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Cystic Fibrosis Patients of Minority Race and Ethnicity Less Likely Eligible for CFTR Modulators Based on *CFTR* Genotype

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Abstract

Background: CFTR modulators are disease-modifying medications for cystic fibrosis (CF) and are shown to be efficacious for only specific *CFTR* mutations. *CFTR* mutation frequency varies by ancestry, which is different from but related to demographic racial and ethnic group. Eligibility for CFTR modulator therapy has not been previously reported by race and ethnicity.

Methods: We conducted a cross-sectional study of patients in the 2018 CF Foundation Patient Registry. We analyzed the percentage of patients in each US Census defined racial and ethnic group eligible for CFTR modulators based on *CFTR* mutations approved by the US FDA and then based on both mutations and FDA-approval by age. We compared lung function based on CFTR modulator eligibility and prescription.

Findings: Based on *CFTR* mutations alone, 92·4% of non-Hispanic white patients, 69.7% of Black/African American patients, 75.6% of Hispanic patients, and 80.5% of other race patients eligible for CFTR modulators. For each CFTR modulator, Black/African American patients were least likely to have eligible mutations, and non-Hispanic white patients were most likely. There was no difference in the disparity between racial and/or ethnic groups with the addition of current FDA-approval by age. The lowest pulmonary function in the cohort was seen in non-Hispanic white, Black/African-American, and Hispanic patients not eligible for CFTR modulators.

Interpretation: Patients with CF from minority groups are less likely to be eligible for CFTR modulators. Because people with CF who are racial and ethnic minorities have increased disease severity and earlier mortality, this will further contribute to health disparities.

Introduction

Recently the treatment of cystic fibrosis (CF) has progressed from treating symptoms and infections to targeting the cause of CF: a defective cystic fibrosis transmembrane

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Author Contributions:

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conductance regulator (CFTR). CFTR modulators stabilize or improve lung function and nutrition and reduce the frequency of pulmonary exacerbation, a major contributor to morbidity and mortality.[1–13] It is hoped that CFTR modulators will markedly increase the lifespan of patients with CF.

CFTR modulators are only approved for specific *CFTR* mutations. Overall, approximately 90% of patients with CF have *CFTR* mutations that are currently FDA-approved for CFTR modulators, although this may not be true for all groups within the CF population.[14,15] CF occurs in all racial and ethnic populations, though incidence and *CFTR* mutation prevalence varies by both geographic region and ancestry.[16–18] Genetic disease prevalence, and specific mutations causing autosomal recessive genetic diseases, are heritable, whereas reported race and ethnicity are imprecise social constructs that differ from ancestry and do not accurately predict genetic variants in individuals.

Given that patients with CF from minority groups have increased morbidity and mortality after adjustment for socioeconomic status, it is important to understand if they are less likely to have *CFTR* genotype for disease-altering CFTR modulator therapy is indicated.[19–23] We sought to determine what percentage of patients of minority groups and non-Hispanic white patients with CF have a *CFTR* genotype for which CFTR modulator therapy is indicated.

Methods

Study Population:

All patients diagnosed with CF and included in the CFFPR in 2018. The Cystic Fibrosis Foundation Patient Registry (CFFPR) is a retrospective observational study of patients from accredited CF centers which include approximately 81–84% of patients with CF in the United States.[15]

Overall Design

This is a cross-sectional study comparing reported race and ethnicity to having *CFTR* mutations for which a CFTR modulator is indicated based on FDA approval in the US. The exposure was patient race and ethnicity defined in accordance to US Census definitions and entered by CF centers: non-Hispanic white, Hispanic, Black/African American, Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and Other/Mixed Race. Hispanic patients included white and non-white races. In the CFFPR, these data are entered by CF Center staff based on participant medical records. Methodology for the entry of these data into medical records at CF Centers is not known.

The primary outcome was having *CFTR* mutations that are FDA-approved for a CFTR modulator regardless of age, since the age of eligibility changes over time after label extension studies. The CFTR modulators are ivacaftor, lumacaftor/ivacaftor, tezacaftor/ivacaftor, and elexacaftor/tezacaftor/ivacaftor. Ivacaftor is FDA-approved for the following *CFTR* mutations as of October 2020: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, R117H, E56K, P67L, R74W, D110E, D110H, R117C, E193K, L206W, R347H, R352Q, A455E, D579G, S945L, S977F, F1052V, K1060T, D1270N, G1349D, A1067T, G1069R, R1070Q, R1070W, F1074L, D1152H.[1,6,24,25] Lumacaftor/

ivacaftor and tezacaftor/ivacaftor are FDA-approved for patients homozygous for the *CFTR* mutation delF508 as of October 2020.[5,8,26] Tezacaftor/ivacaftor is also FDA-approved for delF508 heterozygotes with a residual function second allele as of October 2020 (2789+5G->A, D110E, R352Q, 3849+10kbC->T, D110H, A455E, 3272–26A->G, R117C, D579G, R1070W, 711+3A->G, E193K, S945L, F1074L, E56K, L206W, S977F, D1152H, P67L, F1052V, D1270N, R74W, R347H, K1060T, E831X).[10,11] Elexacaftor/tezacaftor/ivacaftor is FDA-approved as of October 2020for delF508 homozygotes and heterozygotes.[2,4] CFTR modulators were also analyzed based on efficacy: ivacaftor and elexacaftor/tezacaftor/ivacaftor are high-efficacy modulators based on the improvement of pulmonary function and other parameters in clinical trials, and lumacaftor/ivacaftor and tezacaftor/ivacaftor are low-efficacy modulators based on more modest benefits.

Secondary outcomes were qualification for the CFTR modulators based on FDA-approval based on both *CFTR* genotype and patient age as of October 2020. Ivacaftor is FDA-approved for ≥4 months old. Lumacaftor/ivacaftor is FDA-approved for ≥2 years old. Tezacaftor/ivacaftor is FDA-approved for ≥6 years old. Elexacaftor/tezacaftor/ivacaftor is FDA-approved for ≥12 years old. We compared mean FEV_1 percent predicted between patients with a *CFTR* genotype for which CFTR modulator therapy is indicated and are prescribed a CFTR modulator, patients with a *CFTR* genotype for which CFTR modulator therapy is indicated but are not prescribed a CFTR modulator, and patients who do not have a *CFTR* genotype for which CFTR modulator therapy is indicated by race and ethnicity. CFTR modulator data is based on a prescription in the medical record and is recorded in the CFFPR. The following *CFTR* mutations are not listed in the CFF Patient Registry and therefore could not be analyzed: A1067T, E193K, K1060T, S1255P. *CFTR* genotypes are classified by the CFFPR based on phenotype and CFTR protein production[27]. Patients have unclassified *CFTR* genotype if the mutations are known but not classified. Patients are not fully genotyped if they have only 1 or 0 *CFTR* mutations identified.

Statistical Analysis

We first compared the percentage of each racial/ethnic group that have *CFTR* genotypes that are FDA-approved for any CFTR modulator and each individual CFTR modulator based on *CFTR* genotype alone using chi-square. We then compared the percentage of each racial/ethnic group that have *CFTR* genotypes that are FDA-approved for any CFTR modulator and each individual CFTR modulator based on current FDA criteria of both *CFTR* mutations and age using chi-square. In subjects without a *CFTR* genotype that is eligible for CFTR modulator therapy, we compared whether they have known or unknown *CFTR* mutations by race and ethnicity. We compared mean FEV_1 percent predicted between those with a *CFTR* genotype eligible for CFTR modulator therapy and are prescribed a CFTR modulator, patients with a *CFTR* genotype eligible for CFTR modulator therapy but are not prescribed a CFTR modulator, and patients without a *CFTR* genotype eligible for CFTR modulator therapy is indicated by race and ethnicity using linear regression. Because 2018 was the latest year for which CFFPR data were available and elexacaftor/tezacaftor/ivacaftor was not approved until November 2019, use and eligibility were excluded from this analysis. Demographic and clinical data were evaluated using Student's t test for continuous variables and chi-square for categorical variables.

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The study sponsors were not involved in the study design, writing the manuscript, or submission for publication.

The study was approved by the University of California, San Francisco Institutional Review Board (15-17491) and the CF Foundation Registry/ Comparative Effectiveness Research Committee.

Results

The 2018 CF Foundation Patient Registry showed that 25,918 (84.2%) patients were non-Hispanic white, 1,351 (4.4%) were Black/African American, 2,763 (9.0%) were Hispanic, and 743 (2.4%) were other races that were combined for analysis due to small numbers (Table 1). The full analysis with all racial and ethnic groups is in Supplemental Table 1. There was no difference in sex between racial and ethnic groups. Non-Hispanic white patients were older than the other races and ethnicities. Overall, 17.3% of patients either had unclassified *CFTR* mutations or had zero or one mutation reported. Non-Hispanic white, Black/African American, Hispanic, and other race groups had a higher percentage of patients that either had unclassified *CFTR* mutations or had zero or one mutation reported compared to non-Hispanic white patients. The top 3 identified *CFTR* mutations for each race/ethnicity are: delF508, G551D, G542X in non-Hispanic white patients; delF508, 3120+1G->A, A559T in Black/African-American patients; delF508, G542X, 3876delA in Hispanic patients; delF508, G542X, S549N in other race patients.

Modulator Eligibility Based on *CFTR* Genotype

Based on *CFTR* genotype alone, 92.4% of non-Hispanic white patients, 69.7% of Black/African American patients, 75.6% of Hispanic patients, 80.5% of other race patients have a CFTR genotype eligible for at least 1 CFTR modulator therapy ($p<0.001$, Table 2). Only Black/African American patients had a lower percentage (11.4%) of patients eligible for ivacaftor compared to the other races and ethnicities (16.3–17.2%, $p<0.001$). Black/African American patients (19.2%), Hispanic patients (24.0%), and other race patients (31.6%) had a lower percentage of patients with a *CFTR* genotype eligible for lumacaftor/ivacaftor compared to non-Hispanic white patients (47.9%, $p<0.001$). For tezacaftor/ivacaftor, Black/African American patients (21.5%), Hispanic patients (29.8%), and other race patients (35.9%) had a lower percentage of patients with a CFTR genotype eligible for tezacaftor/ivacaftor compared to non-Hispanic white patients (53.9%, $p<0.001$). Black/African American patients (62.5%), Hispanic patients (67.3%), and other race patients (71.9%) had a lower percentage of patients with a *CFTR* genotype eligible for elexacaftor/tezacaftor/ivacaftor compared to non-Hispanic white patients (88.0%, $p<0.001$). Patients with delF508/delF508 genotype qualify for 3 CFTR modulators (lumacaftor/ivacaftor, tezacaftor/ivacaftor, elexacaftor/tezacaftor/ivacaftor). There are racial and ethnic differences in the proportion of the populations with delF508/delF508: 47.9% of non-Hispanic white patients, 19.2% of Black/African-American patients, 24.0% of Hispanic patients, and 31.6% of other races have delF508/delF508 genotype ($p<0.001$).

The full analysis with all racial and ethnic groups is in Supplemental Table 2.

Modulator Eligibility Based on Age and *CFTR* Genotype

For all patient groups and CFTR modulators, there was a slightly lower percentage of patients eligible for CFTR modulator therapy when both age and *CFTR* genotype were taken into account compared to just *CFTR* genotype alone. In comparison of age groups and modulators by efficacy between racial/ethnic groups, the percentage of patients with CFTR genotypes eligible for CFTR modulator therapy increase with age for all groups, however, the disparity between racial/ethnic groups for high-efficacy modulator therapy increases with age (Table 3). In the 0.5–2 year-old group, there was not a significant difference in those with *CFTR* genotype who are eligible for high-efficacy modulator therapy (which is only ivacaftor) and those not eligible for CFTR modulator therapy (p=0.7). In the 2–6 year-old group, Black/African American patients had the lowest percentage of CFTR genotypes eligible for either high-efficacy (only ivacaftor) and low-efficacy modulator therapies (only lumacaftor-ivacaftor), while non-Hispanic white patients had the highest percentage of patients with *CFTR* genotypes eligible for either high-efficacy (only ivacaftor) or low-efficacy modulator therapies (lumacaftor-ivacaftor and tezacaftor-ivacaftor). In the 6–12 year-old group, there was not a difference in those with *CFTR* genotypes eligible for high-efficacy modulator therapies; however a much higher percentage of non-Hispanic white patients had *CFTR* genotypes eligible for low-efficacy CFTR modulator therapies than the other groups, which results in a large disparity in those not eligible for any modulator therapies. The largest disparity in high-efficacy modulator therapies between racial/ethnic groups was in the >12-year-old group with the lowest percentage with eligible *CFTR* genotypes were Black/African American patients, and the highest percentage with eligible *CFTR* genotypes were non-Hispanic white patients. The full analysis with all racial and ethnic groups is in Supplemental Table 3.

Pulmonary Function By Eligibility and CFTR Modulator Prescription

Pulmonary function varied by *CFTR* genotype indicated for modulator therapy and prescriptions for therapy in each racial and ethnic group. In non-Hispanic white patients, FEV_1 percent predicted was lower in the group with eligible *CFTR* genotypes and were on modulators compared to those with eligible *CFTR* genotypes but were not on modulators; however there was no difference in FEV_1 percent predicted with those not eligible for CFTR modulator therapies (Table 4). In Black/African American patients, FEV_1 percent predicted was lower in those with *CFTR* genotypes not eligible for CFTR modulator therapies compared to those with eligible *CFTR* genotypes regardless of whether they were on modulators. Hispanic patients not on modulator therapies had higher FEV_1 percent predicted than either those with *CFTR* genotypes not eligible for CFTR modulator therapies and those on modulator therapies. There was no difference in FEV_1 percent predicted for the other race patients. The full analysis with all racial and ethnic groups is in Supplemental Table 4.

Discussion

In this cross-sectional study, we found that patients of a minority group with CF were less likely to have *CFTR* genotypes eligible for disease-altering CFTR modulator therapies

compared to non-Hispanic white patients. The lowest percentages in patients with *CFTR* genotypes eligible for any CFTR modulator were seen in Black, Hispanic, and other race patients. Only two-thirds of Black and Asian patients and three-quarters of Hispanic patients had *CFTR* genotypes eligible for a CFTR modulator therapy compared to over 90% of non-Hispanic white patients. This pattern was true for all CFTR modulator therapies. The largest disparities were seen for lumacaftor/ivacaftor and tezacaftor/ivacaftor in Black, Hispanic, and Asian patients. Approximately double the percentage of non-Hispanic white patients had *CFTR* genotypes eligible for therapy compared to Black, Hispanic, and Asian patients. The smallest disparity was seen for ivacaftor, which is the only modulator approved for multiple rare mutations in the United States; approval for many of these mutations was granted based on in-vitro evaluation alone. With the addition of FDA-qualified age to *CFTR* genotype, there were overall fewer patients eligible for CFTR modulator therapies, but the differences between racial and ethnic groups did not significantly change. For non-Hispanic white, Black/African-American, and Hispanic patients, pulmonary function was lowest in those with *CFTR* genotypes not eligible for modulator therapy. There is a high need for these patients to be eligible for effective modulator therapy.

One barrier to equality in CFTR modulator therapy eligibility for all races and ethnicities is different *CFTR* mutation frequency between racial and ethnic groups[28]. While delF508 is the most common mutation in all groups, patients of a minority group are less likely to have a copy of delF508 and are more likely to have a deletion or duplication mutation, which can be missed when only DNA panels are used for *CFTR* mutation detection. Mutation frequency is not even uniform within patients of a minority group,[16] for example, it varies among Hispanic populations in different geographic locations.[17] There is not equity in mutation detection in patients of a minority group and non-Hispanic white patients with CF. Patients of a minority group are more likely to have unknown *CFTR* mutations; unknown *CFTR* mutations is associated with mortality in children with CF.[29] CF genetic panels and newborn screens are optimized to detect mutations frequent in non-Hispanic white populations and have lower detection rates in populations of minority groups.[30]

These findings are alarming as patients of a minority group already suffer a greater burden from CF compared to non-Hispanic white patients.[19–21] This disparity in eligibility for CFTR modulators will widen disparities in morbidity and mortality. If a higher percentage of non-Hispanic white patients are on CFTR modulator therapy than patients of a minority group, the disparity will widen. These patients are in high need of the therapeutic benefits to pulmonary function that high-efficacy modulators provide. There are multiple barriers to equality in eligibility for CFTR modulator therapy for all races and ethnicities.[31]

Not only are patients of a minority group less likely to be eligible for CFTR modulator therapy, but even those eligible are under-represented in the pharmaceutical trials.[32] Members of racial and ethnic groups were proportionally under-represented in clinical trials of CFTR modulators compared to the baseline CF population, even with consideration of *CFTR* mutation frequency. For example, for elexacaftor/lumacaftor/ivacaftor,[2,4] only 3.9% Hispanic, 1.5% Black, and 0% other/mixed race patients included in the heterozygote trial[33] and 4.7% Hispanic, 0% Black, and 0% other/mixed race patients included in the homozygote trial,[34] while in comparison, 9.7% of the CF population in 2018 were Hispanic,

5.0% Black, and 4.0% other race.[15] For future pharmacology studies in CF, eligible patients of a minority group should be recruited. Under-representation of patients of a minority group is not unique to CF; this is a problem across all fields of medicine, including other respiratory diseases.[35]

Disparities in eligibility to genomic medicine, such as CFTR modulators, greatly affects patients of a minority group. We found that patients of a minority group were up to five times more likely to zero or one mutation identified compared to non-Hispanic white patients. Patients of a minority group were over twice as likely to have *CFTR* mutations that were not classified compared to non-Hispanic white patients. Patients without two known *CFTR* mutations cannot qualify for CFTR modulators. The barriers to fully genotyping and classifying the function of *CFTR* mutations in patients of a minority group need to be explored, understood, and addressed.

Due to the racial/ethnic differences in CFTR modulator eligibility, there is a greater need in the CF community that are of a minority group for treatments that either target rare mutations or are not mutation specific such as anti-inflammatory, antibiotics, mucociliary clearance agents, or nutritional. The CF Foundation has recognized this need and has put greater resources into developing treatments that are not mutation specific. As patients of a minority group are at a great need for these medications, they should be recruited into these studies at higher percentage than their proportion of the CF population.

Existing CFTR modulators would likely benefit patients with rare *CFTR* mutations that are not currently FDA-approved. Currently, for-profit pharmaceutical companies are financially incentivized to develop drugs and clinical trials for the mutations that occur in the most patients, which are the common mutations in non-Hispanic white patients rather than rare mutations in patients of a minority group. N-of-1 clinical trials have been used with some success to determine response to CFTR modulators in patients with rare *CFTR* mutations.[7,36,37] Traditional clinical trials with a control group are not adequate in studying patients of a minority group with rare or de novo *CFTR* mutations. A limitation of N-of-1 trials is unclear clinical biomarkers (sweat chloride concentration, nasal potential difference, pulmonary function) indicating individual response to CFTR modulators. Cell based assays, such as HBE cells or intestinal organoids, to measure CFTR activity and CFTR modulator response have been used as a tool to predict response to CFTR modulators in individual patients.

This will become a greater issue over the next few years as the demographics of the CF community continue to change. Patients of a minority group are becoming a greater percentage of patients with CF, which is a reflection of the changing demographics of the United States[38], as well as increased detection in minority racial and ethnic groups due to increased sensitivity of genetic testing and newborn screen[30,39,40]. This can be seen in the changing populations in the newborn screen.

Limitations:

A limitation of this study is that reported race and ethnicity are related to but are not the same as ancestry. Genetic disease prevalence, and specific mutations causing autosomal

recessive genetic diseases, are heritable, whereas race is an imprecise social construct used to categorize individuals in a manner that often promotes inequality. An important example of this was seen in a study evaluating pulmonary function prediction utilizing predictive equations for African American race and showed, not surprisingly, that this was less predictive than ancestral genetic markers.[41] Race is frequently used as an explanation for health disparities that actually emanate from social inequities and racism. It is important to note that there are well-documented negative effects of racism on children and adults of a minority group; this alone cannot be remediated by drug therapies.

Another limitation of our study is that patients may have *CFTR* mutations known that are not entered into CFFPR, overestimating the percentage of patients not eligible for CFTR modulator therapy. *CFTR* mutations may also be incorrectly entered into the CFFPR. This limitation should affect patients of all races and ethnicities equally. Another limitation is that patients not included in the CFFPR may be more likely not to have *CFTR* mutations known since they may not be cared for at a CF care center.

CFTR modulator therapy for CF is a landmark example of the benefits of precision medicine. However, it also highlights that precision medicine only benefits those for whom therapies or interventions are developed. Precision medicine can widen health disparities in patients of a minority group who are excluded or under-represented in clinical trials and genetic research. Efforts are being made in the NIH to diversify research to prevent patient groups from being left behind from medical advances[42]. Similar efforts are needed within the CF community to ensure medical advances and treatments benefit all patients in a socially just manner, including those disproportionately affected by CF. Until CFTR modulators can benefit patients equally, continued focus on developing genotype-neutral treatments for CF are essential.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ASL	airway surface liquid
CF	cystic fibrosis
CFFPR	CF Foundation Patient Registry
CFTR	cystic fibrosis transmembrane conductance receptor

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Table 1:

Subject Characteristics

	Non-Hispanic White	Black/African American	Hispanic	Other Races
Number (%)	25,918 (84.2%)	1,351 (4.4%)	2,763 (9.0%)	743 (2.4%)
Sex (male)	13,440 (51.9%)	700 (51.8%)	1,433 (51.9%)	363 (48.9%)
Age, yrs (median, IQR)	21.0 (11.1–32.4)	15.7 (8.1–25.8)	13.6 (7.3–21.8)	15.2 (8.8–26.0)
Class I-III Mutations	18,935 (73.1%)	753 (55.7%)	1,461 (52.9%)	406 (54.6%)
Class IV-V Mutations	3,257 (12.6%)	105 (7.8%)	416 (15.1%)	112 (15.1%)
Unclassified Mutations	2,927 (11.3%)	370 (27.4%)	651 (23.6%)	152 (20.5%)
Not Fully Genotyped	799 (3.1%)	123 (9.1%)	235 (8.5%)	73 (9.8%)

Table 2:

Patients with CFTR Mutations Eligible for CFTR Modulators

	Non-Hispanic White	Black/African American	Hispanic	Other Races	p-value
Any CFTR Modulator	23,940 (92.4%)	941 (69.7%)	2,089 (75.6%)	598 (80.5%)	<0.001
Ivacaftor	4,281 (16.5%)	154 (11.4%)	475 (17.2%)	121 (16.3%)	<0.001
Lumacaftor/ Ivacaftor	12,420 (47.9%)	259 (19.2%)	663 (24.0%)	235 (31.6%)	<0.001
Tezacaftor/ Ivacaftor	13,972 (53.9%)	290 (21.5%)	823 (29.8%)	267 (35.9%)	<0.001
Elexacaftor/ Ivacaftor/ Tezacaftor	22,801 (88.0%)	844 (62.5%)	1,858 (67.3%)	534 (71.9%)	<0.001

Racial and ethnic differences in eligibility for CFTR modulators are analyzed via chi-square analysis.

Table 3:

Eligibility based on *CFTR* Genotype and Age

	Non-Hispanic White	Black/African American	Hispanic	Other Races	p-value
0.5 – 2 years old					0.7
High Efficacy	134 (17.8%)	10 (17.0%)	22 (19.0%)	4 (10.5%)	
Low Efficacy	- 0%	- 0%	- 0%	- 0%	
Not Eligible	618 (82.1%)	49 (83.1%)	94 (81.0%)	34 (89.5%)	
2 – 6 years old					<0.001
High Efficacy	392 (16.8%)	21 (12.7%)	79 (19.5%)	13 16.9%	
Low Efficacy	1,113 47.8%	32 19.4%	97 24.0%	25 (32.5%)	
Not Eligible	823 (35.4%)	112 (67.9%)	229 (56.5%)	39 (50.7%)	
6 – 12 years old					<0.001
High Efficacy	408 (10.8%)	33 (11.4%)	73 (10.9%)	15 (9.7%)	
Low Efficacy	2,068 (54.9%)	64 (22.2%)	175 (26.0%)	54 (35.1%)	
Not Eligible	1,288 (34.2%)	192 (66.4%)	425 (63.2%)	85 (55.2%)	
≥12 years					<0.001
High Efficacy	17,335 (92.0%)	549 (66.7%)	1,157 (75.6%)	369 (79.4%)	
Low Efficacy	10,122 (53.7%)	169 (20.5%)	479 (31.3%)	168 (36.1%)	
Not Eligible	1,515 (8.0%)	274 (33.3%)	373 (24.4%)	96 (20.7%)	

Ivacaftor and elexacaftor/tezacaftor/ivacaftor are considered high-efficacy modulators based on the improvement of pulmonary function and other parameters in clinical trials and lumacaftor/ivacaftor and tezacaftor/ivacaftor are considered low-efficacy modulators based on more modest benefits. Racial and ethnic differences in eligibility for CFTR modulators by efficacy are analyzed via chi-square analysis.

Table 4:

Lung Function by Eligibility and Modulator Use

		Eligible, On Modulator	Eligible, Not On Modulator	Not Eligible	P-value
Non-Hispanic White	**N (%)**	11,143 (43.0%)	5,060 (19.5%)	9,715 (37.5%)	---
	FEV_1%	76.4% (75.9–76.9%)	81.0% (80.1–81.9%)	75.6% (75.0–76.2%)	<0.001
Black/African American	**N (%)**	218 (16.1%)	177 (13.1%)	956 (70.7%)	---
	FEV_1%	84.3% (80.2–88.4%)	87.0% (81.8–92.3%)	77.6% (75.6–79.6%)	<0.001
Hispanic	**N (%)**	657 (23.8%)	441 (16.0%)	1,665 (60.3%)	---
	FEV_1%	78.7% (65.1–92.1%)	86.1% (81.4–90.7%)	78.8% (77.4–80.2%)	<0.0001
Other Races	**N (%)**	219 (29.5%)	121 (16.3%)	403 (54.2%)	---
	FEV_1%	78.7% (65.1–92.1%)	79.8% (63.3–96.1%)	83.4% (77.7–89.0%)	0.5

Eligibility based on CFTR genotype and age.

Racial and ethnic differences in the percentage of patients that are eligible and on modulators determined by chi-square analysis. $p<0.0001$.

Lung function differences determined by linear regression by differences in eligibility and whether on or off modulator for each racial and ethnic group.