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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

cancer immunotherapy that the therapeutic response may be strongly altered by co-medication with drugs interfering with the gut microbiota, such as antibiotics, proton pump inhibitors (PPI), non-steroidal anti-inflammatory drugs (NSAIDs), psychotropic or antidiabetic drugs.

Objectives: Considering the potential role of the gut microbiota in the pathophysiology of SA as in the therapeutic response, the aim was to study the influence of co-medications known to interfere with the microbiota with the therapeutic response to TNF- α in SA patients.

Methods: We retrospectively reviewed the charts of all patients treated in our department with a first TNF- α from 2009 to 2018. Data collected were demographic information, HLA-B27 status, disease characteristics... Patients were classified as responder (R) or non-responder (NR) according to the BASDAI (< 40/100) value at M6 or to the clinician judgment (when BASDAI was not available). Regarding co-medications, we collected all drugs known to interfere with the gut microbiota that were administered 1 month before and during the first 3 months of the TNF- α treatment. We only considered drugs given to more than 5% of patients. Quantitative data were expressed as mean $\pm$ standard deviation, and qualitative variables as percentages. Univariate and multivariate analyses were performed to evaluate the relationship between co-medications and TNF- α . All analyses were computed on STATA 13.1 software with a statistically significant threshold of 0.05.

Results: We included 188 patients suffering from ankylosing spondylitis (n=89) or peripheral SA (n=99). They were 68 women and 120 men, mean aged 46.6 $\pm$ 13; 53% were B27 positive. TNF- α were infliximab (19%), etanercept (44%), adalimumab (34%) golimumab (2%), certolizumab (1%), combined with MTX in 51 patients. 135 patients (72%) were R and 53 (28%) NR. In univariate analysis, 59.1% of patients who received NSAIDs were R, compared to 88.2% of patients not treated with NSAIDs ($p < 0.0001$); 42.2% of patients receiving PPIs were R compared to 86.3% of patients PPI free ($p < 0.0001$); 55.8% of patients who were given antibiotics were R, compared to 75.7% of patients who did not ($p=0.02$); 27.8% of patients treated with psychotropic drugs were R, compared to 75.9% of patients not receiving such treatment ($p < 0.0001$) (Figure 1). Differences were not statistically significant for corticosteroids, MTX, angiotensin-converting enzyme inhibitors and statins. Although 91% of patients taken PPIs were also given NSAIDs, NSAIDs, PPIs and antibiotics intake were considered as independent factors associated with TNF- α failure in multivariate analysis.

Conclusion: Co-medication with NSAIDs, PPIs, antibiotics and psychotropic drugs were significantly associated with a decreased chance to respond to TNF- α . The hypothesis that this effect is due to their interference with the gut microbiota is only speculative but, regardless the reason of this interaction, clinician should be aware of the potential negative effect of these co-medication on TNF- α .

Figure 1.

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AB0662

TREATMENT AND FOLLOW-UP OF AXIAL SPONDYLOARTHRITIS IN DAILY CLINICAL PRACTICE - A SURVEY AMONG DUTCH RHEUMATOLOGISTS

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Background: ASAS-EULAR have developed management recommendations for axial spondyloarthritis (axSpA) to provide guidance to the management of patients with axSpA¹. However, there is limited insight into how rheumatologists treat axSpA patients in daily clinical practice and if these recommendations are used.

Objectives: To get insight into the management of axSpA patients in daily practice in the Netherlands.

Methods: We performed a survey among rheumatologists in the Netherlands with 21 multiple choice questions; 5 general questions on characteristics of their practice and 16 questions addressing treatment and follow-up of axSpA patients in daily practice. The questionnaire was taken during structured face-to-face interviews by employees of the medical department of Novartis NL Rheumatologists in the Netherlands were invited to participate, aiming to get a sample of rheumatologists varying in geographical location and hospital type, as well as a mix of SpA-experts and non-SpA-experts. Rheumatologists gave approval for anonymous use of the data, which were entered in a database and analyzed using descriptive statistics.

Results: Between October 15 2019 and January 16 2020, 36 rheumatologists participated; 6 from university hospitals, 27 from general hospitals and 3 from private care centers.

81% of the rheumatologists referred most of their axSpA patients (76-100%) after diagnosis for information and education concerning axSpA, exercise and lifestyle to a specialized nurse practitioner. Furthermore, 53% of rheumatologists referred most of their axSpA patients (76-100%) to a physiotherapist for exercise therapy. At diagnosis, approximately 55% of axSpA patients used the daily maximum dose of NSAIDs, compared to 25% for patients on biological treatment.

The reported level of importance of different axSpA related aspects for starting a biological was largely similar for AS and nr-axSpA, although some differences could be observed (Figure 1): Most rheumatologists graded insufficient response to 2 NSAIDs during 4 weeks (94% for AS and 92% for nr-axSpA) and bone marrow edema on MRI (75% and 89%) as important for starting a biological. About 60% of rheumatologists considered active disease using ASDAS/BASDAI important for the decision to start a biological, which was similar to the importance of the level of pain. For nr-axSpA, more rheumatologists graded elevated CRP and bone marrow edema on MRI as important for starting a biological, than for AS. Most rheumatologists (67%) do not base a decision that a biological is ineffective on ASDAS or BASDAI. To assess disease activity in axSpA, 86% of the rheumatologists always measured C-reactive protein (CRP), compared to 42% and 31% for BASDAI and ASDAS, respectively. 77% of rheumatologists reported to follow the 2016 ASAS-EULAR treatment recommendations for axSpA for treatment and follow-up of axSpA patients.

Conclusion: This survey among Dutch rheumatologists suggests that ASDAS and BASDAI are as important for starting a biological in axSpA as is the level of pain. Moreover, in contrast to ASAS-EULAR treatment recommendations, most rheumatologists do not use validated disease activity instruments to assess biological ineffectiveness, which may be a topic for increasing awareness and education.

References:

- 1] Van der Heijde D et al, Ann Rheum Dis 2017;76:978-91.

1. Van der Heijde D et al, Ann Rheum Dis 2017;76:978-91.

Figure 1. Level of importance of axSpA related aspects for starting a biological in axSpA
Values given as % of responders (total of 100% per feature)

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