

Cystic Fibrosis Research News

Title:

Immediate Effects of Lumacaftor/Ivacaftor Administration on Lung Function in Patients with Severe Cystic Fibrosis Lung Disease

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What was your research question?

What are the side effects of lumacaftor in combination with ivacaftor (LUM/IVA) treatment, particularly in relation to respiratory symptoms and lung function, in people with cystic fibrosis (CF) who have severe lung disease?

Why is this important?

Lumacaftor combined with ivacaftor is a new treatment that aims to reverse the underlying cell defect of CF. Two clinical trials have demonstrated that LUM/IVA improves clinical outcomes in people who have two copies of the F508del gene mutation. However, people with this mutation but lung function (FEV₁) below 40% predicted were excluded from these studies and the potential benefits and side effects in this more severe disease group remains unknown. Shortness of breath and chest tightness were common in the clinical studies when starting treatment and occurred more frequently in those with lower lung function. Here, we report the safety outcomes in people with severe CF lung disease in our clinic who were prescribed LUM/IVA treatment.

What did you do?

Twelve people attending our CF clinic who were eligible for LUM/IVA therapy and had a lung function of less than 40% predicted were observed in our outpatient clinic for 4 hours after their first dose. We performed spirometry immediately prior and 2 hours following the first dose. Those who had a decline in lung function or had respiratory symptoms were given an inhaled medication called salbutamol to open their airways and spirometry was repeated. Subjects were seen in clinic after 24 hours and at 1 month after commencing treatment. Side effects and lung function were recorded during this period.



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What did you find?

Subjects with severe lung disease reported shortness of breath and chest tightness more frequently than in clinical studies. A decline in lung function was observed in all participants at 2 and 24 hours following the first dose of LUM/IVA therapy but this decline recovered in most patients by 1 month. Salbutamol only improved lung function in a small number of subjects. Increases in respiratory symptoms requiring extra treatment occurred commonly within the first month of starting treatment. Three of the twelve study participants stopped treatment due to persistent shortness of breath and chest tightness after 1 month, however no long-term problems were observed.

What does this mean and reasons for caution?

People with CF and clinicians should be aware of the possible side effects of LUM/IVA if severe lung disease is already established when starting the medication. Based on our experience, we recommend that patients be monitored in the CF clinic closely after commencing the medication, and throughout the first month, so that increases in symptoms and side effects can be identified and treated appropriately. We report findings from only 12 people with CF and this may not reflect everyone with severe CF lung disease who starts LUM/IVA therapy.

What's next?

Our aim is to continue to collect data in this group so the long-term benefit and adverse effects are recorded and recognised. Strategies to reduce the side effects observed following initial treatment are currently being investigated and we await the results from these studies.

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