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Cystic Fibrosis Research News

Title:

AEROSOLIZED LANCOVUTIDE IN ADOLESCENTS (≥12 YEARS) AND ADULTS WITH CYSTIC FIBROSIS – A RANDOMIZED TRIAL

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What was your research question?

Does inhalative lancovutide improve lung function, quality of life and clinical status (including number and duration of hospital admissions, use of antibiotics, etc.) in people with cystic fibrosis (CF) over 12 years old when compared with placebo (just like the treatment drug but with no active medication)?

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Why is this important?

CF is caused by several mutations in the gene which controls how salt (chloride) move between cells through a channel ("CFTR"). New medications allow this channel to work better and about 90% of all people with CF may benefit from these therapies. However, these drugs have no effect in the remaining 10% of people (who have different genetic mutations) and alternative treatment strategies are needed. Lancovutide activates an alternative chloride channel ("TMEM16A") and therefore may be an interesting treatment option for all people with CF, regardless of their underlying mutation. Two small studies showed that treatment with lancovutide was safe and improved lung function in people with CF.

What did you do?

This study was run at 29 centres in 9 countries and included 161 people with CF, who were aged over 12 and had no acute medical conditions (e.g. acute infections). They were randomly assigned to 4 treatment groups (placebo, lancovutide inhalation once daily, every other day or twice a week) and received the treatment for a total of eight weeks. We measured lung function, evaluated quality of life (according to specific questionnaires), and recorded the number and duration of hospital admissions as well as any treatment needed for complications throughout the trial.

What did you find?

In this trial, people in the lancovutide groups did not achieve better results for lung function or the other outcomes mentioned above, such as quality of life or number of hospital admissions. Furthermore, we did not see any positive effects in those with very good lung function at the start of the trial or in children (under 18s) – we had planned in advance to look at these specific groups separately. Lancovutide inhalation was linked to more side-effects than placebo, although most were mild or of moderate severity. So, overall, we think lancovutide is safe.

What does this mean and reasons for caution?

This was the largest trial so far and we considered lancovutide safe overall. In contrast to previous, smaller studies, the current trial did not show positive effects of lancovutide, which speaks against further development of this drug for use in people with CF. A major limitation of this trial was the short duration of only eight weeks. Another problem may be the big differences in how people use their inhalers (and other support devices, such as nebulizers) , so the amount of lancovutide that reaches their lungs and is active may also vary.

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What's next?

These findings argue against further development of lancovutide as treatment for CF. Other drugs that act on alternative chloride channels to CFTR are being developed. A CFTR-independent therapy is particularly desirable as it could benefit all people with CF regardless of their underlying genetic mutation, unlike current treatment strategies.

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