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Original article

Efficiency of treatment with non-steroidal anti-inflammatory drugs according to current recommendations in patients with radiographic and non-radiographic axial spondyloarthritis

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Abstract

Objective. NSAIDs are first-line therapy in axial SpA (axSpA). The proportion of patients responding to NSAIDs and differences between AS and non-radiographic axSpA (nr-axSpA) in this regard have not been studied in detail to date. The aim of this study was to examine the proportion of patients with AS and nr-axSpA responding to NSAIDs according to current treatment recommendations.

Methods. Consecutive anti-TNF-naïve patients with nr-axSpA and AS ($n = 50$ each) were included if their BASDAI score was $\geqslant 4$ without having received maximal NSAID doses. In case of a BASDAI score $\geqslant 4$ 1 week later, another NSAID was prescribed. For the next 3 weeks, continuous intake of maximal doses was recommended but patients could reduce doses in case of intolerance or improvement. MRI of the SI joints was performed at baseline and week 4.

Results. All outcomes except for CRP and MRI scores improved significantly after 4 weeks of NSAIDs, with no difference between axSpA subgroups. An Assessment of SpondyloArthritis international Society 40% (ASAS40) response and partial remission rates were 35 and 16% at week 4, respectively. At the same time point, a BASDAI score $\geqslant 4$ was still present in 44% of patients, 30% of which had reduced NSAID doses, partly due to intolerance (38%). Only 13% of all patients had continuously taken NSAIDs at the maximal dosage, but there was no difference in the efficacy outcome compared with those who had taken reduced doses.

Conclusion. AS and nr-axSpA patients had similar response rates to NSAIDs while objective signs of inflammation did not change over 4 weeks. Only a minority of patients was willing to take maximal doses of NSAIDs, and $\geqslant 40\%$ patients remained candidates for TNF blockers. These results may influence future trial designs.

Key words: axial spondyloarthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, NSAIDs, ASAS40.

CLINICAL SCIENCE

Rheumatology key messages

- The majority of active axial SpA patients benefit from NSAID treatment after 4 weeks.
- Active disease is still seen in 44% of axial SpA patients considered as candidates for TNF blockers.
- There was no difference in the efficiency of NSAIDs between patients with non-radiographic axial SpA and AS.

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Introduction

AS has long been considered as the prototype of a partly heterogeneous group of diseases called SpA. However, the publication of new classification criteria for axial SpA (axSpA) [1, 2] has widened the spectrum of this field, which had been largely determined by the 1984 modified New York classification criteria for AS [3].

The Assessment of SpondyloArthritis international Society (ASAS)/EULAR recommendations for the management of AS [4], and especially the ASAS recommendations for anti-TNF therapy in axSpA [5], have proposed to treat patients for 4 weeks continuously with at least two NSAIDs before considering the initiation of anti-TNF therapy. In the recommended treat-to-target approach for axSpA [6], the treatment strategies should aim for the best possible treatment outcome (defined as remission or, alternatively, low disease activity) while also considering possible safety issues of the applied treatment. This approach also represents the current standard of how to proceed in a clinical situation of increased disease activity in patients with axSpA. However, the clinical outcome of these recommendations and whether the two subgroups of axSpA respond similarly well to NSAIDs is, although probable, still unknown to date. In contrast, the results of the first studies have now been published showing the effect of TNF-α-blocker treatment in the early stages of the disease [7–10].

The main aim of our study was to test the ASAS/EULAR recommendations for the management of AS in a real-life setting. Therefore, we studied the efficiency of NSAIDs in the first 4 weeks at the maximum recommended or tolerated dose unless contraindicated and included a comparison between patients with AS and nr-axSpA. Furthermore, we assessed how many patients were willing and able to take the maximal dose of NSAIDs over the 4 weeks. Finally, we counted how many axSpA patients were candidates for anti-TNF therapy after 4 weeks of NSAID treatment.

Methods

Patients classified to axSpA attending the outpatient department of our specialized centre or referred by the cooperating rheumatology practices were recruited in this prospective observational study. Patients were asked to participate if they were identified with axSpA based on the ASAS classification criteria by their specialized treating rheumatologist and if the clinical and imaging examinations showed the current clinical symptoms were due to axSpA. For differentiation between nr-axSpA and AS, the modified New York criteria were used (with a diagnosis of nr-axSpA if these were negative and AS if these were positive). A total of 100 patients ($n = 50$ each for nr-axSpA and AS) were consecutively included if their BASDAI score was $\geqslant$4/10 and if they had not received the maximally approved dose of NSAIDs nor anti-TNF agents to date.

Informed consent was provided and the maximum dose of NSAIDs was prescribed. In order to closely resemble the real-life situation, there was no specific choice of one NSAID that might have limited participation in the study. Thus the decision of which NSAID to use was left to the discretion of the treating rheumatologist: if the patients had already received an NSAID that was unsuccessful, a different NSAID was prescribed; if patients had problems with the tolerability of COX-2 inhibitors (coxibs) or conventional NSAIDs, the other drug class was prescribed if contraindications were absent.

One week after the patients had received the maximal dose of the first conventional NSAID/coxib, the patient's symptoms were reassessed. In case of a BASDAI score $<$4 and if the rheumatologist felt that the disease activity was sufficiently controlled, patients were told to stick to the current dosage and not change it for the next 3 weeks (or lower the dosage if possible or necessary). In case of a BASDAI score $\geqslant$4 after the first week, the NSAID/coxib was changed (from a coxib to a conventional NSAID or vice versa, both at maximum dose). Since the study was not designed as an efficacy trial, patients were still able to reduce the dose if they felt that they did not tolerate the maximum dose. In that case, they were advised to take the maximally tolerated dose.

NSAID dosages were quantified by the ASAS NSAID index [11]. Briefly, this index quantifies the cumulative dose intake of NSAIDs on a scale of 0–100 over the analysed time period, where 100 represents the maximum approved dose of the NSAID and 0 represents no intake at all.

Clinical visits were performed before treatment initiation (baseline) and after 1 and 4 weeks of treatment with NSAIDs. MRI of the SI joints were performed at baseline in all patients. Due to budget restrictions, a second MRI was performed at the end of the study (week 4) only in the first 60 patients (first 30 with nr-axSpA and the first 30 with AS) who were included in the study. MRIs were performed in a standard protocol using short tau inversion recovery and T1 sequences (slice thickness 3–4 mm, both semicoronal and semi-axial orientations). Technical details of the MRI have been provided in earlier publications from our group [12]. The MRIs were read by two experienced readers who were blinded to the patient's characteristics and to the time point of the MRI. The readers evaluated the MRIs as being positive or not according to the ASAS recommendations [13] and also scored the MRIs by the Berlin method [14]. In case of discrepancies between the two readers with respect to MRI positivity, an adjudication session was conducted with both readers in order to determine whether the MRI was positive according to the ASAS definition or not. For the evaluation of the Berlin score, the mean scores of both readers were taken into account for analysis of the results.

In this study, we wanted to explore the proportion of patients with nr-axSpA and AS who met the inclusion criteria for anti-TNF treatment after treatment with NSAIDs for 4 weeks.

The study was approved by the Ethical Committee of the Ruhr-University of Bochum, Germany. All patients gave written informed consent for participation in the study.

Statistical analysis

Descriptive data are presented as percentages when referring to qualitative variables. Continuous variables are expressed as mean (S.D.) where appropriate. Continuous variables were compared using the Mann–Whitney *U* test, while categorical variables were compared using the chi-square test. *P*-values <0.05 were considered statistically significant.

Results

Baseline characteristics

The patients' baseline demographics are shown in Table 1. Taking into account the last 4 weeks prior to study inclusion, 35 patients were NSAID-naïve and 65 patients were taking NSAIDs [mean NSAID index 37.5 (S.D. 34.7)] at baseline. There were no differences in any of the baseline characteristics between patients with and without MRI examinations available at week 4 of the study (data not shown).

NSAID therapy was started in 51 patients with conventional NSAIDs (51%) and in 49 patients with coxibs (49%).

Follow-up after 1 and 4 weeks of continuous NSAID treatment

All clinical assessments of disease activity improved significantly between baseline and week 4 (Table 2 and Fig. 1) except for CRP values, Berlin SIJ MRI scores and the proportion of patients with a positive MRI, which did not change (Table 3).

After 1 week of treatment, 17 of the 49 patients (34.7%) treated with coxibs were changed to a conventional NSAID, while 18 of the 51 patients (35.3%) who were started on a conventional NSAID were changed to a coxib. Thus there was no difference in these proportions.

When comparing response rates in the two axSpA subgroups, an ASAS 40% (ASAS40) response at week 4 was found in 35 patients [35%; 15 classified as nr-axSpA (30%) and 20 classified as AS (40%)], while ASAS partial remission at week 4 was seen in 16 patients [16%; 7 with nr-axSpA (14%) and 9 with AS (18%)] (see Table 2). Similarly, a BASDAI score $\geqslant 4$ at week 4 was found in 44 patients (44%; 23 (46%) in the nr-axSpA group and 21 (42%) in the AS subgroup]. Thus there were no major differences between nr-axSpA and AS (all $P > 0.05$).

All 44 patients with a BASDAI score $\geqslant 4$ were also judged by the responsible rheumatologist to have active disease and thus were found to be eligible for TNF blocker treatment. Of interest, the majority ($n = 31$) of these patients (70.5%) had not achieved a BASDAI score <4 after the first week of NSAID therapy (Fig. 2).

We did not observe any difference between patients who had already received (low doses of) NSAIDs prior to the study compared with those without previous NSAID treatment. Furthermore, no difference in treatment outcomes was observed between the different compound classes (NSAIDs and coxibs). Patients who changed their treatment from a conventional NSAID to a coxib or vice versa at week 1 showed no differences in disease activity at week 4 as compared with those who remained within the same NSAID class and only changed the compound (data not shown due to the small numbers).

Overall, only a minority [$n = 13$ (13%)] of patients had taken the maximum approved dose of NSAIDs when presenting at week 4. Of these 13 patients, only 6 (46.2%)

Table 1 Baseline demographics for both nr-axSpA and AS patients

Characteristic	nr-axSpA ($n = 50$)	AS ($n = 50$)	*P*-value
Gender, male, % patients	52	70	0.07
Age, years	37.6 (11)	41.9 (12.3)	0.1
Symptom duration, years	7.3 (9.1)	14.6 (11.8)	<0.001*
HLA-B27 positive, % patients	80	74	0.48
BASDAI score, 0–10	6.0 (1.4)	5.6 (1.3)	0.18
NRS for back pain, 0–10	7.1 (1.7)	6.5 (2.4)	0.38
PGA, 0–10	6.9 (1.8)	6.5 (2.3)	0.64
PhGA, 0–10	6.5 (1.7)	6.1 (2.1)	0.42
Mean BASFI, 0–10	4.6 (2.6)	4.8 (2.4)	0.8
AS QoL	10.8 (4.0)	10.0 (4.6)	0.13
CRP, mg/dl	0.6 (0.9)	1.2 (1.1)	0.003*
Berlin SIJ MRI score, 0–24	3.1 (3.0)	6.7 (5.4)	0.01*
ASDAS-CRP >2.1, % patients	76	74	0.82
Positive MRI of the SIJs, % patients	70	78	0.36
NSAID index	19.8 (28.3)	28.9 (37.2)	0.13

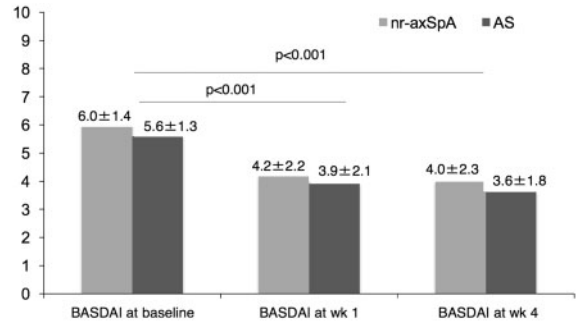
Values are given as mean (S.D.) unless otherwise indicated. There were no statistical differences between the two axSpA subgroups with the exception of symptom duration, mean CRP and mean Berlin SIJ MRI score for activity (asterisks in the table). Positive MRI of the SIJs was defined according to ASAS (see the Methods section). nr-axSpA: non-radiographic axial spondyloarthritis; AS: ankylosing spondylitis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; NRS: numeric rating scale; PGA: patient's global assessment; PhGA: physician's global assessment; BASFI: Bath Ankylosing Spondylitis Function Index; ASQoL: ankylosing spondylitis quality of life index; CRP: C-reactive protein; SIJ: sacroiliac joints; ASDAS: ankylosing spondylitis disease activity score; NSAID: non-steroidal anti-inflammatory drugs.

Table 2 Outcome parameters after 1 and 4 weeks of continuous NSAID treatment in both axSpA subgroups

Outcome parameter	1 week after baseline			4 weeks after baseline		
	nr-axSpA ($n = 50$)	AS ($n = 50$)	axSpA ($n = 100$)	nr-axSpA ($n = 50$)	AS ($n = 50$)	axSpA ($n = 100$)
Mean BASDAI, mean (S.D.)	4.2 (2.2)	3.9 (2.1)	4.0 (2.1)	3.9 (2.3)	3.6 (1.8)	3.8 (2.1)
Mean BASFI, mean (S.D.)	3.4 (1.9)	3.4 (2.1)	3.4 (2.0)	3.2 (2.3)	3.3 (2.2)	3.3 (2.3)
Mean ASDAS, mean (S.D.)	1.8 (0.8)	1.9 (0.9)	1.9 (0.8)	1.7 (0.8)	1.7 (0.7)	1.7 (0.8)
BASDAI <3, % patients	30	40	35	36	44	40
ASDAS <1.3, % patients	30	26	28	36	32	34
ASAS PR, % patients	8	12	10	14	18	16
BASDAI $\geqslant 4$, % patients	48	50	49	46	42	44
ASDAS-CRP $\geqslant 2.1$, % patients	32	42	37	34	32	33
ASDAS clinically important improvement, % patients	26	24	25	32	34	33
ASAS40 response, % patients	24	24	24	30	40	35
BASDAI 50% patients response, % patients	30	36	33	36	40	38

There were no statistical differences in the improvement rates between the axSpA subgroups in any of the assessed outcomes (all $P > 0.05$). PR: partial remission.

Fig. 1 Mean (S.D.) BASDAI values



Mean (S.D.) BASDAI values at baseline, after 1 week and after 4 weeks of continuous NSAID treatment in both axSpA subgroups. The difference between baseline and weeks 1 and 4 was significant but no statistical differences were observed between nr-axSpA and AS at any time point.

reported a BASDAI score $\geqslant 4$ at this time point. Interestingly, this proportion was similar for the 87 patients who had reduced their NSAID dose, with 38 patients (43.7%) reporting a BASDAI score $\geqslant 4$ at week 4.

Among the 44 patients who were found to be eligible for TNF blocker treatment at week 4, 31 patients (70.5%) reported an NSAID index $\leqslant 50$, with 9 patients (29%) stating that the decrease was due to intolerability. In comparison, of 56 patients presenting with a BASDAI score <4 at week 4, 43 patients (76.8%) reported an NSAID index $\leqslant 50$ and 12 patients (27.9%) had reduced the dose because of intolerability. Figure 2 shows the detailed flowchart of patients with BASDAI scores <4 and $\geqslant 4$ after 1 and 4 weeks of the study.

Overall, there were no significant differences in any assessment regarding the response to NSAIDs between nr-axSpA and AS patients (Table 2). Furthermore, the analysis of different subgroups of patients according to their baseline status (MRI positive, CRP positive, gender, symptom duration) did not reveal any factor that would predict outcome and eligibility for anti-TNF treatment after 4 weeks of NSAID treatment (data not shown).

Relationship between NSAID index and clinical response after 4 weeks of continuous NSAID intake

The stratification to different cut-off values of the NSAID index at the end of the study revealed no statistically significant but some numerical differences between groups, independent of the cut-off value used for stratification. In the group with an NSAID index <50 *vs* the group with an NSAID index $\geqslant 50$ after 4 weeks, the mean BASDAI score was 3.7 (S.D. 2.0) *vs* 4.3 (2.3), respectively. Based on the same stratification, the respective proportion of patients with a BASDAI score $\geqslant 4$ was 41.3 *vs* 55%, the proportion of patients with an ASAS40 response was 35% in both groups, the mean patients' global assessment was 4.1 (S.D. 2.3) *vs* 4.2 (2.8) and the physicians' global assessment was 4.0 (S.D. 2.2) *vs* 4.1 (2.5) (all $P > 0.05$). Similar results were found when the patients where stratified by median NSAID indices.

A comparison of patients according to the BASDAI cut-off of 4 showed that in the group of patients with a BASDAI score $\geqslant 4$ at week 4 ($n = 44$), 13 patients (25%) also had an NSAID index $\geqslant 50$, and in the group of patients with a BASDAI score <4 ($n = 56$), 13 had an NSAID index $\geqslant 50$ (23.2%) (all $P > 0.05$).

Course of inflammatory MRI lesions during the 4 weeks of the study

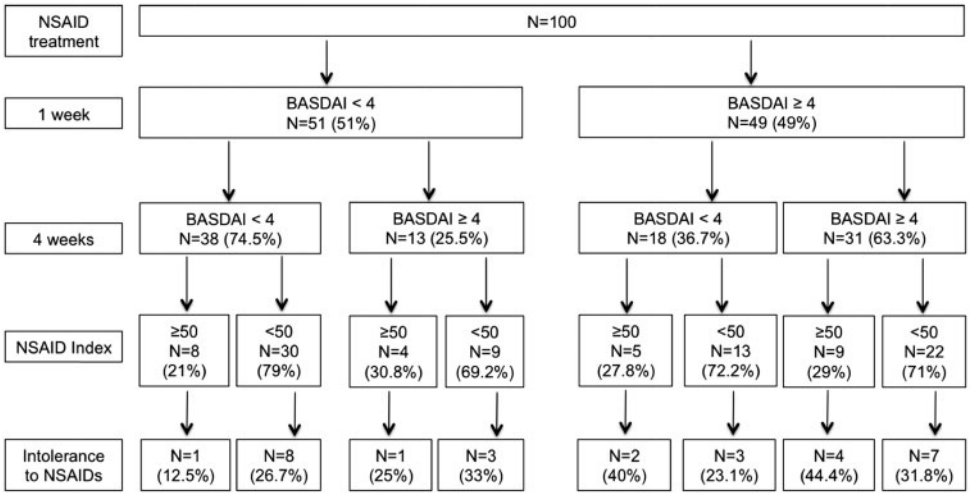
We did not find any association between the NSAID index and the Berlin MRI score. Only minor fluctuation of bone marrow oedema during the 4 weeks of the study period could be observed in both nr-axSpA and AS patients.

Table 3 Course of objective measurements of inflammatory activity

Measurement	Before NSAID treatment		After 1 week of NSAID treatment		After 4 weeks of NSAID treatment	
	nr-axSpA	AS	nr-axSpA	AS	nr-axSpA	AS
CRP, mean (S.D.)	0.6 (0.9)	1.2 (1.2)	0.5 (1.1)	1.3 (1.5)	0.5 (7.7)	1.0 (1.1)
Mean SIJ MRI score, mean (S.D.)[a]	2.1 (2.5)	6.7 (5.4)	NA	NA	2.1 (2.5)	7.1 (5.9)
Number of patients with positive MRI, % patients[a]	60	87	NA	NA	60	83

Inflammatory activity (CRP, MRI) before, after 1 week (CRP only) and after 4 weeks of NSAID treatment. There were no statistical differences in any of the parameters between the assessed time points.
[a]The MRI results in this table refer only to the 60 patients (30 nr-axSpA and 30 AS) who had a follow-up MRI examination available.

Fig. 2 Detailed flow chart of all patients depending on BASDAI scores



Detailed flow chart depending on BASDAI scores after 1 and 4 weeks of continuous NSAID treatment and in relation to NSAID indices and tolerability due to NSAID therapy at the end of the study.

Interestingly, of the 12 patients with nr-axSpA with a normal MRI at baseline (classified via the clinical arm with an additional two or more clinical SpA features), only 2 patients (16.7%) had a positive MRI after 4 weeks. On the other hand, of the 18 patients with nr-axSpA and a positive MRI at baseline, again 2 patients (11.1%) showed a normal MRI after 4 weeks. Of the 12 patients who had a normal MRI at baseline, only 2 (different patients than the ones described previously) showed an ASAS40 response after 4 weeks of NSAID treatment, while 6/12 (50%) had a BASDAI score $\geqslant 4$ at week 4 of the study.

Discussion

This is the first study that has prospectively assessed and compared the response of patients with axSpA using the internationally recommended regimen of continuous therapy with NSAIDs over 4 weeks as proposed by the ASAS/EULAR recommendations [4].

The first clinically relevant result of our study was that there were clearly no differences in the clinical response to NSAIDs in patients classified as nr-axSpA or AS, and there were also no differences in NSAID use as quantified by the ASAS NSAID index. These results are important because they confirm our and others' data [15], where patients classified as nr-axSpA or AS showed many clinical similarities and the same burden of disease but also the same response rates to treatment with anti-TNF [10]. Since the proportion of patients with nr-axSpA and AS who still had a BASDAI score $\geqslant 4$ after 4 weeks of NSAID therapy—in accordance with the physician's opinion—and thus were eligible for anti-TNF therapy, was also almost equal, we argue that these data provide further evidence that axSpA is one rather than two 'separate' diseases.

The second interesting observation is the treatment efficiency of conventional NSAIDs over 4 weeks. The

majority of axSpA patients showed a significant improvement in all clinical indices during this short period of continuous NSAID therapy. However, while an ASAS40 response was observed in 35% of the patients, only 16% of patients reached a status of ASAS partial remission. Obviously this result was not influenced by the class of NSAIDs (coxibs or non-coxibs) used in this study. When comparing our data with results from the Infliximab for Treatment of Axial Spondyloarthritis (INFAST) study [16], in which patients with axSpA received either naproxen or anti-TNF (infliximab) in combination with naproxen, their partial remission and ASAS40 response rates at weeks 2 and 6 were much higher. This may be due to the fact that the patients in the INFAST study had a shorter disease duration ($<$3 years) and had undergone a different preselection process (positive response to NSAIDs prior to the study with NSAID withdrawal prior to study inclusion).

The third important observation is that almost half (44%) of the initially active patients (BASDAI score $\geqslant$4 prior to treatment) still had a BASDAI score $\geqslant$4 after 4 weeks of optimal NSAID therapy and, in combination with the expert opinion for high disease activity, would meet the ASAS criteria for starting a biologic therapy. When interpreting these data, also in comparison with other data, one needs to be clear that the patients included in our study had been pre-selected on the basis of a BASDAI score $\geqslant$4 but had not received a maximum dose of NSAIDs prior to inclusion. This is different from an earlier cross-sectional study using mailed questionnaires in which 64% of patients with AS included independent of disease activity and treatment reported a BASDAI score $\geqslant$4 [17] and also different from the INFAST study, although the exact percentage of patients with a BASDAI score $\geqslant$4 was not reported in the INFAST study [16]. Our study design is also different from studies with anti-TNF agents in which patients have failed NSAIDs prior to inclusion and where NSAID doses have to remain stable during placebo phases—this design is likely responsible for low treatment responses [7, 8, 10, 18, 19]. Interestingly, almost 50% of patients in our study had not reached a BASDAI score $<$4 after 1 week and 63% of these still did not reach a BASDAI score $<$4 after 4 weeks of treatment with NSAIDs. These data suggest that an inadequate BASDAI response after 1 week of NSAID therapy may indicate a low probability of a good response after 4 weeks. The fourth important result of this study is that the majority of patients did not or could not take the recommended dose of NSAIDs over the period of 4 weeks. This has to be regarded as a factor that could possibly influence the efficacy results. However, the ASAS40 response rate was similar in the group that had taken the maximal dose compared with the patients who had decided to reduce the dose. Nevertheless, previous data have also reported high dropout rates over long treatment periods with NSAIDs [20]. It would be interesting to see whether the overall results of such a study would lead to different results and better clinical outcomes if different recommendations with strict application of the need for a maximal NSAID dosage were used.

The fifth and last interesting result of our study is that, in contrast to the clinical efficacy of continuous NSAIDs, there was no influence of this treatment on the degree of bone marrow oedema as assessed by MRI or on CRP levels over 4 weeks. This result adds to the contradictory data on the effect of NSAIDs in axSpA. On the one hand, there is well-documented clinical efficacy [21, 22] and a likely effect on radiographic progression when NSAIDs are given continuously [23]. On the other hand, there is no effect on MRI changes [24] and only a minor effect on CRP [25] despite the fact that patients, especially those with elevated CRP, showed a benefit from continuous NSAID therapy [26]. Similar data were published very recently [27] showing no decrease in the overall SIJ MRI score but an improvement of signal intensity under a 6 week NSAID treatment regimen in a much smaller number of patients. More studies and data will be needed to shed light on this issue. However, we believe that it is important to report that we did not observe a major degree of fluctuation of inflammatory MRI signals in the SIJ, independent of changes observed in clinical disease activity assessments.

The strength of our study is its non-interventional design, which reflects a real-life situation, since we did not further influence patients' decisions to decrease or increase their NSAID intake after the first week of treatment. Indeed, limited compliance and drug adherence has been reported in patients with AS [28]. Furthermore, patients with limited efficacy of NSAIDs are known to frequently change their medication [29]. Since most anti-TNF studies have used an inadequate response to NSAIDs as an entry criterion, these data may influence future trial designs, since the 'real' NSAID intake based on daily dose before the start of anti-TNF therapy has never been studied or reported.

Our study also has some limitations. First, the duration of the study was relatively short. As reported in the INFAST study, it may take 28 weeks for axSpA to reach optimal response rates under treatment with NSAIDs [16]. Thus the follow-up in our study might have been too short to draw 'final' conclusions about the efficacy of NSAIDs in patients with active axSpA. However, as already mentioned, our aim was to assess the outcome of NSAID therapy in patients with active axSpA relative to current international recommendations. Therefore, we opted for a short duration. Nevertheless, we think that in many countries, rheumatologists may follow different strategies in daily practice and evaluate the outcome of treatment with NSAIDs after longer time periods. Indeed, taking into account that the age of onset of axSpA is $<$30 years, that the disease usually takes a chronic course and that it is likely to go on for several more decades, this seems to be the right choice. However, since it seems possible to inhibit structural progression with very early intervention, the short-period strategy may still be the superior one, something that remains to be shown. Data on long-term NSAID therapy are also scarce [24].

The lack of a placebo arm is not a limitation of our study, since the effect of NSAIDs is well established [21,

22] and since the study was not designed to be an efficacy study. Furthermore, the patients in this study suffering from chronic back pain due to axSpA were clearly in need of standard-of-care therapy and the administration of placebos would have been unethical.

In conclusion, in this prospective study we show that many patients with axSpA still have active disease after the recommended 4 weeks of NSAID therapy, although the majority improved. There was no difference between patients with nr-axSpA and AS. Finally, no changes in objective signs of inflammation as assessed by MRI and CRP were observed.

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