

primary studies - published RCT

## **GLPG2737 in lumacaftor/ivacaftor-treated CF subjects homozygous for the F508del mutation: A randomized phase 2A trial (PELICAN).**

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### **Study design (if review, criteria of inclusion for studies)**

Multicenter, randomized, double-blind, placebo-controlled, phase 2a study

### **Participants**

F508del homozygous subjects

### **Interventions**

GLPG2737 as a novel corrector for triple combination therapy.

### **Outcome measures**

The primary outcome was change from baseline in sweat chloride concentration. Other outcomes included assessment of pulmonary function, respiratory symptoms, safety, tolerability, and pharmacokinetics.

### **Main results**

Between November 2017 and April 2018, 22 subjects were enrolled and randomized to oral GLPG2737 (75mg; n=14) or placebo (n=8) capsules twice daily for 28days. A significant decrease from baseline in mean sweat chloride concentration occurred at day 28 for GLPG2737 versus placebo (least-squares-mean difference-19.6mmol/L [95% confidence interval (CI) -36.0, -3.2], p=.0210). The absolute improvement, as assessed by least-squares-mean difference in change from baseline, in forced expiratory volume in 1s (percent predicted) at day 28 for GLPG2737 versus placebo was 3.4% (95% CI -0.5, 7.3). Respiratory symptoms in both groups remained stable. Mild/moderate adverse events occurred in 10 (71.4%) and 8 (100%) subjects receiving GLPG2737 and placebo, respectively. Lower exposures of GLPG2737 (and active metabolite M4) were observed than would be expected if administered alone (as lumacaftor induces CYP3A4). Lumacaftor and ivacaftor exposures were as expected.

### **Authors' conclusions**

GLPG2737 was well tolerated and yielded significant decreases in sweat chloride concentration versus placebo in subjects homozygous for F508del receiving lumacaftor/ivacaftor, demonstrating evidence of increased CFTR activity when added to a potentiator-corrector combination. FUNDING: Galapagos NV. CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov identifier, NCT03474042.

<http://dx.doi.org/10.1016/j.jcf.2019.09.006>

### **See also**

J Cyst Fibros. 2020 Mar;19(2):292-298. doi: 10.1016/j.jcf.2019.09.006. Epub 2019 Oct 5.

### **Keywords**

Adult; Aminophenols; Anti-Bacterial Agents; CFTR Modulators; Genetic Predisposition to Disease; pharmacological\_intervention; Quinolones; GLPG2737; ivacaftor+lumacaftor; Orkambi;