AB0658

PREDICTION OF THE EFFECTIVENESS OF TREATMENT WITH INFlixIMAB BASED ON THE DETERMINATION OF ANTINUCLEAR ANTIBODIES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: The search for new methods for predicting the effectiveness of treatment for biologics is important issue.

Objectives: To study antinuclear antibodies (ANA) levels during of AS treatment by infliximab and evaluate the influence of ANA on treatment outcome

Methods: The presence of antinuclear antibodies (ANA) in 53 ankylosing spondylitis (AS) patients (44 men (83.02%), and 9 women (16.98%), 37.19 ± 9.38 years (95% CI: 34.60-39.78) treated with infliximab was determined by indirect immunofluorescence on an automated AKLIDES system in a serum titer of 1/80 initially (before treatment with infliximab) and at week 30 (before 7 administration). Specific autoantibodies were analyzed on the AKLIDES Cytobead platform using the following antigens SS-A 52, SS-A 60, SS-B, ds-DNA, CENP-B, Sm, RNP / Sm. ANA research was carried out at the Brandenburg Technical University (Senftenberg, Germany). Evaluation of the effectiveness of infliximab therapy was carried out by determining ASDAS-CRP at baseline, at the 14th, 30th and 54th weeks.

Results: A positive nuclear type of ANA was determined initially in 2 out of 53 patients (3.77%) (in one case, the type of luminescence was nucleolar, in the other - speckled), at the 30th week of observation, 16 out of 53 patients became seropositive for ANA (30.18%). The frequency of occurrence of ANA at the 30th week of treatment was significantly higher than the baseline ($p < 0.0001$). Positive results for the determination of specific autoantibodies to at least one nuclear antigen were found in 7 of 16 (43.75%) ANA-positive patients. In all cases, Anti-SS-A 60 (100%) was detected.

In the group of patients in whom treatment with infliximab was ineffective at the 54th week of observation, ANA positivity was observed in 10 (55.5%). In the case of treatment effectiveness at the 54th week of ANA, positivity was not observed at the 30th week. Differences in the incidence of ANA in patients with effective and ineffective treatment at week 54 were statistically significant ($p < 0.0001$). Anti-infliximab antibodies were significantly more common in ANA-positive patients at week 30 of treatment with infliximab ($p = 0.002$, Fisher's exact test).

The appearance of ANA at the 30th week of infliximab therapy was inversely related to the absence of secondary resistance at the 54th week of treatment according to the ASDAS-CRP criteria (OR 0.026; 95% CI: 0.002-0.039; $p = 0.0007$), which allows us to use the results of the determination of ANA at the 30th week of treatment with infliximab as a predictor of secondary resistance to treatment at the 54th week. When testing the method for predicting secondary resistance to treatment with infliximab at week 54 based on the results of determining ANA at week 30 of treatment in a control sample of 12 patients with AS, it was found that the method is statistically significant ($p = 0.0015$, Fisher's exact test).

Conclusion: Assessment of ANA positivity at week 30 of treatment with infliximab can be seen a predictor of the development of secondary resistance to infliximab at the 54th week of treatment.

Disclosure of Interests: None declared

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AB0659

SECUKINUMAB PROVIDES SIGNIFICANT IMPROVEMENT OF SPINAL PAIN IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE 24-WEEK PHASE 3 SKIPPAIN STUDY

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Background: Spinal inflammation causing back pain is a hallmark of axial spondyloarthritis (axSpA) mainly affecting the sacroiliac joints and spine.¹ Spinal pain is the most burdensome symptom resulting in substantial functional limitations and impairment of health-related quality of life.

Objectives: SKIPPAIN (NCT03136861) evaluated efficacy and safety of secukinumab (SEC) in reducing spinal pain in patients (pts) with axSpA who had an inadequate response to NSAIDs.

Methods: SKIPPAIN, a 24 week (wk), randomised, double-blind, multicentre trial, enrolled axSpA pts (aged ≥18 years) with active disease defined by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥4 and average spinal pain numerical rating scale (NRS) score >4 at baseline (BL) and inadequate response to ≥2 NSAIDs ≥4 wks. The trial had a PBO-controlled period from BL to Wk 8 and a SEC 150/300 mg period from Wk 8 to Wk 24. Primary and key secondary endpoints were superiority of SEC 150 mg compared to PBO in achieving average spinal pain score <4 on a 0–10 NRS and BASDAI score <4 at Wk 8, respectively.

Results: 380 axSpA pts (269 (70.8%) AS and 111 (29.2%) nr-axSpA) were randomised to SEC 150 mg (N=285) or PBO (N=95). Demographic and BL characteristics are presented in **Table 1**. Proportion of responders, in terms of average spinal pain, was 31.9% vs. 20.0% for SEC vs PBO ($p < 0.05$) and proportion of pts with BASDAI score of <4 was 33.3% vs. 23.2% for SEC vs PBO ($p < 0.05$), respectively at Wk 8 (**Table 2**). After Wk 8, responder rates increased with SEC treatment. No unexpected safety events were reported.

Conclusion: Secukinumab provided significant improvement of spinal pain in pts with axSpA. SEC was well tolerated with a safety profile consistent with previous reports.²

References:

- [1] Danve A & Deodhar A. *Clin Rheumatol*. 2019;38:625-34.
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Table 1. Patient Demographics and BL Characteristics

Characteristic	SEC 150 mg N = 285	PBO N = 95
Age (years) ¹	42.3 (11.9)	40.9 (12.2)
Female ²	106 (37.2)	39 (41.1)
Time since onset of back pain (years) ¹	13.2 (10.1)	12.3 (9.6)
HLA-B27 positive ²	233 (81.8)	76 (80.0)
hsCRP (mg/L) ¹	13.0 (21.5)	13.2 (23.5)
Elevated hsCRP (>5 mg/L) ²	140 (49.1)	49 (51.6)
Previous exposure to TNF-α inhibitors ²	34 (11.9)	11 (11.6)
Spinal pain NRS Score, 0-10 (average) ¹	7.27 (1.37)	7.31 (1.31)
Spinal pain NRS Score, 0-10 (nocturnal) ¹	7.31 (1.42)	7.40 (1.35)
Spinal pain NRS Score, 0-10 (total) ¹	7.23 (1.51)	7.22 (1.48)
BASDAI ¹	7.09 (1.22)	6.91 (1.38)
ASDAS ¹	3.75 (0.89)	3.67 (0.84)
Peripheral arthritis ²	104 (36.5)	30 (31.6)

¹mean (Standard Deviation), ²n (%).

hsCRP, high-sensitivity CRP; N, number of randomized pts; n, number of evaluable pts; NRS, numerical rating scale

Table 2. Inferential Analysis of Achieving Spinal Pain and BASDAI Score <4.0 Using Logistic Regression Model at Wk 8

Variable	Treatment Group	n/N (%)	Odds ratio versus PBO	95% CI	P-value
Spinal Pain NRS Score (Average)	SEC 150 mg	91/285 (31.9)	1.89	(1.08, 3.33)	0.0264
	PBO	19/95 (20.0)			
Spinal Pain NRS Score (Nocturnal)	SEC 150 mg	77/285 (27.0)	1.72	(0.95, 3.10)	0.0720
	PBO	17/95 (17.9)			
Spinal Pain NRS Score (Total)	SEC 150 mg	92/285 (32.3)	2.38	(1.31, 4.31)	0.0043
	PBO	16/95 (16.8)			
BASDAI score	SEC150 mg	95/285 (33.3)	1.75	(1.01, 3.04)	0.0466
	PBO	22/95 (23.2)			

P-values are from a Logistic regression model with treatment as the principle factor and prior exposure to TNF inhibitors and naïve/inadequate responders to TNF inhibitors as stratification factors.

Missing values were imputed as non-responders. N, Number of randomised pts; n, Number of pts who are responders/evaluable pts.

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AB0660

LONG-TERM CLINICAL OUTCOME OF ANTI-TNF TREATMENT IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: 10-YEAR DATA OF THE ETANERCEPT VS. SULFASALAZIN IN EARLY AXIAL SPONDYLOARTHRITIS TRIAL

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Background: Long-term data on anti-TNF treatment in patients with early axial spondyloarthritis (SpA) is scarce.

Objectives: The objective of this analysis was to assess the long-term clinical efficacy (up to 10 years of treatment) of a tumor necrosis factor (TNF) inhibitor etanercept (ETN) in patients with early axial spondyloarthritis, who participated in the long-term (until year 10) extension of the ESTHER (Etanercept vs. Sulfasalazine in Early Axial Spondyloarthritis Trial) trial.

Methods: In the previously reported ESTHER trial, patients with early active axial SpA [including both non-radiographic axial SpA (nr-axSpA) and radiographic axial SpA (r-axSpA)/ankylosing spondylitis (AS)] with a symptom duration of <5 years and a positive MRI of the sacroiliac joints (SIJs) and/or the spine at baseline) were treated with ETN (n= 40) or sulfasalazine (SSZ) (n= 36) during the first year (1). At year 1, all patients who were not in remission continued with - or switched (in case of SSZ therapy) to - ETN for up to 10 years in total (1). Patients in remission discontinued their therapy and were followed-up until end of year 2; in case of remission loss, ETN was (re)-introduced and continued till the end of year 10.

Figure 1: Observed response rates to etanercept (A) and the course of disease related parameters in study completers (n=19) (B).

Table 1. Baseline characteristics of patients with axial spondyloarthritis who completed the study as compared to patients who dropped out.

	Completer (n=19)	Non-Completer (n=57)	p value
Age, years	32.5 (7.4)	32.8 (8.9)	0.91
Male patients, n (%)	15 (78.9)	29 (50.9)	0.034
Symptombduration, years	1.1 (1.2)	1 (1.7)	0.81
HLA-B27 positivity, n (%)	18 (94.7)	44 (77.2)	0.091
Elevated CRP (CRP>5mg/l), n (%)	7 (38.9)	33 (62.3)	0.088
Fulfilled New York criteria, n (%)	12 (63.2)	27 (47.4)	0.24
Patient global (0-10)	6.1 (1.9)	7.2 (1.7)	0.025
Physician global (0-10)	5.5 (1.5)	6.5 (1.2)	0.007
ASDAS	3 (0.7)	3.5 (0.8)	0.042
BASDAI (0-10)	5.4 (1.1)	5.8 (1.3)	0.27
BASFI (0-10)	4 (2.1)	4.4 (2)	0.41
BASMI (0-10)	1.2 (1.3)	2 (1.6)	0.039
AS-QoL (0-18)	7.6 (3.9)	10.1 (3.9)	0.019

Results: Out of 76 initial patients, 25% (n=19, 12 with r-axSpA and 7 with nr-axSpA) completed year 10 of the study. At baseline, completers were significantly more often male and showed lower values of patient (PGA) and physician global assessments of disease activity (PhGA), ASDAS (Ankylosing Spondylitis Disease Activity Score), BASMI (Bath Ankylosing Spondylitis Metrology Index), and AS-QoL (Ankylosing Spondylitis Quality of Life Questionnaire) as compared to non-completers (Table 1). When analyzing clinical data of the completers, mean BASDAI, BASFI and ASDAS values were constantly <2 during the follow up with no statistically significant differences between the r-axSpA and nr-axSpA sub-groups (Table 2, Figure 1B). In the entire group, a sustained clinical response was observed over 10 years of follow up (Figure 1A). A total of 39 serious adverse events were documented over the 10 years of the study, while six of them were seen as possibly associated with ETN treatment, which lead in five patients (one lymphoma, one sarcoidosis, one demyelinating neurological disease, one elevated liver enzymes and one recurrent minor infections) to an ETN discontinuation.

Conclusion: A sustained clinical response was shown over the 10 years of the study for the completers with comparable rates between r-axSpA and nr-axSpA. ETN was well tolerated across the entire treatment period and showed a good safety profile with no new safety signals.

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AB0661

CO-MEDICATIONS MAY ALTER THE RESPONSE TO TNF-INHIBITORS IN SPONDYLOARTHRITIS PATIENTS: A PHARMACOMICROBIOMIC EFFECT?

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Background: The reason why some spondyloarthritis (SA) patients fail to respond to TNF inhibitors (TNF-i) remains unclear. Recently, it has been shown in