

## EXTENDED REPORT

# An international study on starting tumour necrosis factor-blocking agents in ankylosing spondylitis

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**Objectives:** To determine the type and proportion of patients with ankylosing spondylitis who rheumatologists consider to be candidates for treatment with tumour necrosis factor (TNF)-blocking agents, and to what extent this is in agreement with the ASsessment in Ankylosing Spondylitis (ASAS) international working group recommendations on initiation of treatment with anti-TNF agents.

**Methods:** Participants were rheumatologists from 10 different countries, who were considered to be experts in treating patients with ankylosing spondylitis and in the use of anti-TNF treatment, but were unaware of the ASAS recommendations (unpublished at the time of study in 2003). The first 10 consecutive patients with ankylosing spondylitis seen by the rheumatologist were evaluated as to whether the patient was a candidate for anti-TNF treatment. Thereafter, a metrologist assessed the patient for disease activity and severity, and collected data on demographics and treatment.

**Results:** Complete data were available for 1207 of the 1284 patients and were used for analysis. Overall, the rheumatologists indicated that they would initiate TNF-blocking agents in 49.3% of patients, ranging from 37.2% patients in Canada to 78.3% in Australia. These candidates had higher disease activity, higher levels of acute-phase reactants, worse spinal mobility, worse function, more often hip involvement and a higher prevalence of sick leave. Of all patients considered to be candidates, 40% did not fulfil ASAS recommendations with respect to previous use of non-steroidal anti-inflammatory drugs (NSAIDs; at least two NSAIDs) or Bath Ankylosing Spondylitis Disease Activity Index ( $\geq 4$ ). Conversely, 36% of patients who did not fulfil the NSAID or BASDAI recommendations were still considered to be candidates for TNF-blocking treatment. Objective variables, such as C reactive protein, erythrocyte sedimentation rate or magnetic resonance activity, were considered less important than disease activity in the decision on starting TNF-blocking drugs. The only important objective criterion was rapid radiographic progression.

**Conclusion:** Rheumatologists wanted to initiate TNF-blocking drugs in roughly half of the patients with ankylosing spondylitis. However, there was a wide variation across countries and doctors. Rheumatologists considered both disease activity and severity to be determinants of starting TNF blockers, but their decision was often in disagreement with ASAS recommendations.

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Non-steroidal anti-inflammatory drugs (NSAIDs), education, exercises and other modalities of physiotherapy are considered to be the cornerstone of treatment for patients with ankylosing spondylitis.<sup>1 2</sup> Disease-modifying antirheumatic drugs (DMARDs) are considered second-line treatment, but conclusive evidence for the efficacy of these drugs with respect to spinal manifestations is still lacking.<sup>3 4</sup>

The introduction of tumour necrosis factor (TNF)-blocking drugs has considerably changed the treatment options for patients with ankylosing spondylitis. Etanercept and infliximab seemed to be highly effective in improving signs and symptoms of ankylosing spondylitis, and are well tolerated.<sup>5–12</sup> These drugs are currently registered for the reduction of signs and symptoms of ankylosing spondylitis; however, reimbursement guidelines or mechanisms have not been developed in many countries.

The question of which patients with ankylosing spondylitis are appropriate candidates for TNF-blocking treatment seems important in view of these drug costs and their yet unknown long-term advantages or disadvantages.

To help rheumatologists with this issue, the ASsessment in Ankylosing Spondylitis (ASAS) international working group has recently developed recommendations for the use of anti-TNF $\alpha$  treatment for patients with ankylosing spondylitis.<sup>13</sup> These recommendations were developed by a review of

published reports in combination with expert opinion, including a Delphi exercise,<sup>14</sup> and a consensus meeting of the ASAS international working group. Following these recommendations, TNF-blocking agents should be considered in patients with mainly axial disease, who still have active disease defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of at least 4 on a 0–10 scale, despite an adequate therapeutic trial of at least two NSAIDs at optimal doses for at least 3 months. In addition, a positive expert opinion to start treatment is also required. Before the publication, dissemination and implementation of these international ASAS recommendations, we explored in the international rheumatological community what type of patients with ankylosing spondylitis were considered to be suitable for treatment with TNF-blocking drugs. We examined a representative sample of rheumatologists from several countries in Europe, Canada, Mexico and Australia. A preliminary survey had been conducted in The Netherlands.<sup>15</sup> The treating rheumatologists of patients

**Abbreviations:** ASAS, ASsessment in Ankylosing Spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; DMARD, disease-modifying antirheumatic drug; MRI, magnetic resonance imaging; NSAID, non-steroidal anti-inflammatory drug; TNF, tumour necrosis factor

**Table 1** Main demographic characteristics and disease history of patients with ankylosing spondylitis, with regard to country

Country	n	Sex (male, %)	Age (years)*	Disease duration since first symptoms (years)*	Paid job (yes, %)	Current sick leave (yes, %)	Inflammatory bowel disease (yes, %)	Previous treatment with sulfasalazine (yes, %)	Previous treatment with methotrexate (yes, %)
Australia	120	74	46 (13)	19 (11)	58	4	19	43	19
Belgium	97	75	44 (14)	16 (12)	57	22	7	29	11
Canada	94	79	38 (13)	15 (11)	61	23	10	11	5
France	137	55	41 (14)	13 (11)	59	17	10	38	5
Germany	200	73	45 (14)	16 (11)	67	12	6	32	15
Italy	103	80	47 (13)	16 (9)	62	29	17	35	15
Mexico	128	76	38 (13)	12 (11)	66	35	10	48	10
The Netherlands	98	75	47 (15)	21 (13)	64	20	7	29	1
Spain	183	78	47 (14)	18 (12)	64	42	5	37	9
UK	47	77	48 (12)	20 (13)	65	9	3	19	2
Total	1207	74	44 (14)	16 (11)	63	29	10	34	10

\*Values are mean (SD).

participating in an ongoing long-term observational cohort (Outcome in Ankylosing Spondylitis International Study) were asked whether they would start TNF-blocking treatment on their patients. Demographic, clinical and radiological data of these patients were compared with data of those who were and were not considered to be candidates for TNF-blocking treatment. In this survey, 30% of Dutch patients from the Outcome in Ankylosing Spondylitis International Study were considered to be candidates for TNF-blocking agents by their rheumatologists. Almost all parameters were worse for the candidates than for the non-candidates. Structural damage explained most variation in the practitioners' decision on whether or not to initiate anti-TNF treatment.

The first aim of this study was to obtain insight into the type of patients whom rheumatologists consider to be candidates for TNF blockers. We then analysed the decision whether to start TNF-blocking treatment for an individual patient with demographic characteristics, work status and information reflecting disease activity and disease severity. We also determined the actual proportion of patients with ankylosing spondylitis who were considered to be candidates for anti-TNF treatment in the community and to what extent these decisions were in agreement with the ASAS recommendations.

**METHODS**  
**Rheumatologists**

ASAS members who were not associated with the development of the ASAS guidelines were invited to participate. Ten ASAS members from 10 different countries volunteered to act as national coordinators and to be responsible for the

selection of rheumatologists and collection of data in their countries. The participating countries were: Australia, Belgium, Canada, France, Germany, Italy, Mexico, The Netherlands, Spain and the UK. Each country coordinator had to select rheumatologists who were considered to be experts in treating patients with ankylosing spondylitis and had ample experience with TNF-blocking agents in inflammatory rheumatic diseases. Most rheumatologists had experience with TNF-blocking drugs in ankylosing spondylitis in at least one clinical trial. These rheumatologists were unaware of the ASAS recommendations (unpublished at the time of study in 2003). The aim was to select 20 rheumatologists from each country. Rheumatologists were asked to evaluate 10 consecutive outpatients with a diagnosis of ankylosing spondylitis, and to determine whether they would initiate treatment with TNF blockers, assuming a certain risk-benefit profile for this treatment. This risk-benefit profile was defined as follows:

1. The treatment gives an improvement of at least 50% in at least 50% of the patients.
2. The drugs are available without limitation, and fully reimbursed.
3. There may be an unknown increased risk for (serious) infections, and little information is currently available on long-term safety.

The rheumatologists were asked to make the decision about the patient being a candidate for TNF-blocking drugs or not in the context of their normal routine practice—irrespective of whether this normal routine practice included

**Table 2** Disease activity, function and anti-TNF indicated by the treating rheumatologist, with regard to country

Country	n	BASDAI*	BASFI*	BASG*	Night pain (0–10)*	Patient global (0–10)*	Raised ESR (yes, %)	Raised CRP (yes, %)	Start TNF blockers (yes, %)
Australia	120	5.5 (2.3)	5.5 (2.7)	5.8 (2.5)	4.7 (2.8)	5.7 (2.5)	39.2	55.4	78.3
Belgium	97	4.3 (2.4)	4.2 (2.7)	5.2 (2.3)	3.9 (3.2)	4.9 (2.6)	40.3	58.0	56.7
Canada	94	4.6 (2.3)	3.7 (2.8)	4.8 (2.8)	4.2 (2.7)	4.5 (2.5)	57.1	57.1	37.2
France	137	4.8 (1.2)	3.8 (2.7)	5.4 (2.5)	4.3 (2.8)	5.0 (2.6)	58.8	53.3	45.3
Germany	200	4.2 (2.1)	4.1 (2.6)	5.3 (2.4)	4.5 (2.8)	5.0 (2.8)	55.2	58.9	49.0
Italy	103	4.9 (2.2)	4.6 (2.4)	5.8 (2.4)	4.8 (2.9)	5.9 (2.6)	60.8	62.0	68.0
Mexico	128	4.7 (2.7)	4.5 (3.1)	5.5 (3.0)	4.5 (3.3)	5.5 (2.9)	50.0	45.7	41.4
The Netherlands	98	4.1 (2.3)	4.1 (2.6)	5.0 (2.4)	3.7 (2.9)	4.3 (2.8)	40.5	48.1	40.8
Spain	183	4.3 (2.3)	3.8 (2.8)	5.0 (2.3)	3.8 (3.0)	4.7 (2.6)	56.7	62.0	38.3
UK	47	5.1 (2.2)	5.6 (2.6)	4.7 (2.5)	5.0 (2.9)	5.5 (2.8)	7.7†	42.9	38.3
Total	1207	4.6 (2.3)	4.3 (2.8)	5.3 (2.5)	4.3 (2.9)	5.1 (2.7)	51.5	56.7	49.3

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASG, Bath Ankylosing Spondylitis Global assessment of disease activity; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; TNF, Tumour necrosis factor.

\*Values are mean (SD).

†Data are available for only 13 patients.

questionnaires or specific assessments—and not take the patient's ideas about anti-TNF treatment into consideration. They were also asked to list the information that formed the basis of their decision, by filling a checklist.

### Patients

Consecutive patients with ankylosing spondylitis visiting their rheumatologist at an outpatient clinic visit were included in the study. Patients already treated with TNF-blocking drugs were excluded.

Patients were first seen by their practitioner according to normal clinical routine. Immediately after the consultation, they were examined by a metrologist (another doctor or a research nurse) for full clinical assessment, and the patients completed questionnaires. The assessment profile included instruments selected by the ASAS working group as the core set to assess outcome in ankylosing spondylitis,<sup>16, 17</sup> as well as other widely used instruments, such as BASDAI,<sup>18</sup> swollen joint count (range 0–44) or tender enthesis count (range 0–32), and information on the disease severity, previous and ongoing treatments and work status.

### Statistical analysis

Patients were divided into two groups: the “candidates”, defined as patients in whom the treating rheumatologists wanted to start TNF blockers; and the “non-candidates”, defined as patients in whom the treating rheumatologists did not wish to start TNF blockers (irrespective of the reason). The primary analysis was descriptive: means (standard deviation (SD)) and frequencies, stratified by country and TNF-blocking treatment options (candidate *v* non-candidate), were calculated if appropriate. Univariate between-group differences were statistically tested using Mann–Whitney two-sample U test, Kruskal–Wallis test or  $\chi^2$  test (Fisher's exact test) if appropriate.

Odds ratios (ORs) were calculated to investigate the contribution of various features to the decision to start TNF blockers, and compare settings of candidates with the international ASAS recommendations. Profiles of patients were defined by the BASDAI score, and by NSAID failure. To investigate which variables independently contributed to the decision to judge a patient as a candidate for TNF-blocking treatment, a multivariate logistic regression analysis was carried out with the candidates or non-candidates as the dependent variable, and all disease characteristics, disease activity and disease severity measures as independent variables.

**Table 3** Demographic characteristics, history and work status with regard to the willingness to treat with TNF-blocking drugs

	Anti-TNF indicated by the treating rheumatologist		
	Candidate (n = 595)	Non-candidate (n = 612)	p Value
Sex (male, %)	73.0%	74.4%	0.6
Age (mean (SD), years)	43 (12)	45 (15)	0.08
History of IBD (yes, %)	10.5%	8.7%	0.32
Hip involvement (yes, %)	40.0%	25.3%	<0.001
Previous treatment: sulfasalazine (yes, %)	63.5%	36.5%	<0.001
Previous treatment: methotrexate (yes, %)	67.8%	32.2%	<0.001
Paid job (yes, %)	63.7%	61.9%	0.54
Current sick leave (yes, %)	29.1%	16.6%	0.001

IBD, inflammatory bowel disease; TNF, tumour necrosis factor.

**Table 4** Disease activity and function

	Anti-TNF indicated by the treating rheumatologist		
	Candidate (n = 595)*	Non-candidate (n = 612)*	p Value
BASDAI	5.5 (2.1)	3.8 (2.2)	<0.001
BASFI	5.3 (2.5)	3.3 (2.6)	<0.001
Global pain	5.4 (2.7)	3.7 (2.6)	<0.001
Chest expansion (cm)	4.2 (9.3)	5.0 (10.9)	<0.001
Cervical rotation (degree)	49 (60)	57 (52)	<0.001
Swollen joint	1.9 (3.9)	0.7 (2.0)	<0.001
Tender enthesis	5.3 (6.0)	2.8 (4.4)	<0.001
ESR (mm at the end of the first hour)	33.5 (24.1)	18.8 (16.1)	<0.001
CRP (mg/l)	19.9 (21.8)	9.8 (9.8)	<0.001

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; TNF, tumour necrosis factor.

\*Values are mean (SD).

### RESULTS

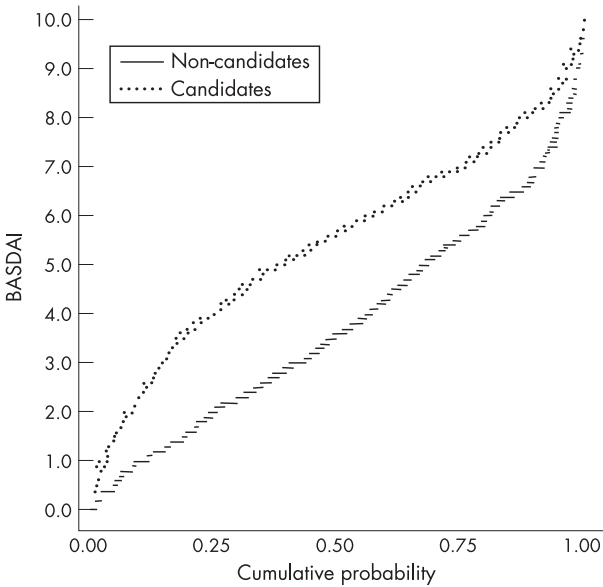
The 145 rheumatologists from 10 participating countries recruited a total of 1284 patients with ankylosing spondylitis. Data regarding the decision of the treating rheumatologists to initiate TNF-blocking treatment were available for 1207 patients, and these patients form the basis of this report. Overall, the rheumatologists indicated that they would start TNF blockers in 49.3% of the patients with ankylosing spondylitis.

High clinical disease activity, severe disease (including structural damage on spinal radiographs, loss of spinal mobility and loss of physical function), raised acute-phase reactants, lack of disease control by ongoing treatment, rapid functional decline and presence of peripheral arthritis (including hip involvement) were the reasons listed most often (in descending order) when considering the patient for TNF-blocking treatment. Rheumatologists rarely based their decision on disease activity on magnetic resonance imaging (MRI), recurrent infections, history of tuberculosis, comorbidity, high risk of adverse events in the patient and expected low compliance.

Tables 1 and 2 summarise the main characteristics of patients with ankylosing spondylitis. Important differences were observed with respect to the willingness to treat patients, ranging from 37.2% in Canada to 78.3% in Australia (table 2). On the basis of the BASDAI score and instruments proposed by the ASAS core set, Australian and UK patients had higher disease activity than patients from other countries. However, Australian and UK patients would have been treated with TNF blockers by their rheumatologists in different proportions (table 2).

Tables 3 and 4 compare the candidates and non-candidates with respect to demographic characteristics, history, work status, disease activity, functioning and spinal mobility. Demographic data were similar in both groups, with 72% men and a mean age of 44 years. Patients with a stated indication for TNF-blocking treatment tended more often to have a history of inflammatory bowel disease and hip involvement than the other patients (table 3). Candidate patients used DMARDs more often than non-candidates (previous DMARD use 89% *v* 47%; current DMARD use 62% *v* 42%) and more often reported sick leave.

All assessments of disease activity and severity (including patients' self-assessments), spinal mobility measures, joint counts, tender enthesis count, and acute-phase reactants scored on average higher in the candidate group, reaching significant differences (table 4). Thus, patients who were considered to be candidates for anti-TNF treatment by their



**Figure 1** Cumulative probability plots of the distribution of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores for the groups of candidate and non-candidate patients for treatment with tumour necrosis factor-blocking agents.

rheumatologist tended to have higher disease activity, higher levels of acute-phase reactants, worse spinal mobility, worse function, hip involvement more often and a higher prevalence of sick leave.

Figure 1 shows the cumulative probability plots of the distribution of the BASDAI scores for the groups of candidate and non-candidate patients. This plot shows that, although candidates have, on average, a higher BASDAI score than non-candidates, 40% of the patients who are not considered to be candidates by their rheumatologist still have a BASDAI score >4. By contrast, 25% of patients who are considered to

be candidates have BASDAI score <4. The minimum and maximum levels of BASDAI scores observed in this study were similar for both candidates and non-candidates.

If compared with the ASAS recommendations, 40% of the patients considered to be candidates for TNF-blocking treatment by their rheumatologists did not fulfil ASAS recommendations for previous NSAID use (at least two NSAIDs) and BASDAI score ( $\geq 4$ ) (tables 5, 6). Conversely, 31% of patients who do not fulfil the NSAID or BASDAI recommendations are still considered to be candidates for TNF-blocking treatment. Interestingly, the OR for being a candidate fulfilling both the BASDAI and NSAID criteria of the ASAS recommendations was not higher than the OR for being a candidate fulfilling either the BASDAI or the NSAID criterion.

Table 7 shows to what extent variables that are considered objective, such as raised acute-phase reactions, and rapid structural progression and activity assessed by ultrasound, scintigraphy or MRI, may have influenced the decision of the rheumatologist—for example, if they failed the criterion of BASDAI score  $\geq 4$ . This is presented for all patients together, as well as stratified for BASDAI score ( $\geq 4$  v <4). All objective variables contributed at least to some extent to the decision to start TNF-blocking drugs (OR >1). Importantly, however, they contributed similarly, or sometimes even less (C reactive protein), in patients with a BASDAI score <4 compared with patients with a BASDAI score  $\geq 4$ . Rapid radiographic progression was the only factor that seemed to affect the decision to start TNF-blocking drugs in an expected direction: the OR for rapid radiographical progression was higher in patients with a BASDAI score <4 than in those with a BASDAI score  $\geq 4$ .

**DISCUSSION**

We showed that, on average, 49% of patients with ankylosing spondylitis attending the outpatient clinic of rheumatologists from 10 countries would have TNF-blocking treatment initiated according to their treating doctor. However, this varied from 38% to 78% of the patients among different

**Table 5** Candidate and non-candidate settings compared with the ASAS recommendations

	Anti-TNF indicated by the treating rheumatologist			
	Candidates, n = 595*	Non-candidates, n = 612*	OR (95%CI)	p Value
ASAS recommendations fulfilled	357 (60)	188 (31)	3.3 (2.6 to 4.3)	<0.001
ASAS recommendations not fulfilled	238 (40)	424 (69)		
Total	595 (100)	612 (100)		

ASAS, ASessment in Ankylosing Spondylitis; TNF, tumour necrosis factor.  
\*Values are n (%).

**Table 6** Candidate and non-candidate settings compared with the components of the ASassessment in Ankylosing Spondylitis recommendations

	Anti-TNF indicated by the treating rheumatologist			
	Candidate (n = 595)	Non-candidate (n = 612)	OR (95%CI)	p Value
BASDAI $\geq 4$	456 (77%) [62%]	282 (46%) [38%]	3.8 (2.9 to 4.9)	<0.001
NSAIDs $\geq 2$	432 (73%) [56%]	345 (56%) [44%]	2.1 (1.6 to 2.7)	<0.001
BASDAI $\geq 4$ and NSAIDs $\geq 2$	357 (60%) [66%]	188 (31%) [34%]	3.4 (2.6 to 4.3)	<0.001

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; NSAID, non-steroidal anti-inflammatory drug; TNF, tumour necrosis factor.  
Percentages in parentheses refer to the percentage of the candidates.  
Percentages in square brackets refer to the percentage of patients fulfilling a certain criterion (eg, BASDAI score  $\geq 4$ ).



**Table 7** Influence of variables on opinions of rheumatologists for all patients together, stratified for the Bath Ankylosing Spondylitis Disease Activity Index criterion

Variables	n (available data)	OR (95% CI)	OR in patients with BASDAI score $\geq 4$ (95% CI) (n)	OR in patients with BASDAI score $< 4$ (95% CI) (n)
Raised ESR	880	3.3 (2.5 to 4.5)	2.9 (2.0 to 4.2) (535)	3.4 (2.1 to 5.6) (345)
Raised CRP	793	3.8 (2.8 to 5.1)	3.9 (2.7 to 5.8) (493)	2.8 (1.7 to 4.8) (300)
Rapid radiographic progression	476	8.6 (5.5 to 13.5)	7.8 (4.2 to 14.6) (276)	9.7 (4.7 to 19.7) (200)
Activity on MRI	156	2.3 (1.2 to 4.5)	2.8 (1.0 to 7.7) (96)	1.5 (0.5 to 4.5) (60)
Activity on scintigraphy	134	2.9 (1.4 to 5.9)	3.1 (1.2 to 7.8) (95)	2.4 (0.6 to 9.0) (39)
Activity on ultrasound	80	2.9 (0.9 to 8.9)	3.4 (0.7 to 17.7) (52)	3.1 (0.6 to 16.9) (28)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; MRI, magnetic resonance imaging.

countries. This study also shows that, in general, patients who are considered to be candidates for TNF-blocking treatment have a higher level of disease activity and more severe disease than those who are not considered to be candidates. But for individual patients, the patterns are less clear. Patients with high levels of disease activity by BASDAI are not always considered to be candidates by their doctors, and rheumatologists sometimes want to start TNF-blocking treatment in patients who currently have low levels of patient-reported disease activity, but who may, for example, have shown a high rate of radiographical progression.

One of the aims of this study was to get insight into what kind of patients with ankylosing spondylitis rheumatologists would like to treat with TNF blockers, before the publication, dissemination and implementation of the international ASAS consensus statement on the use of these drugs.<sup>13</sup> The most important criteria of the international ASAS recommendations are a BASDAI score  $\geq 4$ , the failure of at least two NSAIDs and a positive expert opinion to start treatment. The expert opinion takes into account all clinical, laboratory and imaging information. In this study, rheumatologists seemed to initiate TNF-blocking treatment in patients with active and advanced disease, reflected by high BASDAI scores, high levels of acute-phase reactants and higher degrees of spinal and functional limitation. However, considerable discrepancies exist in opinions of rheumatologists across countries and doctors, irrespective of activity and severity of disease. These results confirm the need for recommendations to standardise management of patients with ankylosing spondylitis.

One of the major criteria defined in the ASAS recommendations for initiation of TNF-blocking agents is a BASDAI score of at least 4 on a 0–10 scale. This cut-off criterion has proven to be robust and to predict, at a group level, patients with worse functional status and quality of life.<sup>19</sup> This starting point for the decision to initiate TNF-blocking treatment meets a high level of face validity in the international ankylosing spondylitis field, because in our study 77% of the patients considered to be candidates by their rheumatologists had BASDAI scores  $> 4$ , and 56% of the non-candidates had BASDAI scores  $< 4$ . Moreover, other domains that were supposed to make up the expert opinion, and were considered to be “hard”, such as high levels of acute-phase reactants or previous failure to NSAIDs, only moderately influenced the decision, with less weight compared with the criterion of BASDAI score  $\geq 4$ . However, the BASDAI criterion does not sufficiently explain by itself the rheumatologist’s opinion. This indicates that the rheumatologist’s opinion considerably adds to patient-reported disease activity rather than just reiterating that information.

Although the evidence that TNF-blocking treatment can retard radiographical progression is lacking, “rapid radiographic progression” seemed to be of importance in driving the rheumatologist’s decision. Landewé *et al*<sup>15</sup> observed this phenomenon in the preliminary survey conducted in The

Netherlands. In addition, we could not find firm evidence that other objective variables, such as C reactive protein level, erythrocyte sedimentation rate or activity on MRI, were considered to be more important than disease activity (BASDAI) in the decision to start TNF-blocking drugs. C reactive protein level and activity on MRI were even less contributory in explaining the decision to start TNF-blocking drugs in patients who did not fulfil the BASDAI criterion than in patients who did.

Rheumatologists do not seem to be influenced in their decision to start TNF-blocking treatment by previous NSAID use. In this study, exactly the same percentages of candidates and non-candidates fulfilled the BASDAI criterion solely and the combined criterion of BASDAI and NSAID. The results as described here should be taken into account in future updates of the international ASAS recommendations.

Our study has a few limitations. Firstly, this study was conducted in the early stages of anti-TNF treatment for patients with ankylosing spondylitis, and the level of experience of rheumatologists may not be similar in all instances. Secondly, although rheumatologists were asked to include patients in an unbiased manner (consecutive inclusion), it cannot be excluded that some selection towards a more active and severe disease course did occur. For example, patients with more active and severe disease, who visit the rheumatologist more often, have a higher prior probability of being included in this survey that spanned a limited period as compared with patients with inactive, quiet disease (sampling bias). Thirdly, rheumatologists had to make their decision under specific assumptions that may not entirely reflect reality. Nevertheless, the results highlight the willingness of the rheumatologists to start TNF-blocking drugs in the treatment of ankylosing spondylitis in a high percentage of patients; results also show that variation in this decision is quite large. This variation cannot be solely explained by differences in characteristics, and activity and severity of disease in patients. This observation indicates that recommendations on the initiation of TNF blockers might prove clinically useful. We intend to repeat this study after the implementation of the international ASAS recommendations in order to test whether these recommendations have contributed to the standardisation of TNF-blocking treatment.

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