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# CYSTIC FIBROSIS CENTER NEWS & NOTES

SPRING 2020, VOL. XXXIV

## NEWS FROM THE FRONT

### Working Together to Improve CF Care in Turkey: *C. S. Mott Children's Hospital and Marmara University CF Center, Istanbul*

By Samya Nasr, MD, Director, Cystic Fibrosis Center

CF outcomes in Turkey have not followed those reported in the US. Most CF patients in Turkey are children and their quality of life is poor. Turkey's current CF care approach indicates that without a systematic and sustained intervention, CF leads to early death, with a high economic and emotional cost to patients and their families. To help improve care in Turkey, guidelines comparable to those in the US need to be established to improve care in all aspects of CF.

Current barriers for improving CF care in Turkey include: limited clinical training of healthcare providers, limited and unreliable microbiologic testing across the country, limited funding for staff support, lack of clinical suspicion by healthcare professionals and lack of referral diagnostic facilities (sweat test and mutation analysis).

Working with the Middle East CF Association (MECFA) and the CF Foundation, a pilot project was started in 2018 between our center and the Marmara University CF center, the second-largest CF center in Turkey, to help improve CF care there. Our work with Marmara CF center is focusing on the following:

1. **Implementing a state-of-the-art multidisciplinary CF Center in Istanbul.** This pilot project will establish a care center able to manage all clinical aspects of patients with CF, following best evidence-based care guidelines and adapting them to Turkey's setting.
2. **Training a multidisciplinary expert CF team based in Turkey.** The project includes visits from the U-M CF team (Samya Nasr, MD, CF Center Director), RT, PT and dietitian in the first year to Marmara CF Center for a week for training in March, 2019. The Marmara CF team visited our center for a week for intensive training this fall following the North American Cystic Fibrosis Conference. In addition, their Pediatric Pulmonary fellow worked and trained at the U-M CF Center in the summer of 2019 for two months, and another fellow will be coming in the summer of 2020 for intensive CF training. The goal is to establish a standard of care at Marmara CF Center and help build the foundation of a quality improvement-led (QI) program. The training takes place at both Marmara and our CF centers. Training includes their pediatric fellows, pulmonologists and faculty, staff and the adult pulmonologists.
3. **Improving clinical outcomes of patients with CF seen at the Center.** Through the multidisciplinary training, we aim to improve outcomes mainly in nutritional and pulmonary status.

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# NEWS FROM THE FRONT

## Working Together to Improve CF Care in Turkey

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4. **Focusing on quality improvement work.** The team at U-M is working closely with Marmara CF team to establish QI projects to reach the goal of improving their care. Areas of QI work include: improving BMI, improving pulmonary function testing and implementing Infection Prevention and Control (IP&C) guidelines. Work started in all QI projects using U-M algorithms and protocols.
5. **Starting a network of CF centers across Turkey.** Once the two-year pilot project has been completed, we will work with Marmara CF center to implement the same approach in other CF centers in Turkey. The goal is to create a National CF Center Network in Turkey. This network will adhere to the requirements of the CFF centers in the US.
6. **Aiming for median life expectancy in Turkey.** This will be accomplished through forming a National CF Center Network, using evidence-based, state-of-the-art healthcare delivery, operating under quality improvement principles, continuing multidisciplinary team training and establishing a meaningful clinical research initiative. The collaborative relationship between Marmara CF Center and others can be guided by the Ministry of Health and Marmara CF Center, depending on the needs. The collaboration could be through online interactions and through developing CF guidelines for Turkey.

In summary, as we work to improve care and outcomes for CF patients in our country, we are excited to share those strategies to improve CF care globally. After the two years of this pilot project are completed, our team is looking to help other CF patients in other countries in the Middle East as well.

Mott team members in Istanbul March 2019. Left to right: Chris Tapley, PT, Dr. Nasr, Sharyn Dagher, RRT

Marmara University and University of Michigan CF Centers in Nashville, TN for the North American Cystic Fibrosis Conference November 2019

Sandra Bouma, Mott Dietitian, mentoring dietitians from Marmara University

# The Work Is Not Yet Done

By Richard H. Simon, MD, Adult Program Director

The development of the triple combination CFTR modulator, elexacaftor-tezacaftor-ivacaftor (elx/tez/iva); Trikafta™), is probably the most important advancement made in the history of cystic fibrosis (CF) treatment. At present, approximately 90 percent of people with CF age 12 years and above are eligible for this highly effective therapy. But despite all the excitement, it is worth remembering that there is still a lot to do. First, studies need to be done in children younger than 12 to determine if elx/tez/iva is safe and effective. Second, approximately 10 percent of people with cystic fibrosis aren't eligible for elx/tez/iva because they don't have at least one copy of the delta F508 (F508del) mutation and therefore will not benefit from it. And third, elx/tez/iva is not a cure but only a highly effective treatment, so the ultimate goal of finding a cure has not yet been achieved.

The standard way to test new drugs is to do the initial clinical trials in people 18 years of age and older. If the treatment proves safe and effective, then the drugs are tested in patients with CF age 12 to 17 years, 6 to 11 years, 2 to 5 years and then below 2 years. The reason for this stepwise testing is that treatments that are safe and effective in older people may not be so in those who are younger. The rapidly growing infant and child may not respond the same way as older people. The previously developed CFTR modulators have already undergone testing in younger patients with CF and have received the following approvals from the US Food and Drug Administration (FDA): Ivacaftor (Kalydeco®) is approved for patients with a subset of mutations for ages 6 months and older, lumacaftor/ivacaftor (Orkambi®) for 2 years and older, and tezacaftor/ivacaftor (Symdeko®) for 6 years and older. Elx/tez/iva (Trikafta™) is currently being tested in patients age 6 to 11 years.

There is a group of mutations in the CF gene that are called "stop" or "nonsense" mutations, which do not respond to any of the available CFTR modulator drugs and are carried by 9 percent of people with CF in the US. These mutations prevent the full length CF protein from being made because they cause its production to be stopped too early. The resulting shortened protein does not function. Treatments are being studied to correct this by producing the protein while ignoring the stop mutations to allow the full length protein to be made.

Another approach to treat CF is to transfer a normal CF gene into the cells of the body that need a functioning CF protein. This strategy, known as "gene therapy," should work in all people with CF, regardless of which mutations they have. Beginning in the 1990s, clinical trials of gene therapy were attempted, but without success. More recently, there have been new tools developed that might be useful for CF. The gene therapy field is being reenergized and studies are ongoing using cultured cells and experimental animals to transfer the normal CF gene into those areas of the lung that need a functioning CF protein.

The ultimate treatment for CF is to correct the mutations in the patient's own CF genes. If this could be done for all cells of the body that need a functioning CF protein, this would be a cure. The approach is called "gene editing." There has been amazing progress at developing tools that can do this in human cells grown in research laboratories. The technique receiving the most attention uses an editing tool called CRISPR that can cut out abnormal parts of the gene and replace them with normal components. The challenge, of course, is to make this work in people with CF.

After considerable discussion, the CF Foundation has decided that scientific knowledge has advanced enough that now is time to invest heavily in the approaches mentioned above. The Foundation has started an ambitious plan they have named "Path to a Cure." The Foundation has committed up to $550 million between now and 2025 for research directed toward these areas. For more information about this exciting endeavor, go to cff.org/Research/About-Our-Research/Path-to-a-Cure-Many-Routes-One-Mission/.

So as we celebrate the approval of elexacaftor-tezacaftor-ivacaftor (Trikafta™) as a true advance in CF treatment, the CF community is rededicating itself to finding treatments that will help all patients as rapidly as possible. In order to emphasize this, the CF Foundation likes to point out that the abbreviation "CF" means not just "Cystic Fibrosis," but also represents the ultimate goal, "Cure Found."

# WHAT'S NEWS

## Food Insecurity: *It's More Common Than You May Think*

By Haley Moraniec, LLMSW, Pediatric Clinical Social Worker

Why is food insecurity so common, especially among CF families? Individuals with CF have much higher fat and caloric needs, greater expenses due to the cost of care, and often cannot work due to poor health.

According to the United States Department of Agriculture (USDA), in 2018, 11.1 percent of families across the nation identified as food-insecure. Many providers note, however, that families do not report food insecurity as often as it is actually occurring. This could be due to the stigma that comes along with being labeled as "food-insecure" or "hungry," or because they do not fully understand the definition.

The official definition of "food insecurity" is not being able to afford enough food or not having reliable access to nutritious foods. Food insecurity can occur for many reasons, and it does not always mean that you simply cannot afford food. Food insecurity also means:

- skipping meals to ensure your children are able to get enough calories
- making portion sizes smaller to ensure the food stretches as long as needed
- choosing between paying for medications, bills, food and other necessities
- not having transportation to get to the store and running out of groceries
- only being able to shop at the local dollar store that doesn't offer fresh options

—and so much more.

Many families minimize their experience with food insecurity because they have food due to skipping other bills, get help from other family members or feel others are "more in need."

The Pediatric Cystic Fibrosis Program began screening for food insecurity in June 2019. We found that 9.7 percent of individuals have indicated on the form that they have had some level of food insecurity over the past year. Additionally, numerous families have verbally shared struggling with food insecurity, but did not circle it on the form. There is a great deal of stigma attached to the idea of not being able to afford enough food.

There are resources available and it is not uncommon to hear that others, too, have questioned where their next meal will come from. Your CF Center social workers are a valuable resource for all patients and families. If you are in need of food assistance, please reach out to your CF Center social worker to discuss options.

## Cystic Fibrosis Liver Disease

By James Abraham, MD, Clinical Assistant Professor, Division of Gastroenterology & Hematology

Cystic fibrosis (CF) is a multi-organ genetic condition affecting over 30,000 individuals in the United States. Typically, CF is diagnosed early in life—often in infancy, due to nationwide newborn screening programs. For many people with CF, health issues affecting the lungs and nutritional status are very common.

As the lifespan of people with CF has increased remarkably over the last few decades, particularly as they've aged further into adulthood, it appears that issues occurring "below the lungs" (specifically affecting the digestive organs) become more frequent and noticeable. Concerns regarding liver and pancreas health, bowel habits, abdominal discomfort and complex nutrition and weight management can sometimes require more discussions with the multidisciplinary CF care team.

Liver involvement in CF (CFLD) is quite common, though its presence and severity can vary widely among the CF population. CFLD can range from mild elevations of serum liver function tests (AST/ALT/GGT, present in 20-30 percent of people with CF), bile sludging or stone formation within the liver, excess fat accumulation in liver cells as well as scarring (multinodular cirrhosis) of the liver. While liver involvement is common, more severe liver disease with multinodular cirrhosis is much less common, occurring in approximately 7 percent of the CF population, and usually developing prior to age 20. Of those who do develop multinodular cirrhosis, 40-60 percent may go on to develop portal hypertension as a complication.

Portal hypertension is a condition that builds pressure within the liver related to severe, prolonged scarring; potential complications include development of esophageal varices (enlarged esophageal veins that may increase risk for gastrointestinal bleeding) and ascites (fluid buildup in the abdomen). If identified early, these complications stand a better chance of being managed appropriately. Liver transplantation is an option for some people with CF who have cirrhosis and portal hypertension; thankfully, this is not required for most patients with CFLD.

Currently, there are no specific tests that can predict which people with CFLD might eventually develop cirrhosis or complications

# WHAT'S NEWS

## Staff Introductions

Ashley Sabourin, PharmD, is an ambulatory clinical pharmacist generalist at the Specialty Pharmacy at Michigan Medicine. She joined the pediatric CF care team in October 2019 and provides comprehensive medication support and clinical care throughout CF patients' treatment course.

Janelle Singletary RN, BSN, Adult Inpatient Nurse, has recently been named CF Liaison for adult inpatients on 6C in University Hospital. She has worked with CF patients in the inpatient setting for 13 years.

of portal hypertension. Because of this, when CFLD is suspected (either by clinical findings, blood work, imaging studies or a combination of these), periodic follow-up with lab studies (at least 1-2 times/year, typically with annual CF studies) and imaging (usually with a non-invasive ultrasound or MRI study) is needed. Ursodiol is a medication that can sometimes be used in certain subtypes of CFLD, although research is not clear if it effectively slows progression. Consultation with a gastroenterology and/or hepatology provider, preferably with CF experience, can be helpful in monitoring and managing CFLD in combination with the multidisciplinary CF team.

Due to the continued and gracious donations from the Gorge family, the CF Center is continuing to offer carrier screening to extended family members of people with CF. Contact the Pediatric Pulmonary Office if interested.

## Michigan Medicine Specialty Pharmacy Services

Michigan Medicine Specialty Pharmacy Services is a full-service specialty pharmacy program. It was developed 10 years ago to support Michigan Medicine providers and patients with high-cost and complex specialty medication needs.

Pulmonary specialty medications we service include: inhaled antibiotics, pancreatic enzymes and modulators.

### Enhanced Patient Services

Michigan Medicine Specialty Pharmacy services are different from neighborhood retail and mail-order pharmacies. Our pharmacists are directly linked to your specialized healthcare providers, and we are dedicated to personally serving you throughout your entire treatment process. In addition, we offer:

- Financial counseling: Access to financial and insurance coverage counseling focused on minimizing your out-of-pocket expense
- 24/7 pharmacist: Access to an on-call pharmacist 24 hours a day, 7 days a week
- Refill reminders: To ensure you don't run out of medications, you will receive monthly telephone calls regarding your refills
- Accurate and efficient assistance with your treatment plan due to our ability to access complete medical records
- Free mail order delivery (see below)
- Value-added clinical support and education services

### Mail Order Delivery

The Michigan Medicine Specialty Pharmacy offers specialized mail order distribution of your medications within the state of Michigan. Your ongoing medications can be delivered in unmarked, temperature-appropriate shipping containers to any address within Michigan at no charge. You can also pick up your prescriptions at the pharmacy during business hours.

### Financial Counseling and Clinical Support

Specialty medications are generally expensive, which can present a significant challenge for some patients to pay for their medication. We offer financial counseling and insurance support services to help you with your insurance, ensuring you are maximizing all available resources.

### Contact Us

**Specialty Pharmacy:**
855-276-3002

**Specialty Pharmacy Services page:**
uofmhealth.org/conditions-treatments/specialty-pharmacy-services

**MAIN LOCATION**
**East Ann Arbor Health and Geriatrics Center**
4260 Plymouth Rd
Ann Arbor, MI 48109
**Hours (EST):**
Mon–Fri, 9:00am–5:30pm; Sat, 8:30am–12:30pm

**ADDITIONAL LOCATION**
**Taubman Center Pharmacy**
1500 E. Medical Center Dr
Ann Arbor, MI 48109
**Hours (EST):**
Mon–Fri, 9:00am–6:00pm

# PATIENT SPOTLIGHT

## From Couch to 5K to Marathon

By Emily Schaller, Adult with Cystic Fibrosis

Exercise. It's good for us. We all know we should do it, but for many of us it is hard to start a new exercise routine or stay in the groove: "I don't have time, I'm too tired, I work too much, I don't know what to do, I just don't want to." In my adult life I've used all of these excuses to get out of exercising, but one excuse that I used for almost a decade is "but I have CF."

When I was diagnosed with CF at 18 months in 1983, my parents made a choice to treat me just like my older brothers, who do not have CF. Little did they know at the time that this decision to keep me active led to a super-healthy childhood. They let me play outside from sunup to sundown, only coming in for necessities like food with salt, drinks and manual chest PT. They also encouraged me to play every sport I wanted to (except hockey, but that is a sore subject so I won't go into that).

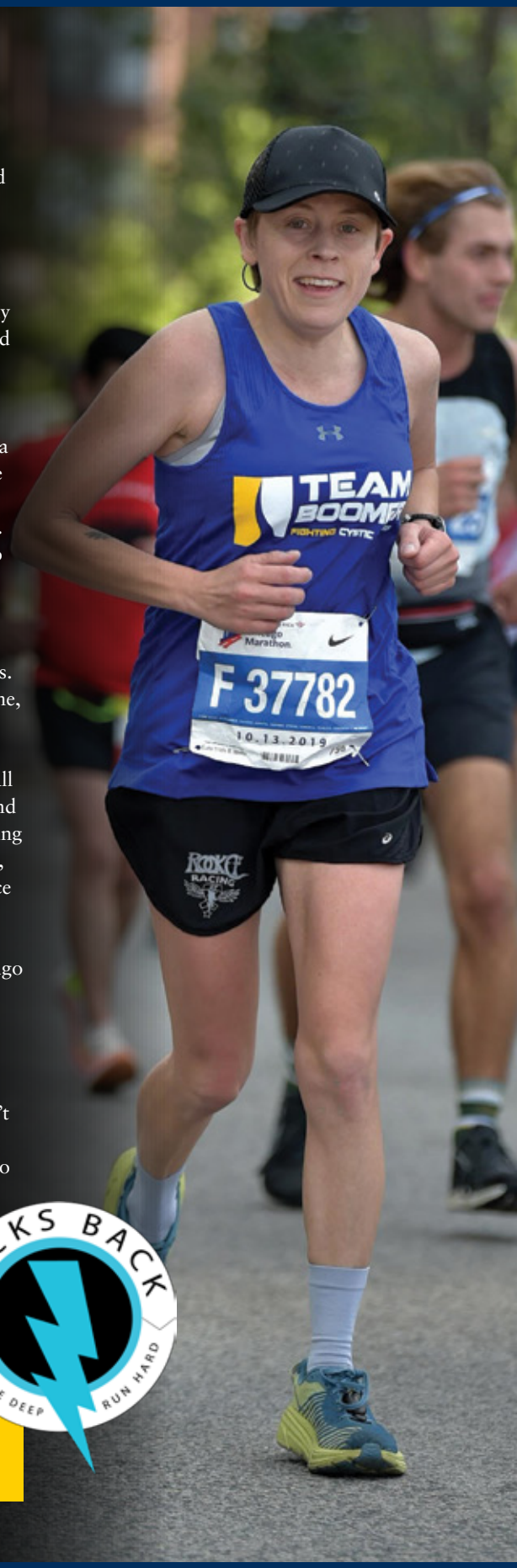
Participating in sports was great for my lungs, but also really helped me feel "normal" and avoid that feeling of isolation that can come along with having CF.

I wish I could say I was a great CF patient who stayed active and exercised to this day, but I can't. In my late teens, my active lifestyle started to slip away. As the effects of CF began catching up with me, recurring lung infections, hospitalization and loss of lung function became my normal. Exercise took a backseat because it was hard—and frankly, I didn't think I needed to do it. Also sitting in the backseat next to exercise was my treatments.

Around 2006, I realized that I needed to get my act together. I began doing my treatments more regularly and decided it was time to try exercising again to see if I could change the direction of my health. Growing up, I would see a few runners in my community and think, "Why would anyone voluntarily run?" So what did I do when I decided to give exercise another shot? I went for a run. I envisioned setting out for a nice two-mile run. In reality, I made it half a block before I keeled over in a full-blown coughing fit. It would have been super-easy to turn around and head home, but I chose to keep going. I slogged on, doing a run/walk combo until I reached a mile.

Once I could run one mile without stopping, I started to push myself a little more until I could run two miles. Just three months into my new routine, I saw my FEV1 increase to numbers I hadn't seen in over a decade. My hospitalizations were also reduced. All of this helped build my confidence and get me to my first 5K. After completing that, I signed up for a 10K, and then, in 2007, my first half-marathon. Since then I have done almost 20 half-marathons and completed three full marathons, the latest being the Chicago Marathon in October 2019.

"I love running" are words I never could have imagined coming out of my mouth, until I realized what it's done for me. But I know running isn't for everybody, so I tell people to find something they like and try to stick to it. Cycling, dance, CrossFit, circuit training, walking, soccer, softball, yoga: it is all good! Just find something you love and stick with it!




**Need something to get you started?** Apply for the Rock CF Kicks Back Program! Kicks Back donates running shoes to people with CF and registers them for a race of their choice. Visit letsrockcf.org/kicksback for more information.

# NACFC Highlights and Inspiration
# Path to a cure: *Together is the way forward*

By Rebekah Raines, Mother of a Child with Cystic Fibrosis, Pediatric Parent Partner and Advisory Board Member

I was happy to attend the North American Cystic Fibrosis Conference [NACFC] in October 2019. It was truly inspiring, humbling and packed with information. There are so many amazing people investing their time, money, talent and intellect to not only work to cure CF, but to find ways to improve the lives of those affected by CF.

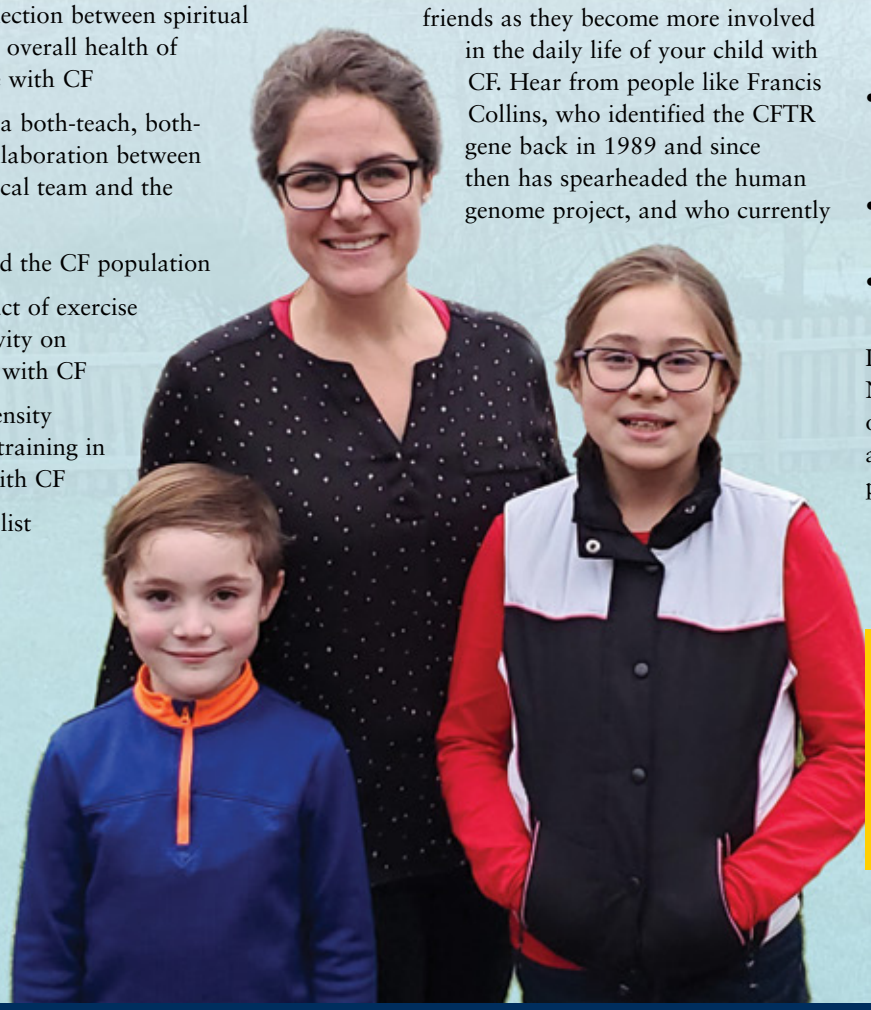
One of the highlights were hundreds of research and quality improvement posters highlighting active studies on:

- psychological effects of CF
- approaches to successfully treat the social, emotional and mental impact of CF
- how antibiotics are affecting the gut microbiome
- how the gut microbiome is connected to mental health
- increasing your FEV1 with modulator therapy
- the connection between spiritual care and overall health of someone with CF
- creating a both-teach, both-learn collaboration between the medical team and the family
- aging and the CF population
- the impact of exercise and activity on children with CF
- high-intensity interval training in adults with CF

… and the list goes on....

I encourage you to take a moment and check out the CF Parent Advisory Facebook Group **facebook.com/groups/AnnArborCFfab** to see information from the 2019 NACFC. The sessions and posters were fascinating, enlightening and hope-filled.

Register here: **arc.nacfconference.org/cff/live/38/page/253** for access to the replay of the livestreamed sessions from the 2019 NACFC. It is worth your time to listen to these sessions. They will help expand your understanding of CF and inspire you to learn more. These sessions can also be a great resource to share with family and friends as they become more involved in the daily life of your child with CF. Hear from people like Francis Collins, who identified the CFTR gene back in 1989 and since then has spearheaded the human genome project, and who currently heads the NIH. Hear from Catherine McCloud, chair of the CFF's Board of Trustees and mother to a man who lost his battle with CF in 2016.



Taking charge of CF begins with each of us. As parents of kiddos with CF we have the opportunity to influence and shape their lives. It starts with simple things like:

- inspiring diligence and grit in our children
- teaching our kids "why" we do what we do; this means that we, as the parents, must first understand
- learning how to keep the gut healthy to help boost immune function and nutrition absorption
- continuously discovering more about and practicing optimal health habits as a family
- play together, be active—learn what inspires your family
- learn to care for your family's emotional/spiritual/mental needs

I wish each of you could experience NACFC. I left the conference with a feeling of awe and hope. Without a doubt, there are wonderful, crazy brilliant, passionate people working to cure CF. I know that together, clinicians, parents and researchers can find a path forward to a cure. For this, I am grateful.

Do you want to learn more about CF Advocacy Day, an opportunity to advocate to state and federal lawmakers in Michigan? Contact Executive Director Shelly Francis sfrancis@cff.org at the CFF NW Ohio and Michigan Chapter.

# TEAM UPDATES

## Pediatric Family Advisory Board Update

By Catherine Enochs, BSN, RN, AE-C, Pediatric Program Coordinator

As parents of children with cystic fibrosis (CF), the Pediatric CF Family Advisory Board (FAB) has brought numerous changes to our clinic to enhance the care of people with CF and their families. Our advisors provide patients' and families' experiences to drive quality improvement in our clinic and hospital.

This year our advisors wanted to focus on the equipment access problems that had surfaced after MedEQUIP, Michigan Medicine's equipment unit, closed its doors. The board met with Binson's—which is one of the major Durable Medical Equipment (DME) companies—to discuss equipment access issues experienced by CF families. The company was very receptive, meeting with the board in person, and is now working to better stock and supply appropriate equipment for people with CF.

While meeting with the FAB, the DME company notified us that the state Medicaid office was causing one of the barriers to gaining access to multiple nebulizer cups per patient. This prompted the CF Center to send supporting research and articles to Medicaid reviewers to prove why one cup per nebulizer treatment would be needed. Medicaid agreed that they would approve, after prior authorization, one nebulizer cup per nebulized medication every six months.

The FAB is also continuing to maintain a private Facebook group for communication and collaboration with the Mott CF community. Their quarterly newsletter began distribution in 2019 and is now being evaluated for improvements that will better serve you as a community of parents and caregivers of children with CF.

Join the private Pediatric FAB Facebook group at **facebook.com/groups/AnnArborCFfab**

We're looking forward to 2020, when we will be focusing on quality improvement projects driven by the FAB. If you are interested in the Family Advisory Board and finding out what serving on the board entails, please email **UM-Peds-CFCenter@med.umich.edu** for more information.

## Adult Patient Advisory Board Update

By Katie Hall, LMSW, Adult Program Coordinator

The Adult CF Center is always looking for ways we can enhance the patient experience in our clinic. We have an active advisory board, which consists of adults who are currently patients in the adult CF clinic here at Michigan Medicine. Our advisory board meets monthly, utilizing an online platform called BlueJeans, where we can all see each other without any infection control concerns. The advisory board also developed a magnet, which you already likely received, that contains information about various signs and symptoms and when to call our clinic or seek urgent medical attention. When members of the CF Center Care Team are working on projects or have ideas they would like to implement, we utilize the advisory board to help make sure we are making changes the board feels would be positive and beneficial for our patients. Our advisory board is also planning to begin work on a clinic brochure for new patients to our care center and for folks who are transitioning from the pediatric program.

The patient voice is crucial to making sure our clinic and our care center are meeting the needs of our patients. We are always looking for new members to join our advisory board! Currently, we meet the second Tuesday of the month from 7-8 pm. If you're interested in joining the advisory board or learning more about it, please contact Katie Hall at **aultkath@med.umich.edu** or call 734-998-6067.

## CFPEERCONNECT

CF Peer Connect is a peer mentoring program for people with cystic fibrosis and CF family members age 16 and older. Through this program, you'll be matched with a peer mentor who has experience with topics that are important to you. Together, you can connect over video, phone or email. Visit **cfpeerconnect.com/about.**

### Want to securely email your doctor?

Sign up for the My U of M Health Portal. Your U-M labs and tests can be reviewed via this portal. You can send messages to your doctor, nurse, dietitian or social worker; request refills; and even reschedule appointments, all via the secure patient portal. Visit **myuofmhealth.org** to get your access code and sign up! *(Please note: The Portal should not be used for sick calls.)*

# New Guidelines for Lung Transplant Referral in People with CF

By Shijing Jia, MD, Adult Program Associate Director

With the many treatments now available for cystic fibrosis (CF), including the new modulator drugs, living with CF is filled with more hope than ever before. For some people, CF lung disease can progress despite conventional therapies such as inhaled hypertonic saline or modulator drugs. For these patients with advanced lung disease, lung transplantation is an option that can be life-saving in some cases.

Of the total patients receiving lung transplants in the US, people with CF account for only a small portion (~15 percent). But people with CF are very different than other patient populations that get lung transplants: CF patients are usually younger, have infectious bacteria such as Pseudomonas, and have other complications of CF disease such as diabetes and pancreatic malabsorption. Experts in the field of lung transplant and cystic fibrosis recognized this, and created consensus guidelines to help guide care for those CF patients with advanced lung disease who may benefit from an evaluation for lung transplantation.

These guidelines were recently published in the Journal of Cystic Fibrosis and then widely distributed to CF care centers across the country and abroad. The recommendations comprise three major themes:

1. Early discussions and education of lung transplantation can help ease the anxiety of the topic for people.
2. Timely and appropriate identification and modification of barriers to lung transplant can help optimize the process when the time actually comes for referral and evaluation for transplantation.
3. Open communication between the patient, the patient's CF care center and the lung transplant center will help improve the quality of care provided collectively.

Since these recommendations were published, the University of Michigan CF Center has been working to align our practice and patient education to these themes. Some of you may be approached for surveys or educational discussions around the topic, even if lung transplant discussions or planning are way off in the distant future. We hope to always be working to improve upon the care we provide to you!

More information about the Lung Transplant Referral Guidelines can be found at the Cystic Fibrosis Foundation website at: **cff.org/Care/Clinical-Care-Guidelines/Respiratory-Clinical-Care-Guidelines/Lung-Transplant-Referral-Guidelines**.

CYSTIC FIBROSIS FOUNDATION®

# Great Strides 2020

Great Strides provides a fantastic opportunity for family, friends, students and colleagues to come together and make a difference. Each year, more than 125,000 people participate in over 400 walks across the country! The event harnesses the power of people with a shared vision and encourages collaboration, team building and leadership as we take steps to find a cure for cystic fibrosis.

Your participation in Great Strides matters a lot! We don't just want to treat CF. We want to end CF. Register now at **cff.org/greatstrides**

GREAT STRIDES®
CYSTIC FIBROSIS FOUNDATION

## Great Strides is coming to a city near you!

**SATURDAY, MAY 2, 2020**
Toledo, OH
Lansing, MI

**SUNDAY, MAY 3, 2020**
Detroit, MI
Kalamazoo, MI

**SATURDAY, MAY 9, 2020**
Ann Arbor, MI

**SATURDAY, MAY 16, 2020**
Auburn Hills, MI

**SUNDAY, MAY 17, 2020**
Grand Rapids, MI
Grand Haven, MI
Davison, MI
Findlay, OH

**FRIDAY, MAY 29, 2020**
Petoskey, MI

**SATURDAY, MAY 30, 2020**
Frankenmuth, MI

**SATURDAY JUNE 6, 2020**
Port Huron, MI
Mount Pleasant, MI

# RESEARCH UPDATES

The CF Foundation's Therapeutics Development Network (TDN) is a driving force in CF research. Michigan Medicine is a CF Therapeutic Development Center, which helps us get involved in clinical research so we can contribute to making improvements in treatments and therapies. But we can only accomplish that with your help! If you have questions about our research program, you may contact Marisa Linn at **mlinn@med.umich.edu** and Dawn Kruse at **dmkruse@med.umich.edu**.

In order to help you better understand some of the studies open to enrollment, below are brief summaries of research we are conducting at Michigan Medicine.

## Antibiotic Studies:

1. TEACH: Adding Chronic Azithromycin to Inhaled Tobramycin to determine whether azithromycin reduces the benefit of inhaled tobramycin by comparing changes in pulmonary function **(recruiting ages 12+)**
2. SAV005-04: Inhaled Vancomycin for the treatment of MRSA **(recruiting ages 6+)**
3. STOP2-IP-15: Standardized Treatment of Pulmonary Exacerbations II to determine the optimal duration of IV antibiotic treatment **(recruiting ages 18+)**
4. STAR-ter: cycled antibiotics for eradication of new cases of MRSA **(recruiting ages 2-45)**

## Anti-inflammatory Studies:

1. APPLAUD: Use of LAU-7B to reduce inflammation in adults **(recruiting ages 18 years+)**

## Enzyme Studies:

1. CF-FC: Fibrosing Colonopathy in US Patients with Enzymes **(recruiting)**

## Behavioral Intervention Studies:

1. Project UPLIFT to Reduce Anxiety and Depression in CF Patients: determining the effectiveness of telephone- or web-based group mindfulness and cognitive behavioral therapy in patients with depression or anxiety **(enrolling ages 13+)**

## Modulator Studies:

1. PTI-801-01: Use of PTI-801 with PTI-808 or Symdeko **(enrollment closed)**
2. PTI-808-01: Use of PTI-808 alone and in combination with PTI-801 and PTI-428 in patients with two copies of the F508del mutation **(recruiting ages 18+)**
3. VX17-659-105: VX-659 Combination Therapy, 1 or 2 copies of DeltaF508 **(enrollment closed)**
4. VX18-561-101: VX-561 (modified ivacaftor) in patients with a gating mutation **(recruiting ages 18+)**
5. VX18-445-104: VX-445 Combination Therapy in patients with one F508del mutation and a gating or residual function mutation **(recruiting ages 12+)**
6. VX18-445-110: open-label extension for participants in the VX18-445-104 study
7. VX18-445-113: open-label extension for participants in the VX17-659-105 study

## Observational Studies:

1. SIMPLIFY: removing hypertonic saline and/or Pulmozyme therapies on patients taking Trikafta **(enrollment not yet open)**
2. CHEC-OB-17: CFTR Modulated Changes in Sweat Chloride and Outcomes- for patients currently taking an FDA-approved CFTR modulator **(recruiting all ages)**
3. PICC: evaluating the factors influencing PICC line problems during treatment of CF exacerbations with IV antibiotics **(recruiting ages 6+)**
4. NTM-OB-17: Evaluation of a standardized approach to diagnosis (PREDICT) and treatment (PATIENCE) of nontuberculous mycobacteria (NTM) **(recruiting ages 6+)**
5. DESIGN CF Phase II: Developing e-Health Systems to Improve Growth and Nutrition in CF **(recruiting parents of CF patients ages 3-12)**
6. PROMISE: evaluating the effects of CFTR modulators on airway inflammation and microbiology **(recruiting ages 12+)**
7. GOAL-e²: G551D Observational Study – Expanded to Additional Genotypes and Extended for Long Term Follow-Up **(enrollment closed)**

# Trikafta™: *What Is All the Excitement About?*

By Amy Filbrun, MD, Pediatric Program Associate Director


Drew holding his first box of Trikafta™

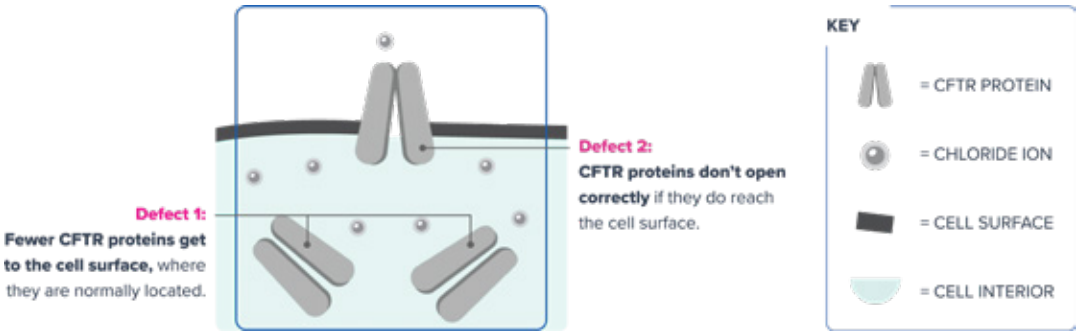



Figure 1; Trikafta.com/how-Trikafta-works

Most of you have probably heard about the newest modulator therapy for patients with cystic fibrosis (CF) who have at least one copy of the F508del mutation and are 12 years or older.

## What is Trikafta™?

Trikafta™ is the trade name for elexacaftor + tezacaftor + ivacaftor, or a "triple-combination" therapy. It is made to help correct the function of the cystic fibrosis transmembrane conductance regulator (CFTR) protein, which pumps chloride across the membrane of CF cells in the lungs. The F508del mutation causes two problems with the CFTR protein (see figure 1). The protein does not fold properly in order to be able to get to the cell surface, and the protein that does make it to the cell surface does not "turn on" or open the chanel at the cell surface properly. Two of the medications in Trikafta™, elexacaftor and tezacaftor, are called correctors, because they fix the protein so it can fold and reach the cell surface. Ivacaftor is called a potentiator, because once the protein is at the surface, it helps to open the channel and allow chloride (and sodium) to flow in and out of the cell.

## What are the benefits?

Two major phase three studies tested how safe and effective Trikafta™ is in people 12 and older with CF; one in people with two copies of F508del and one in people with one copy with another disease causing mutation. The main results of these studies was a significant improvement in lung function (14% increase in forced expiratory volume in one second (FEV1) in patients with one copy of the F508del mutation, and a 10% increase in FEV1 in those with two copies compared to placebo). Other significant improvements included improvement in CF respiratory symptom score and decrease in sweat chloride. These effects were seen across the 24 weeks of the study. In people with a single copy of F508del, there was also a decrease in pulmonary exacerbations and an increase in body mass index (BMI).

## Are there side effects?

One of the more serious side effects is elevated liver enzymes, which can be a sign of liver injury. You will need to have your liver function measured before starting Trikafta™, every three months for the first year, then yearly after that. Another potential serious side effect is the development of cataracts (abnormality in the lens of the eye), which can affect vision. This was most likely in younger patients compared to adults. You should have an eye exam before starting Trikafta™, and regularly while on therapy. Some of the other less serious, but more common side effects include: headache, upper respiratory tract infection, abdominal pain, diarrhea and rash. You should always notify your doctor if you have a concern about possible side effects. Trikafta™ can have interactions with other medications, and you should review your medications, including over the counter supplements, with your doctor before starting Trikafta™. You also need to avoid food or drink that contains grapefruit while taking Trikafta™.

## Can I stop my other medications?

Even though Trikafta™ leads to improvement in lung function, BMI, etc., significant damage that has already occurred in various organs, such as the lungs and pancreas, is unlikely to be repaired. Therefore, it is important to continue to take all your medications and do your routine treatments. You should talk with your doctor as you see how your body responds to treatment with Trikafta™ to see if there are any treatments that can be stopped over time. The CF Foundation will be funding a study called SIMPLIFY to see the effects of stopping certain treatments for a few weeks on lung function in people who are taking Trikafta™. We will all be learning this together over time. Our center is participating in this study so we will be looking for your help in the recruitment.

If you believe you qualify for Trikafta™, and your doctor has not yet spoken with you about starting it, please feel free to speak with your doctor to discuss if this is a good option for you. Visit Trikafta.com if you would like more information.

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