

## Journal club

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### Triple therapy for idiopathic pulmonary fibrosis

This multicentre, randomised, double-blind placebo-controlled trial was designed to address the effectiveness of the antioxidant, N-Acetylcysteine (NAC), alone and in 'triple' therapy (prednisolone, azathioprine and NAC) in idiopathic pulmonary fibrosis (IPF). Patients with IPF and mild to moderate lung function impairment ( $FVC \geq 50\%$  and  $TLCO \geq 30\%$ ) were assigned to receive triple therapy, NAC alone or matched placebo for 60 weeks.

Target recruitment was 130 patients per group, however, following a planned interim analysis (mean follow-up 32 weeks) the triple therapy arm ( $n=77$ ) was halted. Compared with placebo ( $n=78$ ), increased risks of death (8 vs 1), hospitalisation (23 vs 7), and serious adverse events (24 vs 8) were seen. The placebo and triple therapy groups had no significant differences in demographic and clinical characteristics. No clinical or physiological benefit was seen with triple therapy.

This is the first trial to compare triple therapy with placebo, and provides evidence that as a treatment for IPF, triple therapy increases risks of death and hospitalisation. The reasons for this, and which components might be responsible, are uncertain. The shortened duration of this trial limits comparison of mortality rates with previous trials when assessing if an aberrant outcome has occurred.

This trial illustrates the importance of conducting placebo-controlled randomised trials to guide clinical practice when prescribing unproven and potentially harmful therapies. The NAC-only, and placebo groups, continue to recruit. In a disease with such limited treatment options and unmet clinical needs, further evidence for a therapeutic role of NAC is sorely needed.

► The idiopathic pulmonary fibrosis clinical research network. Prednisone, azathioprine, and N-Acetylcysteine for pulmonary fibrosis. *N Engl J Med* 2012;**366**:1968–77.

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