

Treatment of Spondyloarthritides with anti-TNF Biologic Agents

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The spondyloarthritides (SpA) comprise five subtypes: ankylosing spondylitis (AS), reactive arthritis (ReA), major parts of the arthritis/spondylitis spectrum associated with psoriasis (Pso), inflammatory bowel disease (AIBD) and undifferentiated SpA (uSpA). AS is the most frequent subtype of SpA being more prevalent than undifferentiated SpA but psoriatic arthritis (PsA), based on the high prevalence of psoriasis, is also quite frequent, while ReA and AIBD are relatively rare. The prevalence of the whole group of SpA has been recently estimated between 0.6 and 1.9% with an implicated AS prevalence between 0.1 - 1.1%. The prevalence of the whole group of SpA is similar to rheumatoid arthritis (RA). AS and PsA are the SpA subsets with the most severe course of disease. The burden of disease of AS patients equals RA.

Therapeutic options for patients suffering from the more severe forms of SpA have been limited during the last decades. Especially and in contrast to RA, no disease controlling anti-rheumatic therapy (DCART) has been available. Symptom-modifying anti-rheumatic drugs (SMARD) such as non-steroidal anti-inflammatory agents (NSAIDs) are widely used to ameliorate spinal pain. Furthermore, there is a clear role for intensive physiotherapy in most patients. Taken together, there has been a clear need for more effective therapies in the SpA.

There is now accumulating evidence that antitumor necrosis factor (TNF) therapy is highly effective in SpA, especially in AS and PsA. Based on the data recently published on more than 1000 patients with AS and PsA, this treatment seems to be even more effective than in RA. The anti-TNF α agents currently available, infliximab (Remicade), etanercept (Enbrel), and adalimumab (Humira) are approved for the treatment of RA in the U.S. and in Europe. The situation for the SpA is different from RA because there is an unmet medical need, especially

in AS since no therapies with DCARTs are available for severely affected patients, especially with spinal disease. Thus, TNF blockers may even be considered a first-line treatment in a patient with active AS and PsA whose condition is not sufficiently controlled with NSAIDs in the case of axial disease, and sulfasalazine or methotrexate in the case of peripheral arthritis.

For infliximab, a dose of 5 mg/kg was required, and intervals between 6 and 12 weeks were necessary to suppress disease activity constantly—also a major aim for long-term treatment. The efficacy of infliximab remains constant over 3 years and almost all patients relapse after withdrawal.

The standard dosage of etanercept is 2 x 25 mg subcutaneously per week. There are almost no studies yet on adalimumab (standard dose in RA, 20-40 mg subcutaneously every 1-2 weeks) in SpA. Improvement of spinal inflammation as detected by magnetic resonance imaging has been demonstrated for infliximab and etanercept. Both agents are now approved for AS in Europe. The efficacy of etanercept was first demonstrated in PsA, and it is now approved for this indication in the U.S. and in Europe. The studies with infliximab have also been very positive for PsA and psoriasis.

There is preliminary evidence that both agents do also work in other SpA, such as undifferentiated SpA (uSpA). Studies should be performed to document the long-term efficacy of this treatment. There is hope that ankylosis may be preventable, but it remains to be shown whether patients benefit from long-term anti-TNF therapy and whether radiologic progression and ankylosis can be stopped. Severe adverse events have remained rare. Complicated infections including tuberculosis have been reported. These can be largely prevented by appropriate screening. At this time, the benefits of antitumor necrosis factor therapy in AS seem to outweigh these shortcomings.