arthritis (RA) and Ankylosing spondylitis (AS) has been revolutionized with the introduction of tumor necrosis factor alpha inhibitors (TNF-I). Significant reduction in disease activity and achievment of remission resulted in halting of joint damage and improved quality of life. Unfortunately, approximatly 15–30% of patients fail to reach desirable improvement or lose drug effectiveness with time. It may be explained by immunogenicity and production of human anti chimeric antibodies (HACA). Presence of HACA against TNF-I have been associated with low levels of the drug and lose of therapeutic response. The prevalence of HACA in RA is estimated between 20–40%, and in AS between 25–64%. The difference in the pathogenesis of RA and AS as well as diverce approach in using disease modifying anti-rheumatic drugs (DMARDs) may influence HACA production and TNF-I levels in these conditions.

Objectives: To compare the incidence of HACA and Infliximab, Etanercept, Adalimumab levels in patients with RA and AS with respect to concomitant DMARDs.

Methods: Patients' with RA and AS data treated with TNF-I for at least 3 months in whom tests for HACA and Infliximab, Etanercept, Adalimumab levels were available were extracted from patients' files. Data included: demographics, concomitant treatment, and disease activity scores (BASDAI for AS and DAS-28 for RA). Serum for assessment of drugs level (ELISA) and HACA (ADAb;Promonitor, Bridging, ELISA) was obtained before the next drug administration. Univariate comparison was done using Student t test for the continuous variables and Chi square test for the categorical variables (P <.05 was considered significant).

Results: Data on 53 patients with AS (mean age 47.9±11.9 years, 41.5. % female) and 29 patients with RA (mean age 54.8±8.1 years, 75, 9% female) were available: 22 RA patients were treated with Methotrexate and 7 with other DMARDs; no one AS patient was treated with concomitant DMARDs. High level of HACA was found in 22.6% AS patients and in 34.5% RA patients (p>0.05); 86.8% patients with AS reached theurapethic level of drug compared to 69% RA patients (p=0.027). Drugs levels were similar in AS and RA patients (Table). Low disease activity (DAS28-CRP<3.2) was registered in 62.1% RA patients and in 81.4% AS patients (BASDAI <4).

Conclusions: Despite significant difference in the use of concomitant DMARDs, patients with AS and RA had similar prevalence of HACA. Moreover, higher proportion of patients in AS group reached therapeutic level of TNF-I. The data supports the hypothesis, that immune responce to TNF-I may be different in AS and RA and, therefore, the addition of DMARDs to prevent development of HACA in patients with AS may be unnecessary.

Disclosure of Interest: None declared

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THU0393 SECUKINUMAB PROVIDES SUSTAINED REDUCTION IN FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS THROUGH 3 YEARS: LONG-TERM RESULTS OF TWO RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED PHASE 3 STUDIES

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Background: In patients (pts) with ankylosing spondylitis (AS), fatigue is a common symptom negatively affecting health-related quality of life (HRQoL) and social functioning. Secukinumab (SEC), a fully human anti–IL-17A mAb, rapidly improved signs and symptoms, physical functioning, and HRQoL in pts with AS.[1,2]

Objectives: To assess the long-term effects of SEC on fatigue in TNF inhibitor (TNF)-naïve and TNF inhibitor inadequate responder/intolerant (TNF-IR) AS pts in MEASURE 1 and MEASURE 2.

Methods: 371 and 219 pts were randomized to SEC or placebo (PBO) in MEASURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and MEASURE 2 (150 or 75 mg SC), respectively. At Week (Wk) 16, non-responder PBO pts were re-randomized to SEC 150 or 75 mg SC (in MEASURE 1, PBO pts achieving ASAS20 response at Wk 16 were switched to SEC at Wk 24). Fatigue was measured at baseline (BL) and Wks 4, 8, 12, 16, 24, 52, 104 and 156 using FACIT-F, which assesses fatigue in the previous 7 days using 13 questions graded on a 0–4 scale (higher scores=less fatigue). An increase from BL in FACIT-F score of ≥4 points (based on MCID) was used to define "response". Approximately 69% of pts were TNF-naïve and 31% were TNF-IR across both trials. Analyses were based on the full analysis set and subgroups stratified by prior TNF therapy. Correlations between BL characteristics and improvements in fatigue were investigated using a logistical regression model. Only data from the approved dose (SEC 150 mg) are presented.

Results: FACIT-F was 24.5–25.6 and 22.6–24.3 at BL across groups in MEASURE 1 and 2, respectively. Improvements in FACIT-F with SEC at Wk 16 were sustained through Wk 156 in MEASURE 1 and Wk 104 in MEASURE 2 (Table). Rapid and sustained fatigue responses were also seen in subgroups stratified by prior TNF use. In the overall population, LS mean changes (±SEM) from BL in FACIT-F scores were significantly greater with SEC vs PBO at Wk 16 in both MEASURE 1 (7.60±0.99 vs 3.34±1.00, *P*=0.002) and MEASURE 2 (8.10±1.09 vs 3.27±1.09, *P*=0.018); reductions in fatigue were sustained throughout the entire follow up in both trials (MEASURE 1 Wk 156: 9.81±0.95; MEASURE 2 Wk 104: 9.27±1.13). Similar results were reported in both TNF-naïve and TNF-IR pts. Correlational analyses based on pooled data from both trials did not identify any BL factors that

Table: FACIT-F responders in MEASURE 1 and MEASURE 2 with secukinumab 150 mg[a]

	Proportion of Patients with FACIT-F Response[b], % (n/m)			
	Week 16	Week 52	Week 104	Week 156
MEASURE 1[c]				
Overall (N=87)	66.7 (58/87)	73.6 (64/87)	72.2 (57/79)	75.6 (65/86)
TNF-naïve (N=70)	70.0 (49/70)	75.7 (53/70)	70.3 (45/64)	74.3 (52/70)
TNF-IR (N=17)	52.9 (9/17)	64.7 (11/17)	80.0 (12/15)	81.3 (13/16)
MEASURE 2				
Overall (N=72)	77.6 (52/67)	80.6 (50/62)	81.4 (48/59)	–
TNF-naïve (N=44)	86.0 (37/43)	90.0 (36/40)	84.6 (33/39)	–
TNF-IR (N=28)	62.5 (15/24)	63.6 (14/22)	75.0 (15/20)	–

[a]Observed data are shown; [b]Defined as improvement (increase in FACIT-F score) by ≥4.0 points from BL; [c]Data shown are from patients who entered the MEASURE 1 long-term extension study at Week 104 (NCT01863732)
m, number of patients with sufficient data for evaluation; N, number of patients randomized to SEC 150 mg
n, number of responders