

INTRODUCTION

- Cystic fibrosis (CF) is a progressive, genetic disease primarily affecting the respiratory, digestive and reproductive organ systems
- Every year, over 1,000 new CF cases are diagnosed in the United States (US) and in 2017, more than 30,000 individuals were reportedly living with CF in the US
- CFTR modulator therapies, the most advanced CF treatments, act by improving production, intracellular processing, and/or function of the defective CFTR protein. This helps in symptom management and slowing disease progression. However, CFTR modulator therapies are very expensive
- Literature in other chronic diseases provide evidence linking medication nonadherence with adverse clinical outcomes and higher healthcare utilization
- Medication adherence is defined as “the degree to which the person’s behavior corresponds with the agreed recommendations from a health care provider”
- Measures to calculate adherence based on the pharmacy data include medication possession ratio (MPR) and proportion of days covered (PDC). The formulae for calculating these are as follows:
 - MPR = (Sum of days’ supply for all fills in the period/ Number of days in period) * 100
 - PDC = (Number of days in period “covered”/Number of days in period) * 100

OBJECTIVE

- To calculate medication adherence for CFTR modulator therapies using prescription refill data
- To identify reasons for missed doses, medication discontinuation, and CFTR modulator therapy-related adverse events using patient reports

METHODS

- The study was a retrospective analysis of a national specialty pharmacy prescription refill data for CFTR modulator therapies
- Medication name and refill dates from September 2017 till August 2018 (one year data) were utilized to calculate PDC as the adherence measurement, which was further categorized using age (children/adolescents or adults) and insurance characteristics (primary insurance only or primary and secondary insurance)
- PDC was calculated only for patients who haven’t switched CFTR modulator therapies in a year
- PDC values were compared across different categories using a t-test with a significance level of $p \leq 0.05$.
- Routine patient assessments using surveys were conducted by the specialty pharmacy and information regarding medication switching, discontinuation, missed doses and any adverse events associated with CFTR modulator therapies were collected
- Responses of these patient assessments from May 2015 to August 2018 were extracted and analyzed to calculate the frequency of each response
- Statistical analyses were conducted using Statistical Analysis System University Edition (SAS Institute; Cary, NC)

RESULTS

Table 1: PDC calculated for one year (September 2017- August 2018)

	Overall		Children/ Adolescents		Adults		p-value*	Individuals with only Primary Insurance		Individuals with Primary and Secondary Insurance		p-value**
	n	Mean ± SD (%)	n	Mean ± SD (%)	n	Mean ± SD (%)		n	Mean ± SD (%)	n	Mean ± SD (%)	
Total	2548	86 ± 15	1075	86 ± 14	1473	85 ± 15	0.0876	1564	86 ± 15	984	86 ± 15	1.00
Ivacaftor	789	84 ± 16	330	85 ± 15	459	84 ± 16	0.3744	455	84 ± 16	334	84 ± 16	1.00
Lumacaftor/ivacaftor	1361	84 ± 15	684	86 ± 14	677	83 ± 15	0.0001	869	85 ± 15	492	84 ± 15	0.24
Tezacaftor/ivacaftor + ivacaftor	398	92 ± 11	61	96 ± 10	337	91 ± 11	0.001	240	92 ± 12	158	92 ± 11	1.00

*Comparing children/adolescents versus adults using t-test

** Comparing individuals with only primary insurance versus individuals with primary and secondary insurance using t-test

Table 2: Frequency of missing doses

Questions	How frequently did you miss doses of lumacaftor/ivacaftor in the past 28 days?		How frequently did you miss doses of ivacaftor in the past 28 days?	
	Frequency	Percent (%)	Frequency	Percent (%)
Response	n=25840		n=14905	
0	24443	92.23	13985	93.83
1 to 5	1273	4.80	686	4.60
6 to 11	55	0.21	47	0.32
12 or more	69	0.26	33	0.22
Not filling drug today	509	1.92	150	1.01
Unsure	153	0.58	4	0.03

Table 3: Reasons for missing doses

Question	What causes you to miss your ivacaftor?		What causes you to miss your lumacaftor/ivacaftor ?		What causes you to miss your tezacaftor/ivacaftor + ivacaftor?	
	Frequency	Percent (%)	Frequency	Percent (%)	Frequency	Percent (%)
Response	n= 802		n= 1147		n= 54	
Forgetfulness	366	45.64	688	59.98	29	53.70
Too busy/Unable to fit into daily routine	157	19.58	222	19.35	6	11.11
Vacation/Away from home	34	4.24	81	7.06	1	1.85
Insurance issues (Prior Auth)	36	4.49	76	6.63	1	1.85
Infection/Illness	32	3.99	38	3.31		
Administration difficulties	2	0.25	7	0.61	2	3.70
Side effects	2	0.25	7	0.61	1	1.85
Other (document in comments section below)	117	14.59			13	24.07
Lapse in access or waiting for delivery	38	4.74			1	1.85

Table 4: Discontinued medications

Question	Which medication was discontinued?	
	Frequency	Percent (%)
Response	n=327	
Ivacaftor	62	18.96
Lumacaftor/ivacaftor	205	62.69
Tezacaftor/ivacaftor + ivacaftor	10	3.06
Non-CFTR modulator therapies	50	15.29

Table 5: Reasons for discontinuing medications

Question	Why was the medication discontinued?	
	Frequency	Percent (%)
Response	n=247	
Switched medication	185	74.90
Other	23	9.31
Uncertain	22	8.91
Side effects	12	4.86
Lab abnormalities	2	0.81
Administration difficulties	1	0.40
Allergic reaction	1	0.40
Financial issues	1	0.40

Table 6: Side effects reported for CFTR modulator therapies[#]

Questions	What side effects, if any, are you experiencing with your ivacaftor?		What side effects, if any, are you experiencing with your lumacaftor/ivacaftor ?		What side effects, if any, are you experiencing with your tezacaftor/ivacaftor + ivacaftor?	
	Frequency	Percent (%)	Frequency	Percent (%)	Frequency	Percent (%)
Response	n= 9823		n= 14474		n= 1699	
None	8947	96.36	13531	93.48	1412	82.96
Not filling drug today ⁺	156	1.68	537	3.71	197	11.57
Other	97	1.04	152	1.05	57	3.35

[#]Option provided if the patient is not filling any particular medication during an assessment
⁺Responses reported only with frequencies >1%

CONCLUSIONS

- Compared to PDC values reported for patients with CF in the literature, the PDC values of the CFTR modulator therapy regimen calculated for the specialty pharmacy population demonstrated good adherence
- Using self-reports, patients taking CFTR modulator therapies reported low frequency of missing doses and adverse events, thus supporting adherence data calculated using PDC values
- While outside the scope of the research, potential reasons for increased adherence in children/adolescents compared to adults may be attributed to parental monitoring of timely consumption and refilling of CFTR modulator therapies
- Similarly, the overall high adherence values could also be attributed to the specialty pharmacy CF program, which provides regular reminders for refilling CFTR modulator therapies and counselling on medication adherence. Future studies are required to validate these assumptions.