0.3–0.4 mg/kg at increasingly frequent intervals (once every 3 weeks to once weekly) for 15 months. Bone turnover was reduced, cortical bone mass was increased, and both patients reported a subjective decrease in bone pain. When treatment was ceased, bone turnover reverted to an accelerated pattern. There were no local reactions associated with treatment, although symptoms of mild transient hypocalcemia were noted. There was no evidence of antibodies against recombinant osteoprotegerin.

This trial corroborates evidence that juvenile Paget's disease results from osteoprotegerin deficiency. The investigators deduce that recombinant osteoprotegerin as once-weekly, self-administered subcutaneous injections could be a valuable treatment for juvenile Paget's disease.

Rachel Murphy

Original article Cundy T *et al.* (2005) Recombinant osteoprotegerin for juvenile Paget's disease. *N Engl J Med* **353:** 918–923

GnRH analogue protects against cyclophosphamide-induced ovarian failure in SLE

Depot leuprolide acetate, a gonadotropin-releasing hormone (GnRH) analogue, protects against premature ovarian failure (POF) in women receiving cyclophosphamide for systemic lupus erythematosus (SLE), a recent trial has found.

SLE affects a disproportionately large number of women of child-bearing age, but severe manifestations of SLE are often treated with cyclophosphamide, a drug associated with significant toxicities including POF. Continuous administration of a GnRH analogue suppresses ovulation and reduces estrogen and progesterone to prepubertal levels, and has been shown in animal and pilot human studies to prevent chemotherapy-induced ovarian damage.

In this latest trial, 40 women under the age of 35 years were enrolled: 39 with severe SLE and one with systemic vasculitis. All participants were treated with monthly intravenous cyclophosphamide plus a tapering dosage of daily oral prednisone. In 20 women, a GnRH analogue injection was also given 10 days prior to cyclophosphamide, although some women did not receive this until the second monthly cycle. The remaining 20 women were age-matched and cyclophosphamide-dose-matched controls.

Results showed that the GnRH analogue significantly reduced POF compared to the control treatment. The GnRH analogue was generally well tolerated, although two patients developed thrombocytopenia and experienced severe dysfunctional bleeding.

Further investigations are needed to confirm the efficacy and mechanism of the ovarian protection, but GnRH-analogue injection has the potential to be a safe, cost-effective, easily administered method for ovarian preservation in women undergoing chemotherapy for various indications.

Rachel Murphy

Original article Somers EC *et al.* (2005) Use of a gonadotropin-releasing hormone analog for protection against premature ovarian failure during cyclophosphamide therapy in women with severe lupus. *Arthritis Rheum* **52:** 2761–2767

Rituximab is an effective treatment for Sjögren's syndrome

There are currently no evidence-based treatments for Sjögren's syndrome (SS), an autoimmune disease characterized by chronic inflammation of the salivary and lacrimal glands that leads to malignant B-cell lymphoma in 5% of patients. Salivary gland function attenuates early in the disease, accompanied by altered salivary composition. Although associated with side effects and the production of antichimeric antibodies, the anti-CD20 monoclonal antibody rituximab has shown promise in the treatment of SS in this small, open-label, phase II study.

Four rituximab infusions were given at weekly intervals to eight patients with early primary SS and seven patients with both primary SS and mucosa-associated lymphoid tissue type (MALT) lymphoma, with the aim of depleting B cells and thereby reducing disease severity. Three early-SS patients did not complete the protocol, owing to antichimeric antibody production and serum-sickness-like symptoms, which are rarely described in the rituximab literature.

In patients with residual stimulated salivary production >0.10 ml/min (all early-SS patients and two with MALT lymphoma), treatment resulted in a significant increase in stimulated salivary secretion, persisting for up to 48 weeks in three patients. Three patients with MALT lymphoma achieved remission, and subjective factors including mouth dryness and physical functioning improved in the early-SS group.