FRI0416

THE EFFICACY AND SAFETY OF ANTI-TNF α TREATMENT IN ANKYLOSING SPONDYLITIS PATIENTS WITH LATE ONSET COMPARED TO THOSE WITH ADULT ONSET; THE DATA FROM TURKBIO REGISTRY

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Background: The first symptoms of ankylosing spondylitis (AS) patients usually begin prior to 45 years, but can occur later in life.

Objectives: The purpose of this study is to evaluate the efficacy and safety of anti-TNF α treatment in late-onset AS (LoAS) patients in comparison to those with adult onset AS (AoAS).

Methods: We studied AS patients in TURKBIO registry between the dates of January 2011 and November 2018. All the patients fulfilled the modified New York criteria for AS¹ and were classified into 2 groups based on their age at symptom onset: AoAS (age $\geq$ 16 but $\leq$ 45 years); and LoAS (age $\geq$ 45 years). In both groups, the following data were compared: (1) epidemiological variables (2) clinical manifestations, including signs and symptoms at diagnosis; (3) laboratory results (4) disease activity markers and follow-up parameters (BASDAI, ASDAS-CRP and HAQ); (5) previous and current treatments (6) adverse events.

Results: A total of 2551 AS patients (91.1% with AoAS and 8.9% with LoAS) were included in the study. LoAS group had more female patients, older age, shorter disease duration and diagnostic delay, higher initial ESR and less HLA-B27 positivity compared to the AoAS (Table 1). Peripheral arthritis (not statistically significant) and dactylitis was seen more common in the LoAS. The frequency of other involvements was similar between the groups (Table1). The frequency of using drugs was similar between each groups although the use of glucocorticoids and sulphasalazine was more common in the LoAS. Switching from the first anti-TNF α treatment to the second one was more common in the AoAS. However, there was found no significant difference between the two groups in 2 or more switch ratios (Table 1). At the latest visit after the anti-TNF α therapy, the mean improvement in BASDAI was significantly higher in the AoAS (Table 2). A total of 10 (4.4%) serious adverse events were reported in LoAS and 39 (1.7%) in AoAS patients in the follow-up (HR: 2.62; 95% CI: 1.32–5.18). Severe infections were the most commonly seen serious adverse events (1.3% in LoAS and 0.8% in AoAS), followed by allergic reactions (0.9% in LoAS and 0.3% in AoAS). Tuberculosis was observed in 2 patients (0.9%) in LoAS and 9 (0.4%) in AoAS, malignancy in 3 patients (1.3%) in LoAS and 6 (0.3%) in AoAS.

Conclusion: Our data showed that almost 8.9% of the patients with AS had late-onset of symptoms. The results suggested that LoAS patients might have different demographic, clinical features, disease activity parameters at baseline. The frequency of anti-TNF α use and response rate to the treatment was also similar in LoAS to those in AoAS patients. The LoAS patients seem to have more common severe adverse events compared to the AOAS patients possibly related to their older age.

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Table 1. Demographic and clinical characteristics of patients with AoAS and LoAS

	AoAS ($\leq$ 45 yrs)	LoAS ($\geq$ 45 yrs)	p-value
N	2324	227	
Sex (male), n (%)	1411 (61)	109 (48)	0.000
Age, yrs	43.07 $\pm$ 10.26	62.10 $\pm$ 8.59	0.000
Duration of disease, yrs	14.50 $\pm$ 9.42	8.53 $\pm$ 6.27	0.000
Delay of diagnosis, yrs	6.12 $\pm$ 6.61	3.59 $\pm$ 4.37	0.000
HLA-B27 positivity, (%)	64	44	0.000
C-reactive protein (mg/L)	16.66 $\pm$ 24.32	19.20 $\pm$ 26.37	0.169
Erythrocyte sedimentation rate (mm/hr)	26.83 $\pm$ 21.56	34.47 $\pm$ 24.56	0.000
BASDAI	38.9 $\pm$ 22.6	34.6 $\pm$ 22.1	0.007
BASFI	29.3 $\pm$ 22.7	30.4 $\pm$ 23.8	0.535
ASDAS-CRP	2.70 $\pm$ 1.19	2.69 $\pm$ 1.21	0.454
HAQ	0.78 $\pm$ 0.60	0.92 $\pm$ 0.69	0.008
Uveitis, n (%)	192 (8)	14 (6)	0.328
Peripheral arthritis, n (%)	389 (17)	50 (22)	0.055
Enthesitis, n (%)	339 (15)	31 (14)	0.779
Dactylitis, n (%)	77 (3)	15 (7)	0.019
Inflammatory bowel disease, n (%)	41 (2)	7 (3)	0.254
Psoriasis, n (%)	30 (1)	0 (0)	0.162
Treatment, n (%)			
NSAIDs	762 (33)	70 (31)	0.600
Sulphasalazine	176 (8)	35 (15)	0.000
Methotrexate	111 (5)	16 (7)	0.179
Glucocorticoid	62 (3)	15 (7)	0.002
Anti-TNF α	1467 (63)	134 (59)	0.252
Secukinumab	31 (1)	2 (1)	0.788
Anti-TNF α switch, n (%)			
One switch	359 (15)	22 (10)	0.026
Two switch	113 (5)	7 (3)	0.297
Three switch	25 (1)	3 (1)	0.996
Four switch	8 (0.3)	0 (0)	0.792

AoAS: adult-onset ankylosing spondylitis, LoAS: late-onset ankylosing spondylitis
*Continuous variables were presented as mean $\pm$ SD for both tables

Table 2. Changes in follow-up parameters between the baseline and the latest visits in patients on biologicals

	AoAS ($\leq$ 45 yrs)			LoAS ($\geq$ 45 yrs)		
	Baseline (mean $\pm$ SD)	Latest follow-up (mean $\pm$ SD)	Change (mean $\pm$ SD)	Baseline (mean $\pm$ SD)	Latest follow-up (mean $\pm$ SD)	Change (mean $\pm$ SD)
BASDAI	38.9 $\pm$ 22.6	23.7 $\pm$ 21.6*	15.2 $\pm$ 23.6	34.6 $\pm$ 22.1	23.4 $\pm$ 21.1*	11.2 $\pm$ 20.8**
BASFI	29.3 $\pm$ 22.7	20.9 $\pm$ 19.9*	8.3 $\pm$ 20.2	30.4 $\pm$ 23.8	24.1 $\pm$ 23.4*	6.3 $\pm$ 20.3
ASDAS-CRP	2.70 $\pm$ 1.19	1.98 $\pm$ 1.08*	0.72 $\pm$ 1.23	2.69 $\pm$ 1.21	2.03 $\pm$ 1.08*	0.65 $\pm$ 1.17
CRP (mg/L)	16.66 $\pm$ 24.32	11.33 $\pm$ 18.87*	5.33 $\pm$ 24.60	19.20 $\pm$ 26.37	13.71 $\pm$ 18.27*	5.49 $\pm$ 25.25
HAQ	0.78 $\pm$ 0.60	0.59 $\pm$ 0.47*	0.19 $\pm$ 0.52	0.92 $\pm$ 0.69	0.71 $\pm$ 0.58*	0.21 $\pm$ 0.55

*Baseline vs the latest visits, p<0.05

**Change between the baseline and the latest visits in AoAS vs LoAS groups, p<0.05

FRI0417

ETANERCEPT TREATMENT IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND AN INADEQUATE RESPONSE TO NONSTEROIDAL ANTI-INFLAMMATORY DRUGS: PERIOD 1 RESULTS FROM THE RE-EMBARK TRIAL

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Background: Etanercept (ETN) is efficacious in patients with non-radiographic axial spondyloarthritis (nr-axSpA).¹ However, little is known² about the effect of ETN withdrawal in patients with nr-axSpA who achieved a significant clinical response.

Objectives: The primary objective of this ongoing, 3-period study is to estimate the proportion of patients with nr-axSpA who experienced a flare (Ankylosing Spondylitis Disease Activity Score with erythrocyte sedimentation rate [ASDAS-ESR] $\geq$ 2.1) within 40 weeks post-ETN withdrawal, after achieving inactive disease (ASDAS with C-reactive protein [ASDAS-CRP] $<$ 1.3). Here, we report results of the 24-week Period 1, whose goal was to generate a population of ETN-treated patients with inactive disease.

Methods: RE-EMBARK (NCT02509026) is a multicenter, open-label trial in 18-50-year-old patients with active nr-axSpA (defined as fulfillment of Assessment in Spondyloarthritis International Society [ASAS] criteria, but not modified New York criteria, plus ASDAS-CRP $\geq$ 2.1), with an inadequate response to $\geq$ 2 nonsteroidal anti-inflammatory drugs (NSAIDs),

who were on a stable NSAID dose for ≥ 2 weeks. In Period 1, all patients received ETN (50 mg/week) plus NSAID for 24 weeks. At week 24, patients who achieved inactive disease qualified for Period 2 and were withdrawn from ETN treatment for 40 weeks. In Period 3, patients who experience a flare during Period 2 will be retreated with ETN for 12 weeks. Efficacy outcomes for Period 1 included the proportions of patients achieving inactive disease and 20% and 40% improvements in ASAS disease activity (ASAS20 and ASAS40), as well as the changes from baseline in the Spondyloarthritis Research Consortium of Canada (SPARCC) scores for the sacroiliac joint (SPARCC-SIJ) and the spine (SPARCC-Spine). Efficacy analyses presented here were performed on the observed cases.

Results: Of 209 treated patients, 112 (54%) were men, 186 (89%) white, 142 (68%) had MRI-evident sacroiliitis, and 162 (78%) were HLA-B27-positive. The mean baseline score for ASDAS-CRP was 3.5, 8.5 for SPARCC-SIJ, and 2.7 for SPARCC-Spine. Twenty-one (10%) patients discontinued the trial. A significant decrease in ASDAS-CRP score was observed at all post-baseline visits (Panel A). At Week 24, 62% (117/188) of patients achieved inactive disease (Panel B), 86% (163/190) and 76% (144/190) achieved ASAS20 and ASAS40, respectively, and there was a significant reduction from baseline in SPARCC-SIJ (-5.8; $P < 0.001$) and SPARCC-Spine (-1.5; $P = 0.002$). Seventy-nine (38%) patients experienced TEAEs, and 1 (0.5%) patient experienced a serious TEAE (cellulitis).

Conclusion: Majority of patients with active nr-axSpA and an inadequate response to NSAIDs achieved inactive disease and reduction of inflammation in both the SIJ and the spine with 24-week open-label ETN treatment. There were no unexpected safety signals.

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FRI0418

SECUKINUMAB PROVIDED SIMILAR EFFICACY IN MALES AND FEMALES WITH ACTIVE ANKYLOSING SPONDYLITIS OVER 52 WEEKS: POST HOC POOLED ANALYSIS OF THE MEASURE TRIALS

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Background: The burden of ankylosing spondylitis (AS) is reported to be higher in female patients (pts). In addition, females show less improvement in AS outcome measures as compared to males when treated with tumour necrosis factor (TNF) inhibitors.^{1,2} Currently, there are no data available on the efficacy of secukinumab (SEC) in males versus females.

Objectives: To compare the efficacy of SEC in pts with active AS by gender (male vs female) from data pooled from four phase 3 studies (MEASURE 1-4).

Methods: This *post hoc* analysis pooled data from the MEASURE 1-4 trials. Baseline (BL) demographics and disease characteristics were summarized across genders. Efficacy outcomes assessed at Week (Wk) 16 and 52 were ASAS20, ASAS40, ASDAS-ID, BASDAI, BASMI, BASFI, SF-36 PCS and FACIT-F. BL predictor analysis used multivariable logistic regression (binary variables) or generalized linear model (continuous variables) to assess the impact of gender as an independent variable on ASAS40, ASDAS-ID, and BASDAI at Wk 52, after adjusting for treatment group and other baseline factors in a pooled analysis across studies and treatment groups.

Results: Overall, 647 males and 322 females who received SEC 300mg IV load (LD) (n=76), 150mg IV LD (n=199), 150mg s.c. LD (n=188), 150mg no LD (n=117), and placebo (n=389), respectively, were included in the analysis. At BL, significant differences in TNFi, HLA-B27, and smoking status were observed between genders. MASES scores were significantly higher in females; hs-CRP, BASMI-occiput to wall, and BASMI tragus to wall distance scores were significantly higher in males. Efficacy outcomes were generally similar in males and females (Figure 1). There was no significant impact of gender as an independent predictor of SEC efficacy at Wk 52 as measured by ASAS40 (Odds ratio [OR] 1.1; $P = 0.50$), ASDAS-ID (OR 1.32; $P = 0.16$) or change in BASDAI (treatment effect, -0.17; $P = 0.82$).

Conclusion: Similar efficacy outcomes were observed in male and female patients with active ankylosing spondylitis treated with secukinumab over 52 weeks.

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Figure 1. Summary of Efficacy Responses by Gender: A. BASDAI Mean Change from Baseline and B. ASAS40 Response Rates

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