



# Cystic Fibrosis Research News

## **Citation:**

Gifford AH. Heltshe SL. Goss CH. CFTR Modulator Use is Associated with Higher Hemoglobin Levels in Individuals with Cystic Fibrosis. Ann Am Thorac Soc. 2019 Mar;16(3):331-340.

## **What was your research question? (50 words maximum)**

Is the use of CFTR modulators associated with higher hemoglobin (Hgb) levels in individuals with cystic fibrosis (CF)?

## **Why is this important? (100 words maximum)**

Anemia is a condition in which blood Hgb levels are low. Anemia can cause fatigue and shortness of breath, two symptoms reported by many people with CF. Several processes can cause anemia, including iron deficiency, poor nutrition, blood loss, and chronic inflammation in the body. Many adults and some children with CF have anemia, but we cannot totally explain why anemia develops in certain people with CF.

## **What did you do? (100 words maximum)**

Using data from the CF Foundation Patient Registry, we developed statistical models to explore whether the use of CFTR modulator drugs was associated with higher Hgb levels. Because Hgb is generally lower in women than in men, we tested this theory separately in females and males. Specifically, we studied the effect of ivacaftor (IVA, Kalydeco) on Hgb in people with the G551D mutation and the effect of ivacaftor/lumacaftor (LUM/IVA, Orkambia) on Hgb in people with two copies of the F508del mutation. We also used statistical models to adjust the effects of IVA and LUM/IVA on Hgb for other features.

## **What did you find? (100 words maximum)**

We identified 1,347 patients (707 males, 640 females) with G551D who had data for both Hgb levels and CFTR modulator use. In addition, 12,582 patients (6,640 males, 5,942 females) with two copies of F508del had data on both Hgb levels and CFTR modulator use. We found a small increase in Hgb levels with the use of IVA or LUM/IVA. Looking at the same associations but accounting for other features, we saw a positive effect of IVA on Hgb in males but not females. In addition, we found a positive effect of LUM/IVA on Hgb in males and females.

## **What does this mean and reasons for caution? (100 words maximum)**



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Our study suggests that restoring CFTR function using CFTR modulator drugs may increase Hgb levels in people with CF. This should theoretically reduce the severity of anemia. However, our study does not identify a mechanism for this observation and doesn't consider that people with CF might have other reasons to be anemic. We also did not include data from people with CF who had undergone lung transplantation. Because of these limitations, our findings should be interpreted cautiously.

### **What's next? (50 words maximum)**

We next want to study the effects of taking medications that reduce stomach acid on Hgb levels in people with CF. Theoretically, these medications, called H2-blockers and proton-pump inhibitors, reduce iron absorption from the intestine, which might cause anemia due to iron deficiency.