

Cystic Fibrosis Research News

Title:

AZD5634, an inhaled ENaC inhibitor, in healthy subjects and patients with cystic fibrosis

Lay Title:

Evaluation of a novel compound, AZD5634, in healthy volunteers and patients with cystic fibrosis

Authors:

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What was your research question?

We aimed to confirm that AZD5634 was safe and well tolerated in healthy volunteers and test that the drug works in patients with cystic fibrosis (CF).

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Why is this important?

In patients with CF, mutations in a key gene affect sodium channels in the airway lining, increasing the absorption of sodium. This results in the accumulation of thick, sticky mucus that is characteristic of CF and an increased risk of chronic or repeated lung infections. Previous studies have shown that blocking these sodium channels could potentially help to prevent or reduce the build-up of this sticky mucus. In turn, this should allow the normal clearance systems of the lungs to remove bacteria and particles, reducing the risk of lung infections and improving lung function in patients with CF. AZD5634 is an inhaled drug which blocks these sodium channels, and was investigated for the treatment of CF.

What did you do?

We conducted a study, testing a range of single doses of AZD5634 in healthy volunteers, to better understand how well tolerated and safe it is, and how it is metabolized by the body. A further study was carried out to investigate the effect of one dose of AZD5634 on lung mucus clearance and confirm how the drug works in patients with CF.

What did you find?

The first study showed that inhaled AZD5634 was rapidly absorbed and was safe and well tolerated, causing no more side effects than placebo. No volunteers discontinued the study because of side effects and there were no findings of any concern reported in doctors' assessments, lung function testing or laboratory tests, with no change in sodium and potassium handling in the kidneys in all but one patient, which is a common problem for this group of compounds. The second study showed that AZD5634 works as expected, by blocking the sodium channels in the airway lining, although this beneficial mechanism of action did not lead to an improvement in lung mucus clearance after a single dose for patients with CF. AZD5634 was safe and well tolerated in these patients.

What does this mean and reasons for caution?

These studies provide initial evidence suggesting AZD5634 is a safe and well tolerated inhaled drug to block sodium absorption in the airways of patients with CF. However, the lack of improvement in lung mucus clearance in the patient study means that the potential of AZD5634 as a new treatment for CF was not proven.

What's next?

In the patient study, a single dose of AZD5634 failed to increase lung mucus clearance. Hence, no further studies are planned at this time.



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Original manuscript citation in PubMed

<https://pubmed.ncbi.nlm.nih.gov/35227647/>

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