canakinumab for gout attacks

Too risky

- There are no clinical trials of canakinumab in patients with gout attacks refractory to several prior treatments. Adverse effects mainly include infections, hypersensitivity reactions and dizziness.

Gout attacks are due to accumulation of uric acid crystals in the joints (1). If left untreated, the associated inflammation and pain subside after a few days. When ice, paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, and colchicine are not sufficiently effective or cannot be used, systemic corticosteroids are another option (1). Adding an opioid cannot be used, systemic corticosteroids are ineffective and corticosteroid treatment of gout when NSAIDs and/or colchicine have failed (2-5). Both NSAIDs and colchicine were ineffective, not tolerated or contraindicated in only about one-third of patients. Patients had experienced at least three gout attacks in the year prior to enrolment, and 42% were taking a preventive treatment (mainly allopurinol).

At baseline, pain intensity in the most painful joint averaged 74 mm on a visual analogue scale ranging from 0 mm to 100 mm. In a pooled analysis of the two trials, 72 hours after the injection, pain intensity was 25 mm with canakinumab versus 36 mm with triamcinolone (p < 0.0001) (2-5). The clinical relevance of this difference is uncertain. Full pain relief was achieved in respectively 46% and 37% of patients in the canakinumab and triamcinolone groups, a non-significant difference. Recourse to paracetamol, codeine or corticosteroids was less frequent with canakinumab than with triamcinolone (37% versus 55%, p < 0.0001).

Infections, hypersensitivity reactions, dizziness. The immunosuppressive effect of canakinumab, and its long elimination half-life (nearly a month), create a risk of infections and possibly cancer (6).

In the two trials, 19% of patients receiving canakinumab developed an infection, versus 13% of patients receiving triamcinolone. The infections mainly included nasopharyngitis, upper respiratory tract infections, urinary tract infections, and bronchitis (2,3). Four patients receiving canakinumab and none treated with triamcinolone developed serious infections, while respectively 3.2% and 2.4% of patients developed opportunistic infections. It is also noteworthy that two patients treated with canakinumab, one for juvenile idiopathic arthritis and one for periodic syndrome, died of septic shock and disseminated tuberculosis (3).

Overall, 63% of patients treated with canakinumab versus 51% of those receiving triamcinolone experienced at least one adverse event (severe in respectively 7% and 3% of patients) (2,3). The most common adverse effects associated with canakinumab were hypersensitivity reactions (including angioedema), dizziness, haematological disorders (especially neutropenia), and hepatic disorders (2,3). Elevation of serum uric acid levels was more frequent with canakinumab than with triamcinolone.

The canakinumab risk management plan calls for special monitoring of infections and malignancies.

In practice. Given its uncertain efficacy on gout-related pain, canakinumab is too risky to use for treatment of gout attacks. Its price is also exorbitant. It is better to stick with existing symptomatic treatments, which should be initiated as early as possible.

Selected references from Prescrire’s literature search

- Scientists consulted by the US Food and Drug Administration (FDA) voted unanimously against authorising canakinumab for the treatment of gout (ref 4).

- Prescrire Editorial Staff “Treatment of gout attacks” Prescrire Int 2008; 17 (95): 123.