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Cystic Fibrosis Research News

Title:

Lumacaftor/Ivacaftor Reduces Pulmonary Exacerbations in Patients Irrespective of Initial Changes in FEV_1

Authors:

Susanna A. McColley,[a] Michael W. Konstan,[b] Bonnie W. Ramsey,[c] J. Stuart Elborn,[d] Michael P. Boyle,[e] Claire E. Wainwright,[f] David Waltz,[g] Montserrat Vera-Llonch,[g] Gautham Marigowda,[g] John G. Jiang,[g] Jaime L. Rubin[g]

Affiliations:

[a]Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, 225 East Chicago Avenue #43, Chicago, IL 60611, USA;
[b]Case Western Reserve University School of Medicine and Rainbow Babies & Children's Hospital, 11100 Euclid Avenue, Cleveland, OH 44106, USA;
[c]Seattle Children's Hospital and University of Washington School of Medicine, 4800 Sand Point Way NE, Seattle, WA 98105, USA;
[d]Imperial College and Royal Brompton Hospital, London and Queens University Belfast, 97 Lisburn Road, Belfast, UK BT9 7AE;
[e]Johns Hopkins Medical Institution, 600 North Wolfe Street, Baltimore, MD 21287, USA; [f]Lady Cilento Children's Hospital and Child Health Research Centre, University of Queensland, 62 Graham Street, South Brisbane, Queensland 4104, Australia;
[g]Vertex Pharmaceuticals Incorporated, 50 Northern Avenue, Boston, MA 02210, USA

What was your research question?

Improved lung function and fewer pulmonary exacerbations (worsening of symptoms) were observed with lumacaftor/ivacaftor therapy in people with cystic fibrosis (CF) homozygous for *F508del*. We intended to examine whether individuals who did not experience short-term improvement in lung function, in this case lung function measured after 15 days of therapy, would still benefit from treatment with lumacaftor/ivacaftor.

Why is this important?

We thought that while a short-term improvement in lung function might not be evident in some people receiving lumacaftor/ivacaftor, they might still have less pulmonary exacerbations compared with those not receiving treatment. This is important because pulmonary exacerbations negatively affect people with CF, who often miss work or school, are hospitalized, and may lose lung function permanently. When people do not experience

short-term results after starting a new treatment, they may be more inclined to stop taking it. Furthermore, physicians or payers may believe that the treatment is not worthwhile if improvement is not observed quickly.

What did you do?

Using the data collected from the TRAFFIC and TRANSPORT clinical trials for lumacaftor/ivacaftor, 1108 participants were divided into groups based on their lung function changes in the first 15 days after starting lumacaftor/ivacaftor therapy or placebo. The rates of pulmonary exacerbations, intravenous (IV) antibiotic use, and hospitalizations due to pulmonary exacerbations for each group were then calculated and compared between groups.

What did you find?

As shown in the TRAFFIC/TRANSPORT manuscript, patients treated with lumacaftor/ivacaftor had fewer pulmonary exacerbations and improved lung function compared with those receiving placebo. In this new analysis, those treated with lumacaftor/ivacaftor who did not experience an early increase in lung function had higher pulmonary exacerbation rates than those who had an increase in lung function. Both groups of participants receiving lumacaftor/ivacaftor experienced significantly lower rates of pulmonary exacerbations than participants receiving placebo. The rates of IV antibiotic use and hospitalization for pulmonary exacerbations were also similar in both groups of patients receiving lumacaftor/ivacaftor, whether or not they showed early improvement in lung function, and all rates were lower than those receiving placebo.

What does this mean and reasons for caution?

This study shows that individuals who do not experience early increases in lung function can still benefit from continued treatment with lumacaftor/ivacaftor. Effects were not dependent on age, initial lung function, additional medication use, or airway infection. These results are limited to individuals with two *F508del-CFTR* mutations and not all people with CF as a whole. Since this is an analysis after the study results were available (post hoc), there may be unidentified factors that affected patients' response to therapy that we could not evaluate.

What's next?

While improving lung function is important, additional benefit may be seen with lumacaftor/ivacaftor therapy. Evaluation of each individual's response to a therapy like lumacaftor/ivacaftor, which has demonstrated improvement across a multitude of endpoints,

should consider a range of outcomes. Additional ways to monitor therapy response should continue to be investigated.

Original manuscript citation

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