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Cystic Fibrosis Research News

Title:

Measuring the effect of elexacaftor/tezacaftor/ivacaftor combination therapy on the respiratory pump in people with CF using dynamic chest radiography

Lay Title:

Measuring how the drug elexacaftor/tezacaftor/ivacaftor affects the muscles of breathing, using dynamic chest radiography

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What was your research question?

The drug elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA, sold as Trikafta™ or Kaftrio™) has been shown to have many benefits for people with CF, such as fewer flare ups of CF, and better lung function as measured by spirometry. We wanted to investigate whether ELX/TEZ/IVA also affects the muscles of breathing.

Why is this important?

Understanding if and how the muscles of breathing change after starting drugs such as ELX/TEZ/IVA might help us better understand how these drugs work on the body. It might also be useful for studies of these types of drugs in the future, as a means of telling if the drugs are working or not. As more and more people start taking drugs such as ELX/TEZ/IVA,

we may also need to develop ways to monitor lung health that can detect small changes in lung function early on.

What did you do?

We used a new type of X-ray machine, called dynamic chest radiography (DCR for short), to look at the lungs of people with CF, before and after starting ELX/TEZ/IVA. Rather than a single snapshot like a standard X-ray, DCR takes a 10-second X-ray video of the chest, during breathing. DCR can identify and follow the movement of the diaphragm (the main muscle of breathing) and the outline of the lungs. It is quick to do (around five minutes). This was part of a larger study, called DYNAMIC-CF, which is looking at the lung health of people with CF using DCR.

What did you find?

In total, we looked at the DCR X-rays of 24 people with CF, before and after starting ELX/TEZ/IVA. After starting ELX/TEZ/IVA, the diaphragm moved out significantly further and faster during a deep breath. The diaphragm also returned to its resting position at a significantly higher speed after a deep breath. The lungs were also significantly smaller after taking a breath out. This suggests that after starting ELX/TEZ/IVA, the lungs can expand more, and have less trapped air. The muscles of breathing move significantly faster and further. The improvements seen with DCR were mirrored by significant improvements seen in spirometry.

What does this mean and reasons for caution?

So far, no other studies have investigated how the muscles of breathing or the size of the lungs are affected by ELX/TEZ/IVA. No other studies have used DCR in people with CF before. In this study, we used DCR to show that ELX/TEZ/IVA improves the mechanics of breathing in people with CF. DCR might be a useful X-ray technique in future studies of CF drugs. However, this study was small (24 people with CF). We took only one DCR before and after starting ELX/TEZ/IVA.

What's next?

Larger studies with more follow-up DCR X-rays are needed to confirm the findings of our study. We also need to continue to refine the way in which we take DCR images. As part of the DYNAMIC-CF study, we are doing work to calculate the volume of the lungs using DCR.

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