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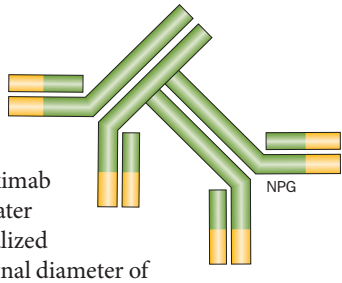


INFLAMMATION

Phase III trial of infliximab in Kawasaki disease

Primarily affecting children aged <5 years, Kawasaki disease is thought to be an exaggerated immune response to one or more infectious triggers. If left untreated, approximately one-quarter of patients develop coronary artery aneurysms, which can mean a life of antithrombotic therapy and regular follow-up.

Standard initial treatment for patients with Kawasaki disease involves aspirin and a single infusion of intravenous immunoglobulin. Unfortunately, however, the inflammatory process is not sufficiently interrupted in 10–20% of treated patients, and these 'immunoglobulin-resistant' individuals remain at high risk for coronary artery aneurysm. Various investigators, therefore, hypothesize that intensification of the initial anti-inflammatory therapy might reduce the chances of an insufficient therapeutic response and subsequent coronary artery aneurysms in patients with Kawasaki disease.

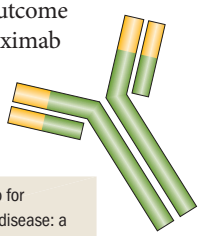
In a phase III randomized, controlled trial, Dr Adriana Tremoulet and colleagues assessed the utility of adding infliximab, a chimeric monoclonal antibody that specifically binds tumor necrosis factor, to standard initial therapy in patients with Kawasaki disease. In the two-centre trial, 196 children with Kawasaki disease, who had experienced fever for 3–10 days, were randomly assigned to undergo intravenous administration of either infliximab or placebo (saline) immediately before receiving standard initial therapy.

Treatment resistance—the primary outcome of the study—was similar for the two groups. Notably, however, duration of fever was shorter, and reductions in the concentration of C-reactive protein, the absolute neutrophil count, and the erythrocyte sedimentation rate were more rapid in the infliximab group. Moreover, no patients who received infliximab experienced a reaction to the intravenous immunoglobulin infusion, compared with 13.4% of patients assigned to placebo.

The proximal left anterior descending coronary artery is the most frequent site of coronary artery aneurysm in patients with Kawasaki disease. At 2 weeks, patients in the infliximab group showed a greater decrease in a normalized measure of the internal diameter of this artery than patients in the placebo group; however, the difference between the two groups was no longer significant at 5 weeks. No significant differences were observed for the internal diameters of the proximal right coronary artery or the left main coronary artery at these time points.

The investigators point out that the low rate of immunoglobulin resistance in the placebo group (11.3%) would have decreased their power to detect a difference in the primary outcome measure. They also speculate that "the primary outcome of a larger multicentre trial of infliximab should perhaps be adverse coronary artery outcomes".

Bryony M. Mearns



Original article Tremoulet, A. H. *et al*. Infliximab for intensification of primary therapy for Kawasaki disease: a phase 3 randomised, double-blind, placebo-controlled trial. *Lancet* doi:10.1016/S0140-6736(13)62298-9