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Original article

Six-month response to anti-TNF drugs in axial spondylarthropathy according to the fulfillment or not of New-York criteria for ankylosing spondylitis or French recommendations for anti-TNF use. A "real life" retrospective study on 175 patients

Stéphanie Gérard, Benoît le Goff, Yves Maugars, Jean-Marie Berthelot*

Rheumatology Unit, Nantes University Hospital (CHU Nantes), Place Alexis Ricordeau, 44093, Nantes Cedex 01, France

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Abstract

Objectives: To assess in clinical practice the 6-month outcome in patients with axial spondylarthropathy (SpA) treated by anti-TNF, according to the fulfillment of New-York criteria (NY) for the diagnosis of ankylosing spondylitis (AS), or agreement with French recommendations (SFR) for anti-TNF use in SpA.
Methods: Outcome could be retrospectively assessed according to the updated ASAS score (improvement of at least 50% or two units of the BASDAI) and the percentages of patients reaching at 6 month the patient BASDAI acceptable symptoms state (PASS) of 3.5.
Results: A total of 175 out of 203 patients could be retrospectively assessed at 6 month. Fifty-eight percent fulfilled the NY criteria, and 81% satisfied SFR recommendations. After 6 months of anti-TNF treatment, patients with NY criteria (NY+) met the updated ASAS outcome more often than NY− (70% versus 58%) (chi-square: 0.041): reduction of BASDAI of 2.86 ± 2.18 (NY+) versus 2.48 ± 2.39 (NY−) (NS). PASS of 3.5 was reached in 64% (NY+) versus 49% (NY−). ASAS outcome was met in 45%/60%/69%/88% of patients with 0/1/2/≥3 parameters to guide physician's opinion from SFR: raised ESR or CRP was present in 66%, active enthesitis or arthritis in 49%, coxitis in 13%, active or relapsing uveitis in 11%, inflammation of sacro−iliac or spine on MRI in 12%, and worsening of articular damage in 5%.
Conclusion: The effectiveness of TNF-blockers was slightly better in patients fulfilling the NY criteria for AS or SFR recommendations, but 58% of axial SpA not fulfilling NY criteria, and 48% of patients not satisfying French recommendations also met ASAS outcome.

Keywords: Axial; Spondylarthropathy; Ankylosing spondylitis; Anti-TNF; ASAS; Guidelines; Outcome; PASS; Undifferentiated; BASDAI

Spondylarthropathies (SpA) share common features, including preferential involvement of spine and sacro−iliac joints, enthesitis, genetic background, and association with other conditions like psoriasis, uveitis, and inflammatory disorders of the digestive tract [1,2]. Anti-TNF drugs have been a breakthrough in the treatment of ankylosing spondylitis (AS), the most achieved subset of SpA [3], especially for those patients whose disorder is no longer relieved by non-steroidal anti-inflammatory drugs (NSAID). Since several double-blind studies of anti-TNF in AS could demonstrate highly significant improvement in ASAS and BASDAI scores [4–9], which lasted much longer than the study period [10,11], a consensus was quickly reached for their extensive use in AS [12]. It was later confirmed that TNF-blockers induced improvement of health-related quality of life (HRQOL) in AS even more than in rheumatoid arthritis [13]. Therefore, infliximab, etanercept and adalimumab were approved to treat AS, and were licensed in France from 2003 to 2006. However, undifferentiated SpA (uSpA) are more frequent than typical AS, and many of these patients have not improved enough by taking NSAID. Therefore, many patients with axial uSpA not fulfilling AS criteria [3], can ask for anti-TNF [14]. There are still very few studies on the effectiveness of anti-TNF

* Corresponding author. Tel.: +33 240 08 48 22 or 01; fax: +33 240 08 48 22 30.
E-mail address: jeanmarie.berthelot@chu-nantes.fr (J.-M. Berthelot).

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drugs in SpA not fulfilling the criteria for AS [15–17]. Therefore, we sought to determine in patients treated by a TNF-blocker for axial SpA in our unit (i.e., outside of trials): (1) how often they satisfied New-York criteria (NY) for the diagnosis of AS and/or recommendations from the French Society for Rheumatology for anti-TNF use in SpA [18] (SFR) (which are very similar to those of the ASAS consensus) [12,19], e.g., 'who is having anti-TNF' for SpA in ''real life''; (2) the magnitude of their response to anti-TNF according to the satisfaction of the NY criteria or SFR recommendations. Indeed, anti-TNF use is allowed in France for patients fulfilling the ASAS consensus criteria, which gives French rheumatology units the opportunity of exploring the outcome of anti-TNF treatment according to the fulfillment or not of NY criteria.

The response to anti-TNF was assessed according to the updated ASAS outcome score (improvement of at least 50% or two units of the BASDAI) [20], the percentages of patients reaching at 6 month the patient BASDAI acceptable symptoms state (PASS) of 3.5, and the reduction of BASDAI values between baseline and M6.

1. Methods

1.1. Recollection of patients

All patients diagnosed as axial SpA and treated by a TNF-blocker from January 2003 to September 2006 in the single rheumatology unit of our university hospital (societal financing in all) were included in this retrospective cohort study. The decision to treat by anti-TNF had relied on the judgments of both office-based and hospital-based rheumatologists of the need for a trial of anti-TNF. All medical records featuring the chemical or brand name of at least one of the three anti-TNF drugs were first retrieved from the hospital database, using its software facilities. Then patients firmly diagnosed as spondylarthropathy (SpA) (fulfillment of ESSG [2] or Amor's [1] criteria in all cases) who had already been treated for at least 1 week by any of these three anti-TNF drugs were selected. Patients with predominantly peripheral SpA, and/or diagnosed as psoriatic arthritis, were finally excluded. None of these patients were involved in a clinical trial.

1.2. Outcome assessment

BASDAI scores [21,22], both at baseline and 6 months, could be extracted from the charts of 175 patients (BASDAI and BASFI assessments are routinely performed in our unit for patients treated by anti-TNF drug). The 6-month response of the 175 patients for whom BASDAI at baseline and M6 were both available, was assessed using several tools: difference in BASDAI scores between baseline and M6; reduction of two points of the BASDAI score; ratio of improvement of the BASDAI score; updated ASAS outcome (improvement of at least 50% or two units of the BASDAI) [12,20]; percentage of patients with BASDAI below the thresholds of 'patient acceptable symptoms state' (PASS) of 4.8 [23], 4.0 and 3.5 [24] after 6 months of treatment by the TNF-blocker.

1.3. Fulfillment of NY criteria or SFR recommendations

Fulfillment or not of New-York criteria, ASAS, and spondylarthritis French recommendations (SFR), was assessed using published guidelines [3,18]. SFR for anti-TNF use required in 2006: (a) a diagnosis of axial SpA (based either on New-York criteria or unequivocal inflammatory changes in the spine or the sacro–iliac joint on MRI); (b) a BASDAI score above 4.0 for 1 month; (c) failure to respond to at least three NSAID during a 3-month period each; (4) active disease (above 4/10 on an analogical scale) as assessed by the physician using six parameters: raised ESR or CRP, active enthesitis or arthritis, coxitis, active or relapsing uveitis, inflammation of sacro–iliac or spine on MRI, and worsening of articular damage [18]. An updated version has been published in December 2007 [25], which also includes characteristic involvement of the sacro–iliac joints, spine or peripheral sites documented by radiographs or computed tomography (structural damage) [25], but this version was not available at the end of our study and only unequivocal inflammatory changes in the spine or the sacro–iliac joint on MRI were considered.

1.4. Statistical analysis

Data were analysed using the SPPS-12.0 software. Outcomes were compared by chi-square for categorical outcomes (ASAS modified) or Student's *t*-test for continuous outcomes (mean of improvement in BASDAI scores at 6 months according to the fulfillment or not of New-York criteria or SFR recommendations). In Table 2, Student's *t*-test was used for continuous outcomes (age, disease duration, baseline ESR, baseline CRP, baseline BASDAI) and chi-square for categorical values.

2. Results

Complaints predominated either in the buttocks (73% of patients) and/or the back (93% of patients) in each of those 203 axial SpA treated by anti-TNF. The features of these 203 patients appear in Table 1 (left column). BASDAI and BASFI at baseline and 6 months were available in 175 of those 203 patients, who had been treated by infliximab ($N = 48$), adalimumab ($N = 13$), or etanercept ($N = 114$) (Table 1, right column). BASDAI at 6 months could not be retrieved in 28 cases either because of drug discontinuation ($N = 12$), or other reasons ($N = 16$) (information lost, or BASDAI not fulfilled at 6 months). Twelve out of 175 patients (7%) had previously been treated by another anti-TNF drug.

2.1. Compliance with ASAS and SFR recommendations for anti-TNF initiation in patients with axial SpA

New-York (NY) criteria were satisfied in only 58% (101/175) of patients. Differences between patients with and without NY criteria appear in Table 2. Significant differences were noticed for several items: patients without NY criteria were more females, had more frequent past episodes of reactive arthritis,