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Journal club

CFTR potentiator for cystic fibrosis

This multicentre, double blinded, randomised controlled trial assessed the efficacy of ivacaftor, a cystic fibrosis transmembrane conductance regulator (CFTR) protein potentiator.

The primary outcome of the trial was the change in the forced expiratory volume in 1 s (FEV_1). The secondary outcomes were time to the first pulmonary exacerbation and subject-reported respiratory symptoms. The trial included 161 subjects who were 12 years of age or above with the G551D mutation.

The study showed a treatment effect of 10.6% in FEV_1 ($p<0.001$) in patients with a starting FEV_1 <70% predicted. There was a 55% reduction in the risk of pulmonary exacerbation and a statistically significant improvement in subject-reported respiratory symptoms by 48 weeks. The study showed no significantly increased rate of adverse effects or dropout rate associated with ivacaftor. The study was not powered to assess the treatment effects in different demographic subgroups.

The G551D mutation is present only in approximately 4%–5% of cystic fibrosis patients and produces a defective CFTR protein which localises onto the epithelial cell surfaces. In the commonest CFTR mutation, F508del, the CFTR protein is however unable to reach the cell surfaces. Ivacaftor, given its mechanism of action, is therefore not applicable to this larger patient group.

The study has shown potential clinical applications which have arisen through our increased understanding of the CFTR gene. The effects of ivacaftor beyond 48 weeks and in combination therapy for individuals with other CFTR mutations would be interesting areas of research and may broaden the clinical application of ivacaftor.

► **Ramsey BW,** Davies J, McElvaney G, *et al.* A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. *N Eng J Med* 2011;**365**:1663–72.

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