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Background: According to previous studies, the effectiveness of interleukin-17 (IL-17) inhibitors was higher in anti-TNF-naïve patients with ankylosing spondylitis (AS) [1,2]. Netakimab (NTK) is a humanized anti-IL-17A antibody approved for the treatment of AS, psoriatic arthritis, moderate-to-severe plaque psoriasis in Russia and Belarus.

Objectives: To compare the efficacy of NTK in anti-TNF-naïve patients with anti-TNF-experienced patients with active AS at week 16 of therapy.

Methods: ASTERA (NCT03447704) is an ongoing phase 3 placebo (PBO)-controlled clinical study, aimed at evaluating NTK efficacy in AS [3]. 228 adult patients with active AS (BASDAI ≥ 4) were randomly assigned (1:1) to receive 120 mg NTK or PBO subcutaneously at week 0,1,2 and then q2w. This analysis includes 112 patients in NTK group. Efficacy endpoints included ASAS20/40, ASAS5/6 and ASAS partial remission (PR) at week 16 of therapy.

Results: 28 (25.0%) of 112 patients in NTK group had previous inadequate response/intolerance to anti-TNF (anti-TNF-IR): 24 (21.4%) – one anti-TNF, and 4 (3.6%) – two anti-TNF. 84 (75.0%) patients were TNF-naïve. Achievement of ASAS criteria response at week 16 was similar in both groups (Table 1).

Table 1. Efficacy of NTK at week 16

Parameter	TNF-naïve (n = 84)	anti-TNF-IR (n = 28)	p-value*
ASAS20, n (%)	52 (61.9%)	17 (60.7%)	0.91
ASAS40, n (%)	35 (41.7%)	11 (39.3%)	0.82
ASAS5/6, n (%)	39 (46.4%)	11 (39.3%)	0.51
ASAS(PR), n (%)	15 (17.9%)	4 (14.3%)	0.78

*. Fisher's exact test

Conclusion: NTK 120mg provided sustained improvements in signs and symptoms of AS in anti-TNF-naïve and anti-TNF-IR patients at 16 weeks of therapy.

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FACTORS ASSOCIATED WITH THE DEVELOPMENT OF ANTI-DRUG ANTIBODIES TO TUMOUR NECROSIS FACTOR INHIBITORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A TWO YEAR FOLLOW-UP STUDY

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease affecting sacroiliac joints and spine as well as peripheral joints and entheses. Tumour necrosis factor inhibitors (TNFi) are widely used in patients with

persistently high disease activity despite non-steroidal anti-inflammatory drugs. Some patients fail to respond or loose responsiveness during therapy with TNFi. The development of anti-drug antibodies (ADA) might play a role in non-response or some adverse events. However it has never been evaluated for 2-years period.

Objectives: Therefore, the aim of the present study was to evaluate the development of ADA against TNFi longitudinally during 2-years period in axSpA patients and factors associated with it.

Methods: In total 180 axSpA patients according to ASAS classification criteria with a new TNFi prescription in the last two weeks period were included in this observational study. Clinical data and serum samples were collected at baseline and at every 12 weeks. Serum drug levels and ADAs were measured on 12, 24, 52 and 104 weeks of treatment by ELISA in one center to avoid inter-assay variability. The development of ADA over time was investigated by using generalized estimating equations (GEE) which is a technique for longitudinal data analysis allowing the use of all available data even deviated from normality.

Results: 180 biologic naïve axSpA patients (116 male, median [IQR] 44.5 [14,5] years) who started anti-TNF agents (infliximab [20%], adalimumab [27.2%], etanercept [32.2%] and golimumab [20.6%]) were included in the analysis. In comparison to baseline values BASDAI, ASDAS-CRP and CRP values were significantly decreased in third months of follow-up (Figure 1). In total 172 patients had at 12 weeks, 154 at 24, 121 at 52, and 73 at 104 week serum samples available for ADA determination. In longitudinal analysis; baseline age and TNFi type, as well as longitudinal BASDAI, ASDAS, serum CRP levels and the development of adverse events and discontinuation of the drug were found to be associated with the development of ADA. In order to determine independent association/s with the development of ADA two longitudinal multivariable models were run; (a) with ASDAS as an activity measure, (b) with BASDAI and CRP levels and produced that all the variables were independently associated with longitudinally development of anti-drug antibodies (Table 1). Antibodies to adalimumab were related with lower serum drug levels.

Conclusion: The results of the present study with up to 2 years of follow-up, revealed that the development of ADA against TNFi therapy is associated with high disease activity, the development of adverse events and treatment discontinuation in patients with axSpA. And etanercept might be negatively associated with the development of ADA.

Table 1. Factors associated with the development of anti-drug antibodies

	Model 1			Model 2		
	B	95% CI	P	B	95% CI	P
Age years	-0.061	-0.109;-0.012	0.015	-0.058	-0.107;-0.010	0.018
TNFi Treatment						
ETN	-1.981	-4.369;-0.134	0.104	-2.475	-4.791;-0.076	0.036
ADA	1.438	-0.002;0.407	0.073	1.275	-0.119;-0.160	0.064
INF	1.550	3.010;3.102	0.050	1.255	2.666;2.629	0.073
GOL	0 ^a			0 ^a		
Presence of adverse event, no	-0.824	-1.451;-0.198	0.010	-0.835	-1.461;-0.208	0.009
TNF treatment discontinuation	1.289	0.043;2.534	0.043	1.248	-0.075;2.571	0.065
BASDAI	0.035	0.015;0.055	0.001			
CRP	0.020	-0.035;0.005	0.008			
ASDAS-CRP				0.852	0.466;1.238	0.000

0^a:set to zero because this parameter is redundant.

Figure 1. Mean change in disease activity and CRP levels during follow-up duration. (P values for 3rd months BASDAI<0.0001, CRP<0.001, ASDAS-CRP<0.001 respectively)

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