Etanercept therapy was discontinued in 11 patients; inefficacy was reported as the reason for seven of these patients (five with soJIA and two with nsJIA). Only two adverse events were reported; neither was regarded as severe.

The authors report that the response in younger children was similar to that in older children, suggesting that etanercept therapy is a suitable and efficacious treatment option for patients with JIA under the age of 4 years.

Original article Tzaribachev N *et al.* (2008) Safety and efficacy of etanercept in children with juvenile idiopathic arthritis below the age of 4 years. *Rheumatol Int* **28:** 1031–1034

Anti-osteopontin monoclonal antibody improves and prevents arthritis in a mouse model

Previous studies have demonstrated that osteopontin, a proinflammatory cytokine, has an important role in the pathogenesis of rheumatoid arthritis (RA). To exploit osteopontin as a potential therapeutic target, Fan *et al.* examined the efficacy of two novel anti-osteopontin monoclonal antibodies (mAbs; 23C3 and F8E11) in the treatment of murine collagen-induced arthritis (CIA), an animal model of human RA.

CIA was induced in DBA/1J mice by administration of two doses of type II collagen, 21 days apart. The mice were treated with anti-osteopontin mAb or control IgG, either from the time of the first immunization (control group), or after the second immunization (established CIA treatment group). Both mAbs were effective in inhibiting the development of CIA, whereas reversal of established disease was only achieved with mAb 23C3. Osteopontin was observed to prevent apoptosis of type II collagen-activated T cells and of T cells in the synovial fluid of patients with RA. On addition of mAb 23C3, T-cell apoptosis was drastically increased. The authors identified the epitope ATWLNPDPSQKQ (the binding site for mAb 23C3) within osteopontin as being directly involved in protection of activated T cells.

According to Fan and colleagues, the ability of mAb 23C3 to promote apoptosis of activated T cells indicates that the mAb could provide a new treatment option for RA.

Original article Fan K *et al.* (2008) Treatment of collagen-induced arthritis with an anti-osteopontin monoclonal antibody through promotion of apoptosis of both murine and human activated T cells. *Arthritis Rheum* **58:** 2041–2052

Bortezomib eliminates antibody-producing plasma cells in mice with lupus-like disease

Long-lived plasma cells, which produce autoantibodies in diseases such as systemic lupus erythematosus (SLE), are an as yet unexplored therapeutic target in such antibody-mediated disorders. Bortezomib (a proteasome inhibitor) has recently been approved for treatment of relapsed multiple myeloma, a plasma cell neoplasia, owing to the sensitivity of immunoglobulin-synthesizing myeloma cells towards proteasome inhibitors. Neubert and colleagues hypothesized that bortezomib could also target autoantibody-producing plasma cells implicated in the pathogenesis of SLE, and investigated the outcomes of proteasome inhibition in mice with lupus-like disease.

The researchers found that, for the depletion of total and long-lived plasma cells in mouse bone marrow, bortezomib was more efficient and specific than the standard SLE treatments dexamethasone and cyclophosphamide. A marked decrease in plasma cells (>60% in spleens, >95% in bone marrow) was observed within 48 h of bortezomib treatment, indicating that the proteasome inhibitor acts directly on these cells. Bortezomib treatment also significantly decreased double-stranded-DNA-specific autoantibody production after 7 days, whereas the standard treatment had no effect. Mice treated with bortezomib remained healthy and survived much longer than control mice treated with phosphate buffer solution only.

Neubert *et al.* conclude that elimination of autoantibody-producing plasma cells by proteasome inhibitors might represent a new treatment strategy for antibody-mediated diseases, and warrant further careful clinical studies.

Original article Neubert K *et al.* (2008) The proteasome inhibitor bortezomib depletes plasma cells and protects mice with lupus-like disease from nephritis. *Nat Med* **14:** 748–755