

Cystic Fibrosis Research News

Title:

Lumacaftor/ivacaftor in patients with cystic fibrosis and advanced lung disease homozygous for *F508del-CFTR*

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What was your research question?

Is combination therapy with lumacaftor/ivacaftor safe, tolerable, and effective in patients with cystic fibrosis (CF) aged 12 years and older with advanced lung disease?

Why is this important?

Patients with CF and more severe lung dysfunction have a greater disease burden and risk of death than patients with better lung function. No FDA (Food and Drug Administration)-regulated studies have been conducted to determine the safety, tolerability, or efficacy of lumacaftor/ivacaftor in patients with CF who also have advanced lung disease. These patients may be at more risk of side effects from lumacaftor/ivacaftor treatment.

What did you do?

We conducted a clinical study that included patients with CF aged 12 years and older who had two copies of the *F508del-CFTR* gene mutation and who also had advanced lung

Cystic Fibrosis Research News

disease. All patients underwent medical tests, including spirometry (which measures how well the lungs are working) before and after taking lumacaftor/ivacaftor. Patients received lumacaftor 400 mg/ivacaftor 250 mg every 12 hours (full dose) for 24 weeks. To improve study drug tolerability, dose modification to half-dose for 1 to 2 weeks was permitted at the discretion of the study doctor. Safety, tolerability, and efficacy were assessed in this study.

What did you find?

Treatment benefits associated with lumacaftor/ivacaftor were observed in patients with CF and advanced lung disease similar to those seen in patients with CF without advanced lung disease. Patients receiving lumacaftor/ivacaftor had less need for antibiotics to treat their symptoms and fewer hospitalizations. An increased incidence of side effects (including dyspnea and chest tightness) was observed in patients receiving full-dose lumacaftor/ivacaftor. However, patients who initiated treatment with half-dose lumacaftor/ivacaftor prior to increasing to full dose experienced fewer side effects and did not discontinue study drug treatment.

What does this mean and reasons for caution?

Although this study had only a small number of patients, these data demonstrated that lumacaftor/ivacaftor is safe and tolerable in patients with CF and advanced lung disease. The findings from this study suggest that patients with CF and advanced lung disease might benefit from treatment initiation at a lower dose of lumacaftor/ivacaftor, with a gradual increase to full dose. This study should be interpreted with caution because no direct comparison was made to patients with CF and higher lung function.

What's next?

This study showed that lumacaftor/ivacaftor can potentially be a safe and effective therapy in patients with CF and advanced lung disease. Additional studies are needed to observe a larger patient population over an extended study period in order to provide more evidence for our findings.

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