Use of abatacept in autoimmune diseases (systemic lupus erythematosus and other systemic autoimmune diseases)

Evidence-based Medicine | Official Recommendations | Expert opinion

Rationale

In systemic lupus erythematosus (SLE), the T cells contribute to initiate and to perpetuate the autoimmune response (114). They may be directly involved in the development of tissue damage. Interactions between T cells and B cells are involved in the production of the high-affinity autoantibodies implicated in the pathogenesis of SLE.

T cells also activate B cells and other effector cells, most notably dendritic cells, which produce the cytokines associated with SLE flares (115). B- and T-cell activation are associated with disease flares (116). Experimental studies showed increased survival after T-cell response modulation by CTLA4-Ig (abatacept) in the NZB/NZW mouse model of SLE (117), whereas in the Lyn-/- model, inhibition of T-cell co-stimulation failed to prevent immune complex deposition or the development of tissue lesions (118).

Clinical data

Few data are available.

- A prospective controlled double-blind study evaluated the efficacy and safety of abatacept versus placebo, in combination with conventional treatment, in patients who had SLE with polyarthritis, discoid lesions, or serositis (119). Patients with central nervous system or renal involvement were not eligible. The study patients received a predefined schedule of glucocorticoid therapy starting with 30 mg of prednisone-equivalent per day for 1 month. The primary efficacy criterion was the flare rate over one year, with flares being defined as a BILAG category A or B. This study showed no beneficial effects of abatacept on this primary criterion or on the secondary efficacy criteria. In addition, abatacept had no effect on the flare rate (BILAG A/B or BILAG A) in any of the three clinical subgroups (polyarthritis, discoid lesions, and serositis), except in a post hoc analysis, which showed a decrease in BILAG A flares over one year in the subgroup with joint involvement (36.5% with abatacept versus 62.5% with the placebo; treatment-related difference, -26.1 [95%CI, -47.4;-4.8]). Further post hoc analyses showed that the proportion of patients according to physician's judgment to have experienced flares during the treatment year was lower with abatacept (63.6% versus 82.5% with the placebo; treatment-related difference, -19.3 [95%CI, -30.6;-8.0]) (119). The beneficial effect of abatacept was more marked in the subgroup with polyarthritis at baseline (treatment-related difference,-28.3 [95%CI,-46.1;-10.5]) (119). An exploratory analysis of patient self-assessments (physical and mental components of the SF-36, fatigue, and sleep disturbances) showed significant improvements in the abatacept group in the physical SF-36 component, fatigue, and sleep disturbances (119).

  On the other hand, serious adverse events were significantly more common with abatacept (19.8%) than with the placebo (6.8%), particularly during the first 6 months and usually in the setting of an SLE flare.

- A double-blind placebo-controlled trial of abatacept added to mycophenolate mofetil or cyclophosphamide is ongoing in patients with lupus nephritis.

Official recommendations

In the EULAR recommendations, T-cell co-stimulation inhibitors are not listed among the drugs used to treat SLE but are mentioned in the ongoing research program (120). Abatacept is not listed among the drugs for SLE in the National Diagnosis and Management Protocol developed by the French High Health Authority (121).

Expert opinion

Given the absence of proof of efficacy in the first controlled trial and the increased rate of serious adverse events seen with abatacept in the same trial, until the results of the placebo-controlled trial in lupus nephritis become available, abatacept should not be used to treat patients with SLE. However, in patients with predominant joint manifestations who are dependent on glucocorticoid therapy and have failed all other treatment options, abatacept therapy may be discussed with specialists at a reference center.