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Cystic Fibrosis Research News

Title:

Retrospective observational study of French patients with cystic fibrosis and a Gly551Asp-*CFTR* mutation after 1 and 2 years of treatment with ivacaftor in a real-world setting

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What was your research question?

What are the benefits of ivacaftor treatment in patients with cystic fibrosis (CF) and a G551D CFTR mutation (the first mutation eligible for this new treatment) in a real-world setting? Can we confirm the clinical benefits reported in clinical trials? Could it contribute to reducing overall treatment burden?

Why is this important?

Large placebo-controlled clinical trials demonstrated that ivacaftor treatment improved lung function and nutritional status, and decreased the number of pulmonary exacerbations in patients with a CFTR "gating" mutation (G551D was the first studied). These clinical trials required that recruited individuals be in stable condition and those with severe lung

function were not eligible. Because there is only limited experience with ivacaftor outside clinical trials, we sought to obtain data on ivacaftor effectiveness and tolerance in a more heterogeneous CF population in order to confirm previous results and to look for other potential benefits such as a decrease in treatment needs.

What did you do?

We contacted each of the 45 French CF centres in order to recruit individuals with CF and a G551D mutation who had initiated ivacaftor before 1st June 2013. They were included in a multicentre observational study. We studied changes from baseline to 12 and 24 months after ivacaftor initiation in the following clinical parameters: FEV_1, weight, bacteria isolated in sputum, IV and oral antibiotic courses, and concomitant treatments. We also looked for a change in pancreatic insufficiency and diabetes mellitus status and collected data on ivacaftor interruption or discontinuation and on adverse events, excluding pulmonary exacerbations.

What did you find?

Fifty-seven patients (mean age 21.5) were included: 30 children and adolescents and 27 adults. Mean absolute change in FEV_1% predicted improved from baseline to Year 1 (8.4%) and Year 2 (7.2%). Other benefits included increased weight and body mass index, fewer *Pseudomonas aeruginosa* and *Staphylococcus aureus* positive cultures, as well as fewer IV antibiotic courses and maintenance treatment prescriptions (including azithromycin after 12 months, and DNase and nutritional supplements after 24 months of ivacaftor treatment). No change was observed for inhaled antibiotics or pancreatic enzymes. No significant adverse events were reported. There were two treatment discontinuations and 10 interruptions.

What does this mean and reasons for caution?

The improvements in respiratory function and nutritional status that were observed with ivacaftor treatment in interventional studies were confirmed in this real-world setting. A slightly lower increase in FEV_1 was observed but could be due to variable compliance over time, and/or to the inclusion of patients with severe or high respiratory function whose increase in FEV_1 was lower. The decrease in *P. aeruginosa* and IV antibiotics confirms the results of previous observational studies. Importantly, we also show a decrease in some maintenance treatments, which is likely the result of clinical symptoms improvement after an extended period of time on ivacaftor.

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What's next?

Further studies with a larger number of patients, including those with other gating CFTR mutations, are necessary to improve our knowledge of the long-term effectiveness and safety of ivacaftor. Observational studies should also include young children (from age 2) to determine if ivacaftor can prevent respiratory decline when initiated early.

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