University of Wisconsin
Clinical Sciences Center

Center Focus

Winter, 2020

Newsletter of the
Cystic Fibrosis Center

Abbvie CF Scholarship Winner

One of this year's Abbvie CF scholarship winners attends our Pediatric CF Center. Her name is Alyssa B. Here is a bit about Alyssa and her entry.

One quote that has helped me through my journey with cystic fibrosis is "Someone always has it worse than you." While this might seem extreme to many, this is a quote that I now live by. When I was a child, I always felt insecure about my condition. I was the only kid who had to take enzymes with meals, consume extra supplements in my school classes to help gain weight, and was asked why I always coughed constantly. I was self conscious about performing my lung treatments in front of my friends because I thought that I would be portrayed as different. I started asking myself "Why me?" and "What did I do to deserve this?". One day I was feeling sorry for myself and my mother approached me and said a quote that I would soon never forget. "Someone always has it worse than you." Later that night while I laid in bed, I started to think about my attitude on life. I was extremely healthy for a kid with cystic fibrosis, I had a loving and caring family accompanied by many friends, and I had a lifestyle that was preparing me a bright and successful future. I realized how lucky I actually was. From that day forward instead of asking "Why me?", I started asking "Why not me?". I realized that cystic fibrosis didn't define me in a bad way. It made me work harder, achieve more goals, and made me into who I am today.

Alyssa B.'s Achievements

Varsity Softball Team, Captain, First-Team All Conference, MVP, All-Star, 2015-2019

4-H, President, Secretary, 2015-2019

FFA, Vice President, Reporter, 2015-2019

Quiz Bowl, Manager, 2016-2019

National Honor Society, 2017, 2019

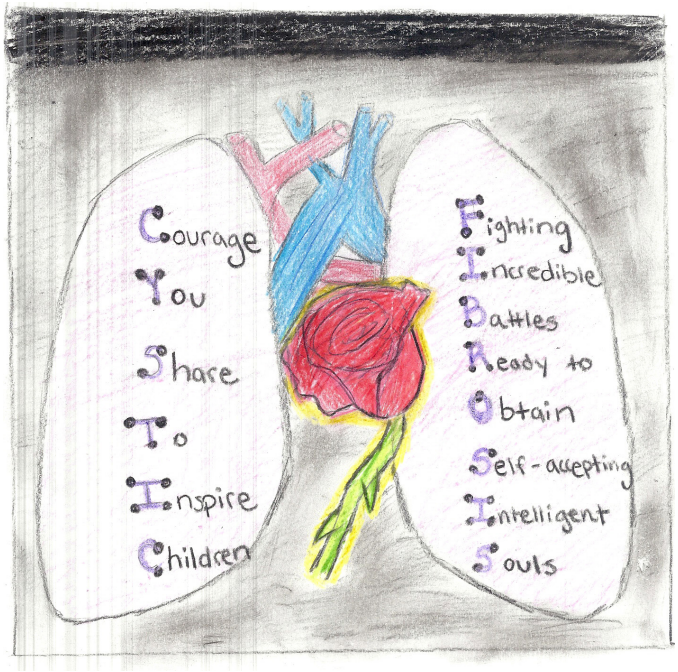
Student Council, Class Vice President, 2015, 2017

Church Server, 2015-2018

Varsity Basketball, Captain, Offensive MVP, 2015-2019

Varsity Volleyball, Captain, 2017-2018

Mentor for Troubled Children, 2018-2019



Adult CF Pulmonary Clinic to Stay at Current Location

At this time UW has made the decision to keep the adult pulmonary clinic at its current location. We apologize for any confusion as our previous newsletter had announced an upcoming new location. *See you all in our current location (B/2) for adult pulmonary function testing and all adult CF clinic visits!*

2019 CF Family Education Day Video Archive

CF Family Education Day 2019 was held on Saturday October 19 at the Fluno Center on UW Madison Campus. If you were unable to attend no worries. Most all the presentations are archived on our CF Center Website. Simply go to: *https://videos.med.wisc.edu/events/206*

Did you happen to see this on Fox 47 News?

It is a story about one of our adult patient s who is a competitive marathon runner.

http://fox47.com/sports/content/barrett-conquers-marathons-cystic-fibrosis

A Sad Goodbye…

As many of you may know, Jordan Foster, RN has left our outpatient CF Clinics. She has accepted a job as an inpatient nurse and will be caring for our kids on the 7th floor. We miss her but wish her well. It's interesting to know that she left clinic for the inpatient experience and two of our new nurses, Jenny Liter and Becky Steinmetz, left the 7th floor inpatient unit to have the outpatient experience. You will be able to see familiar faces in different places!

New Team Members

Nikki Dondlinger

Hey! My name is Nikki Dondlinger, I am a Cystic Fibrosis Research Coordinator in both the adult and pediatric clinics. My job involves running clinical trial visits and coordinating with all the people it takes to conduct them, including the patients! I have a bachelor's degree from University of Wisconsin – La Crosse in Biology. I grew up in the Madison area, and as much as I love to travel, I knew I wanted to move back here for the health care career opportunities, and I enjoy all the outdoor activities the area has to offer year-round.

I am very excited for the future of the CF community in research and look forward to working with you and your families. If you have any questions regarding CF clinical trials, please feel free to reach out at ndondlinger@pediatrics.wisc.edu! -Nikki

Rebecca Steinmetz

Hi, my name is Becky and I am a Registered Nurse with the pediatric pulmonology team. I met many of you when I was working inpatient on P7 (Universal Care Unit), and I have also worked as a nurse at the VA, where my patients were just a little bit older than they are at AFCH! In my free time I love hiking with my husband and dogs, and training for the Ironman! I am so excited to get to know you all better as a member of the clinic team!

Jenny Liter

Hi my name is Jenny Liter. I'm a Registered Nurse new to the Pediatric Pulmonary Clinic. I've been lucky to meet many of you and your children in clinic or speak to you on the phone already since I started in August! Prior to joining the pediatric clinic team I worked for four years on the inpatient unit P7 (The Universal Care Unit) that cares for patients with CF when they're admitted to the hospital. I'm excited to focus more on caring for patient's with CF and being a part of our Quality Improvement Group and Parent Advisory Group. Outside of work I enjoy going on hikes, baking (*and eating!*) cookies, and playing volleyball.

Silver Linings

Did you know?: If you have CF and are flying anywhere you can call 1-855-787-2227 72 hours before travel and request to speak with a travel support specialist? They are part of the TSA Cares program and they can help you to move quickly through security and screening.

THANK YOU!

THANK YOU TO EVERYONE WHO FILLED OUT OUR SURVEY! WE WOULD LIKE TO TAKE THIS OPPORTUNITY TO UPDATE YOU ALL ON THE STUDIES BEING PERFORMED HERE AT UW FOR PATIENTS WITH CF.

trikafta™
(elexacaftor/tezacaftor/ivacaftor and ivacaftor)

Study Opportunities for Adults

Study & Drug Name	Duration	Placebo	Goal of Study	Genotype
VX18-445-104 & 110 Trikafta	4 months 96 weeks	YES* NO	Assessing ELX/TEZ/IVA in pts with class III and class IV/V mutations	1 copy F508del & gating or residual function
PROMISE	6 visits over 2 years	N/A	Observation of patients on Trikafta	Homozygous/ heterozygous F508del
STOP-2	24-35 days	N/A	Evaluating differing durations of IV treatment	Any

Boehringer Ingelheim

CYSTIC FIBROSIS FOUNDATION™

Study Opportunities for Adults and Kids

Study & Drug Name	Duration	Placebo	Goal of Study	Genotype
CHEC-OB-17 Observation of sweat chloride	1 visit	N/A	Observation of patients on modulator therapy for 3+ months	Modulator eligible
BALANCE-CF-1 BI 1265162 delivered via Respimat inhaler BID	4 weeks	YES	Improved mucocilliary clearance via ENaC	Any
CFFC Fibrosing colonopathy	Followed in CF clinic	N/A	Observation of incidence of fibrosing colonopathy	Any

kalydeco (ivacaftor)

ORKAMBI® (lumacaftor/ivacaftor)

Study Opportunities for Kids

Study & Drug Name	Duration	Placebo	Goal of Study	Genotype
VX15-770-124 & 126	24 weeks 96 weeks	NO	Evaluate Ivacaftor in infants 0-2 years of age	1 Gating mutation
VX16-809-122 & VX19-809-124	24 weeks 96 weeks	NO	Evaluate Orkambi in children 1-2 years of age	Homozygous F508
HyPOINT	Up to 7 visits over 3 years	N/A	Hyperpolarized Imaging for New Treatments	Any

Brought to you by the CF Research Coordinators:

Melanie Nelson / 608-265-4617

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Blaze a trail to better treatments and a cure for cystic fibrosis.

Cystic Fibrosis Center Outcomes Data

The University of Wisconsin Cystic Fibrosis Center in Madison, Wisconsin, is one of more than 115 care centers across the country accredited by the Cystic Fibrosis Foundation. We work closely with the Foundation to continue to improve the care and quality-of-life of our patients and publicly report our center-specific data to give patients, families and ourselves an opportunity to look for areas of improvement.

Pulmonary Function and Nutritional Outcomes

Pulmonary function and nutrition are important indicators of the health of cystic fibrosis patients. The Forced Expiratory Volume in 1 second (FEV_1, the volume of air a person is able to forcefully blow out in a second) is considered a good indicator of lung function.

The following is data from 2018 and displays lung function for patients treated at the UW Cystic Fibrosis Center compared to the average score for all centers in the United States.

	UW Health	U.S. Average
6-12 years old	93.7%	96.8%
13-17 years old	94.2%	90.4%
18 years and older	70.0%	69.4%

Of note is that in 2013, the CF Foundation started using the Global Lung Initiative reference equations. (The previous reference equations were by Wang and Hankinson.) This change results in lower FEV_1 percent predicted values for preteens and teens.

The Body Mass Index (BMI, a ratio of body weight to stature) is considered a good indicator of nutritional status. The following is data from 2013 and displays BMI for patients treated at the UW Cystic Fibrosis Center compared to the average score for all centers in the United States.

	UW Health	U.S. Average
Median BMI percentile for patients 2-19 years old	65.0%	57.6%
Median BMI for patients 20 years and older	23.5 kg/m^2	23.3 kg/m^2

Care Provision Performance

Current guidelines of care recommend that patients with cystic fibrosis be evaluated at an accredited CF Center at least quarterly. In addition, patients should undergo pulmonary function testing at least two times a year and have a culture of their respiratory secretions performed at least once a year. The recommendation is also to increase the frequency of follow up for those patients that have more severe disease.

We believe that more frequent clinic visits and more frequent monitoring of pulmonary function and sputum cultures can lead to better outcomes. Thus, we strive to exceed the Cystic Fibrosis Foundation's recommended testing and obtain pulmonary function test and a sputum culture (or throat swab culture for patients who cannot cough out sputum) at every clinic visit.

The table represents two groups of patients who had four or more visits, four or more cultures and two or more PFTs.

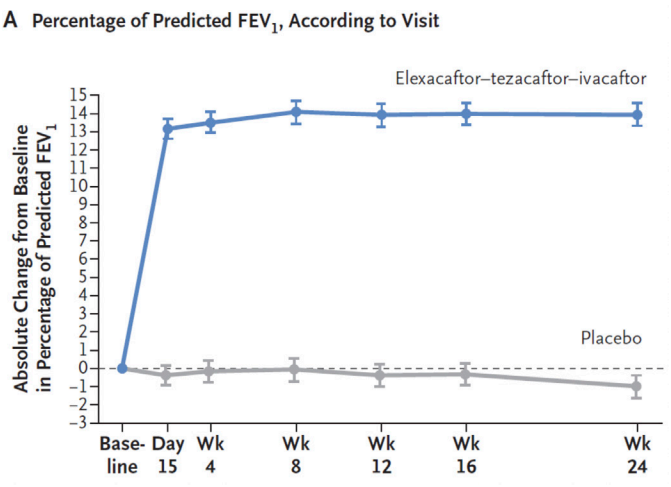
	UW Health	U.S. Average
Children 7-17 years with ≥4 visits, ≥1 culture, ≥2 PFTs	65.8%	58.4%
Adults ≥18 years with ≥4 visits, ≥1 culture, ≥2 PFTs	63.2%	58.4%

Our data is shown compared to the average outcomes reported by the Cystic Fibrosis Foundation for all accredited CF Centers in the U.S. (2018 data)

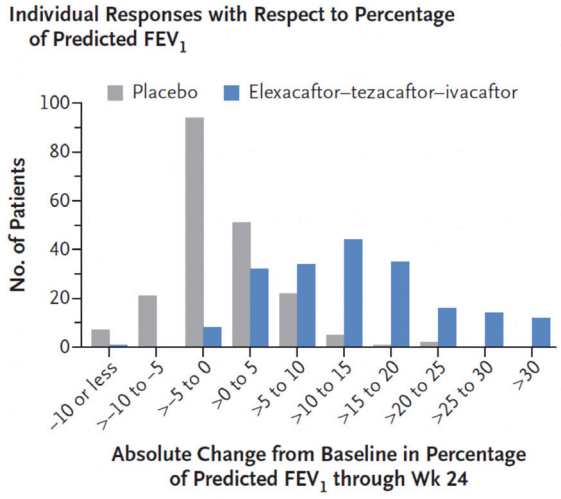
Trikafta Approval Highlights the 2019 North American Cystic Fibrosis Conference

There was an air of excitement in Nashville in late October/early November when approximately 5,000 health care professionals gathered for the 2019 North American Cystic Fibrosis Conference. One of the most important topics of the conference was the unexpectedly rapid approval by the FDA of Trikafta (elexacaftor/tezacaftor/ivacaftor plus ivacaftor). The data from the phase 3 clinical trials was so compelling that the FDA approved this new CFTR modulator only 3 months after the application had been submitted.

Trikafta is approved for individuals with CF who are at least 12 years of age and who have a minimum of one copy of the F508del variant. (Note: the term "variant" is now preferred over the term "mutation".) Two phase 3 studies were conducted simultaneously. One of these studies enrolled subjects who had one F508del variant and a second variant that would result in minimal function of CFTR protein. (For example, class one variants such as G542X or R553X in which no CFTR protein is produced.) In this randomized, double-blind, placebo-controlled trial, subjects who received Trikatfa had an FEV_1 improvement of 13.8% compared to placebo at 4 weeks and an improvement of 14.3% at 24 weeks:



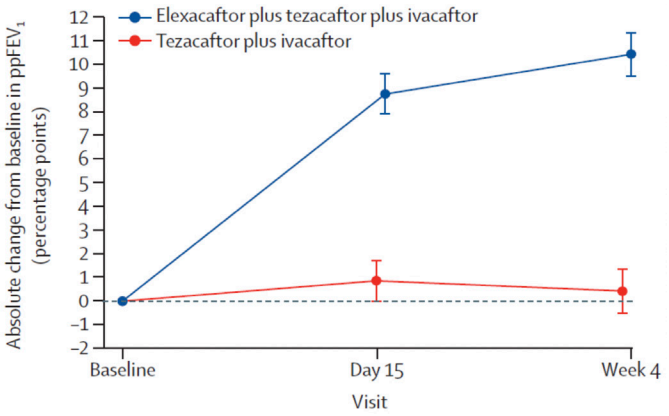
The improvements in FEV_1 listed above are averages. There were subjects who had improvements in FEV_1 at 24 weeks that exceeded 20% to 30%:



There was also a decrease in pulmonary exacerbations by 63%, sweat chloride values decreased by 41.8 mmol/L and quality of life scores significantly improved in subjects treated with Trikafta compared to placebo. The figures above come from the New England Journal of Medicine publication: Middleton PG, Mall, MA, Dřevínek P, et al: Elexacaftor-tezacator-ivacaftor for cystic fibrosis with single phe508del allele. *NEJM 2019;381:1809-19.*

Importantly, Trikafta is the first modulator approved for patients who have a minimal function mutation. The previously approved modulators Kalydeco, Orkambi and Symdeko are not effective for patients with minimal function mutations.

The second study of Trikafta enrolled subjects who had two copies of the F508del variant. Orkambi and Symdeko are approved modulators for people with CF who have two copies of the F508del variant. These modulators are useful because long term use of these modulators slows down the decline of lung function. However, the FEV_1 improvement is only approximately 3 to 4%. In the Trikafta study, subjects were first placed on tezacaftor plus ivacaftor (Symdeko) for 28 days. Thereafter, approximately one-half of subjects were administered Trikafta and the other half of subjects continued tezacaftor plus ivacaftor. The assignment of drug was blinded, meaning that neither the subjects nor the direct research team knew who was receiving which drug combination. At 28 days, the subjects receiving Trikafta had improvement in FEV_1 of 10% compared to the group that continued Symdeko:



Please note that with the 3 to 4% improvement in FEV_1 with Symdeko, the total improvement in FEV_1 with Trikafta is close to 14% (the same as that seen in subjects with F508del and a minimal function variant). Similar to the data in the New England Journal of Medicine article for F508del/minimal function, there were statistically significant improvements in sweat chloride values and quality of life scores. The data above was published in the Lancet: Heijerman HGM, McKone EF, Downey DG, et al: Efficacy and safety of the elexacaftor plus tezacaftor plus ivacaftor combination regimen in people with cystic fibrosis homozygous for the F508del mutation: a double-blind, randomised, phase 3 trial. Lancet 2019 Oct 30 [Epub ahead of print]

As stated above, there is a useful place for Orkambi and Symdeko in people with CF because over the long-term, these medications slow down the progression of lung disease. However, Kalydeco and Trikafta are known as highly effective modulator therapy. Our goal is to prescribe Trikafta for all eligible patients (those who are at least 12 years of age and who have at least on F508del variant). We look forward to the future approval of Trikafta in people with CF who are younger than 12 years of age.

There are people with CF who have two variants, neither of which is F508del. Unfortunately, these patients are not eligible for any of the FDA approved modulators. The CF Foundation wants all patients to have a highly effective treatment. Thus, at the North American Cystic Fibrosis Conference, the CF Foundation announced the Path to a Cure research initiative. This research initiative will devote 500 million dollars through 2025 to ensure that there is a cure for every patient with CF.

A special guest at the North American Cystic Fibrosis Conference was Dr. Francis Collins, the Director of the NIH and one of the co-discoverers of the CFTR gene. You can watch plenary 2 where Dr. Collins appeared, and can watch the other plenary sessions, by going to *https://www.nacfconference.org/*. Hover your mouse over "Content" and go to "Archive" in the drop-down menu.

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