Use of abatacept in ankylosing spondylitis and other spondylarthropathies

Evidence-based Medicine | Official Recommendations | Expert opinion

Rationale

More than a decade after TNF antagonists were introduced to treat ankylosing spondylitis (AS) and psoriatic arthritis, the clinical effectiveness of these biologic agents has been confirmed in daily practice. However, as expected, the number of patients with primary or secondary failure of one, then two, and finally three TNF antagonists has increased steadily over time. Consequently, questions have arisen over the last few years about possible alternatives to TNF antagonists for use as second-line biological therapy. A few data on abatacept are available.

Clinical data on axial spondylarthritis

- The first case of abatacept treatment in a patient with spondylarthropathy who had failed TNFα antagonist therapy was published in 2009 (105). The good response to abatacept encouraged further use of this drug in spondylarthropathies

- A second case was reported (106) and an open-label study in 9 patients was presented at the 2009 meeting of the French Society for Rheumatology (107). Again, these preliminary results suggested that abatacept might hold promise in this indication.

- More recently, the first open-label pilot study was reported. For 6 months, 30 patients meeting modified NY criteria for SA received abatacept (108). Among them, 15 patients with a mean age of 45.3±9.8 years had failed treatment with at least one TNFα antagonist and the 15 others, with a mean age of 38±7.2 years, were naive to biological agents. All 30 patients had active axial AS (BASDAI >4 and VAS axial pain score >4). Patients received Abatacept according to the schedule recommended in RA, until week 24. At week 24, in the group with prior failure of TNFα antagonist therapy, an ASAS 20 response was achieved in 20% of patients and no patients had an ASAS 40 response, BASDAI 50 response, or partial ASAS remission. In the group naive to biologics, 26.7% of patients had an ASAS 20 response, 13.3% an ASAS 40 response, 6.7% a BASDAI 50 response, and 6.7% a partial ASAS remission. There were no significant changes in the BASDAI, patient overall assessment, or C-reactive protein level in both treatment groups.

- Another open-label study in 7 patients meeting ASAS criteria for AS also showed no clinically relevant response after 6 months of treatment (109). Overall tolerance was good.

These results leave little hope that abatacept may induce a major response in patients with active axial AS, particularly in patients with a previous failure to a TNFα antagonist therapy.

Clinical data on psoriatic arthritis

The level of evidence available for peripheral psoriatic arthritis is higher, since after anecdotal case-reports of good responses to abatacept (110-112), a Phase II placebo-controlled trial was conducted (113). In this trial, 170 patients with peripheral psoriatic arthritis were randomized to one of the 4 treatment arms for 6 months with:

- abatacept 10 mg/kg/infusion (as in RA),
- abatacept 10 mg/kg/infusion after two infusions of 30 mg/kg,
- abatacept 3 mg/kg/infusion,
- or placebo

according to the schedule used in RA.

The patients had active disease with at least three tender joints, and three swollen joints, and at least one psoriasis plaque. Failure of at least minimal DMARD therapy was required. Patients with a history of TNFα antagonist therapy were eligible.

After 6 months, the proportion of ACR20 responders was significantly higher in the two abatacept 10 mg/kg groups than in the placebo group (48% with 10 mg/kg, 42% with 10 mg/kg after a loading dose, and 19% with the placebo). No significant difference was found between the abatacept 3 mg/kg group and the placebo group (33% and 19%, respectively). The response rate was higher in the group naive to TNFα antagonists than in the group with a history of failure to one or more TNFα antagonists.

This study shows that abatacept in the doses used in RA had a greater effect on symptoms than did a placebo.

However, this study is not sufficient to determine whether the frequency of response and magnitude of response e are sufficient to warrant the use of this biological agent.