European Cystic Fibrosis Society

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Cystic Fibrosis Research News

Title:
Use of elexacaftor/tezacaftor/ivacaftor among cystic fibrosis lung transplant recipients

Lay Title:
Use of the CFTR modulator combination elexacaftor/tezacaftor/ivacaftor after lung transplant

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What was your research question?
Is elexacaftor/tezacaftor/ivacaftor (ETI) being prescribed to treat cystic fibrosis (CF) for people living with a lung transplant? If so, who is being prescribed ETI after lung transplant and why? Are there clinical effects of ETI in lung transplant recipients?

Why is this important?
People living with CF (pwCF) still have signs and symptoms of CF after lung transplant. It is possible that use of CFTR modulators, such as ETI, after lung transplant could lead to improvements in non-lung aspects of CF. ETI is not routinely prescribed after lung transplant because the primary benefit studied in clinical trials was in lung function and transplanted lungs do not receive a benefit from CFTR modulators. Drug interactions and potential side effects of ETI must be considered when prescribing ETI in transplant recipients.

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What did you do?

We performed a medical records-based study at the 15 centres within the Cystic Fibrosis Lung Transplant Consortium. We identified all lung transplant recipients who were prescribed ETI after transplant from October 2019 to September 2020. We collected information about reasons ETI was prescribed and when/if/why it was stopped. We also analysed laboratory data to determine whether there was a meaningful change in diabetes control, anemia, or liver enzyme levels. We measured the change in body mass index (BMI), number of courses of antibiotics, and frequency of acute cellular rejection before and after ETI was started.

What did you find?

Use of ETI after lung transplant was variable across the centres, some centres had 0% while others had up to 35% of CF lung transplant recipients who were prescribed ETI. On average, only 13% of recipients were prescribed ETI. Sinus disease and gastrointestinal symptoms were the most common reasons for prescribing ETI. More than 40% of recipients stopped ETI due to side effects or lack of benefit. Immunosuppression management was challenging (requiring extra blood tests) for 4 patients (4%). Hemoglobin A1c (measure of average blood sugar level) improved on average for everyone, and hemoglobin (red blood cell count) increased on average for people with anemia. Body mass index (BMI) and liver enzymes were not statistically different. The number of antibiotic courses and number of episodes of lung transplant rejection decreased after ETI initiation.

What does this mean and reasons for caution?

Use of ETI after lung transplant was rare. While there remains potential for improvement in non-lung clinical outcomes, our data provided limited evidence of benefit. Only a small number of people had data both before and after ETI. Other factors that influenced the clarity of the data included the fact that there were fewer clinic visits and people were less likely to be exposed to non-COVID-19 respiratory viruses due to early pandemic isolation. These pandemic factors likely influenced observed clinical outcomes. We did not capture sinus or gastrointestinal symptom data, which were the most common reasons ETI was started.

What's next?

We plan to study the pharmacokinetics (blood concentrations over time) of ETI in lung transplant recipients to determine whether drug interactions affect ETI levels in the blood. We hope to prospectively study the use of ETI in lung transplant recipients in order to capture clearer data about potential benefits and/or harms of ETI in this setting.

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