European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

GLPG2737 IN LUMACAFTOR/IVACAFTOR-TREATED CF SUBJECTS HOMOZYGOUS FOR THE F508DEL MUTATION: A RANDOMIZED PHASE 2A TRIAL (PELICAN)

Authors:

Silke van Koningsbruggen-Rietschel[a], Katja Conrath[b], Rainald Fischer[c], Sivagurunathan Sutharsan[d], Axel Kempa[e*], Wolfgang Gleiber[f], Carsten Schwarz[g], Andreas Hector[h], Nancy Van Osselaer[b], Arian Pano[b*], Sam Corveleyn[b], Dieudonné Bwirire[b], Eva Santermans[b], Karine Muller[b], Susan Bellaire[i], Olivier Van de Steen[b]

Affiliations:

[a]Cystic Fibrosis Center, Children's Hospital, University of Cologne, Faculty of Medicine and University Hospital Cologne, Germany;
[b]Galapagos NV, Mechelen, Belgium;
[c]Cystic Fibrosis Center Munich-West, Munich, Germany;
[d]Cystic Fibrosis Division, Department of Pulmonary Medicine, University of Essen, University Duisburg-Essen, Ruhrlandklinik, Germany;
[e]Cystic Fibrosis Center, Klinikum Stuttgart, Stuttgart, Germany;
[f]Cystic Fibrosis Center, Department of Pulmonary Medicine, University Hospital, Goethe University, Frankfurt, Germany;
[g]Cystic Fibrosis Center, Charité – Universitätsmedizin, Berlin, Germany;
[h]Children's Hospital of the University of Tübingen, Tübingen, Germany;
[i]Galapagos BV, Leiden, The Netherlands

*The affiliation details listed here indicate the author's affiliation at the time the study was conducted.

What was your research question?

How effective is GLPG2737, a new medicine being developed for cystic fibrosis (CF), when given together with two existing CF treatments? Does GLPG2737 help correct the underlying problem in CF and improve lung function? How safe is GLPG2737? Also, what levels of GLPG2737 are reached in the blood?

Why is this important?

CF is caused by genetic faults in a protein called CF transmembrane conductance regulator (CFTR). In healthy people, CFTR helps to balance levels of salts and fluids inside and outside

cells. In people with CF, this protein does not work properly, or not enough is present, and thick secretions gather in the lungs and other parts of the body. Existing medicines that increase the levels or activity of CFTR improve CF symptoms to some extent, but further treatments are still needed. GLPG2737 is a new medicine being developed for CF that works by partially correcting the faulty CFTR protein.

What did you do?

Twenty-two adults with CF and a certain type of CFTR gene (*F508del* homozygous) were included in this clinical trial (PELICAN). Participants took either GLPG2737 or placebo (no active drug) twice a day for 28 days. They were also being treated with two existing CF medicines (lumacaftor and ivacaftor). The amount of chloride (a component of salt) in participants' sweat was measured, to see how well CFTR worked after treatment (the study's main aim). Breathing tests were done to measure how well the lungs worked. Blood tests were done to measure the concentration of GLPG2737. All side effects were recorded.

What did you find?

Compared with placebo, GLPG2737 decreased the amount of chloride in participants' sweat, suggesting that there was more active CFTR. Overall, after 28 days of treatment, the lungs of those people taking GLPG2737 were working (functioning) a little better than those taking placebo. Blood levels of GLPG2737 were lower than if the drug had been given alone (without the other CF treatments). Side effects of GLPG2737 were not severe and were like those seen in clinical trials of other CF treatments. No side effects led to treatment being stopped.

What does this mean and reasons for caution?

Combining three CF medications may be beneficial for patients, but larger trials are needed to confirm this. Although only a small improvement in lung function was seen when GLPG2737 was added to lumacaftor and ivacaftor, this was not the main aim of this small trial. The lower GLPG2737 blood levels seen when the drug was taken with lumacaftor and ivacaftor might have limited the effects of the GLPG2737. Different results might be seen if GLPG2737 was given with other CF drugs.

What's next?

The results of the PELICAN trial suggest that adding GLPG2737 to the existing combination of lumacaftor and ivacaftor for 28 days was well tolerated, but the improvement in lung function is small. Further studies are needed to find out how well GLPG2737 works when given with other CF treatments.

Cystic Fibrosis Research News

Original manuscript citation in PubMed

https://www.ncbi.nlm.nih.gov/pubmed/?term=GLPG2737+IN+LUMACAFTOR%2FIVACAFTOR-TREATED+CF+SUBJECTS+HOMOZYGOUS+FOR+THE+F508DEL+MUTATION%3A+A+RANDOMIZED+PHASE+2A+TRIAL+(PELICAN)

cfresearchnews@gmail.com