

Cystic Fibrosis Research News

Title:

GLPG1837, A CFTR POTENTIATOR, IN p.Gly551Asp (G551D)-CF PATIENTS: AN OPEN-LABEL, SINGLE-ARM, PHASE 2a STUDY (SAPHIRA1)

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What was your research question?

How safe is GLPG1837, a medicine being developed for cystic fibrosis (CF)? Does GLPG1837 help the underlying problem in CF and help the lungs function (work) better? Are GLPG1837 levels in the blood high enough between doses? Are patients willing to stop current medication temporarily, to participate in a trial?

Why is this important?

CF is a disease involving faults in a protein called CF transmembrane conductance regulator (CFTR). CFTR maintains the balance of salts and fluids inside and outside cells. When it does not work properly, thick secretions build up in the lungs and elsewhere. Ivacaftor is a medicine that works by increasing the activity of CFTR in patients with certain types of gene mutations (changes). This drug improves CF symptoms, but it is costly and not available in all countries. GLPG1837 is a possible new medicine for treating CF. Like ivacaftor, GLPG1837 works by increasing CFTR activity for patients with certain mutations.

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What did you do?

In this clinical trial (SAPHIRA1), 26 adults with CF and a mutation called G551D were given GLPG1837 twice daily. Patients received 125 mg for 7 days, then 250 mg for 7 days, and finally 500 mg for 14 days. All except one patient were taking ivacaftor before joining SAPHIRA1. Patients stopped taking ivacaftor 1 week before starting GLPG1837 (and began taking ivacaftor again after the trial).

Side effects were monitored and lung function was measured using breathing tests. The amount of chloride (a component of salt, which is raised in CF) in sweat was measured, as were GLPG1837 blood levels.

What did you find?

Most side effects were like those often seen in clinical trials in patients with CF. One patient unexpectedly had an increase in a protein called creatine phosphokinase. This can suggest injury/stress in muscles. Some patients had high levels of a liver enzyme (protein) called gamma glutamyl transferase. These changes disappeared on their own and did not cause any signs of illness.

GLPG1837 decreased the amount of chloride in sweat and improved lung function. These effects appeared similar to those of ivacaftor. At the 500 mg dose, blood levels of GLPG1837 stayed high enough for treatment effects to be sustained.

What does this mean and reasons for caution?

At the start of GLPG1837 treatment, patients had high sweat chloride levels, typical of CF. GLPG1837 decreased chloride levels and improved lung function, suggesting it helped CFTR to work better. However, this was a small trial and the main aim was to assess safety. Larger trials, which also include patients taking a placebo (dummy drug), are needed. GLPG1837 was shown to be safe enough for testing in more people with CF. However, the chance of increased levels of creatine phosphokinase or gamma glutamyl transferase shows a need for caution. Further clinical trials are needed to learn more about these effects.

What's next?

Many people with CF take ivacaftor; it's important to test new medications in these individuals (not just untreated patients). To participate in most clinical trials, patients must stop current treatment temporarily. In SAPHIRA1, for a short period, patients were prepared to stop ivacaftor. These findings can help design new trials.



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