RESEARCH HIGHLIGHTS

OSTEOARTHRITIS Inhibitor of nerve growth factor relieves OA pain

Treatment with tanezumab, a humanized monoclonal antibody against nerve growth factor (NGF), has been shown to reduce pain and improve joint function in patients with osteoarthritis (OA) of the knee in a proof-of-concept study. The results of the trial, which was led by Nancy Lane, are published in the *New England Journal of Medicine*.

"NGF has been known for over 20 years to be an important protein for inducing sensory nerve pain," explains Lane. Animal studies conducted in the past decade showed that blocking NGF provides effective analgesia, and in a phase I trial tanezumab induced rapid and long-lasting pain relief. The results of the phase II trial support these findings, and show that tanezumab treatment is associated with mild or moderate adverse effects.

The study enrolled 450 patients with moderate or severe knee OA, who were randomly allocated to receive one of several doses of tanezumab (10, 25, 50, 100 or 200 µg per kg body weight) or placebo. As the primary outcome measure, the investigators chose the patients' assessment of global response and of knee pain when walking on days 1 and 56 of the study. "Individuals with moderate-tosevere knee OA frequently have more pain when they walk and less pain when they are not active, but most studies just ask about knee pain independent of activity," Lane points out.

After 16 weeks, patients who received two injections of tanezumab 8 weeks apart reported greater average reductions in pain while walking than those who received placebo (45-62% with various doses of tanezumab vs 22% with placebo; P < 0.001). The efficacy was dose dependent, with the greatest reduction in pain occuring with the higher doses. Patients' global assessment scores also increased more in the tanezumab groups as compared with the placebo group. Adverse events with tanezumab therapy,



which were most commonly headache, upper respiratory tract infection and paresthesia, occurred in 68% of patients, compared with 55% in the placebo group.

"The future is bright for non-narcotic analgesics for pain reduction in this pathway, but we need to know more," says Lane. Determining how NGF is involved in joint pain will be key to the success of this approach to the treatment of OA.

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Original article Lane, N. E. *et al.* Tanezumab for the treatment of pain from osteoarthritis of the knee. *N. Engl. J. Med.* **363**, 1521–1531 (2010)