



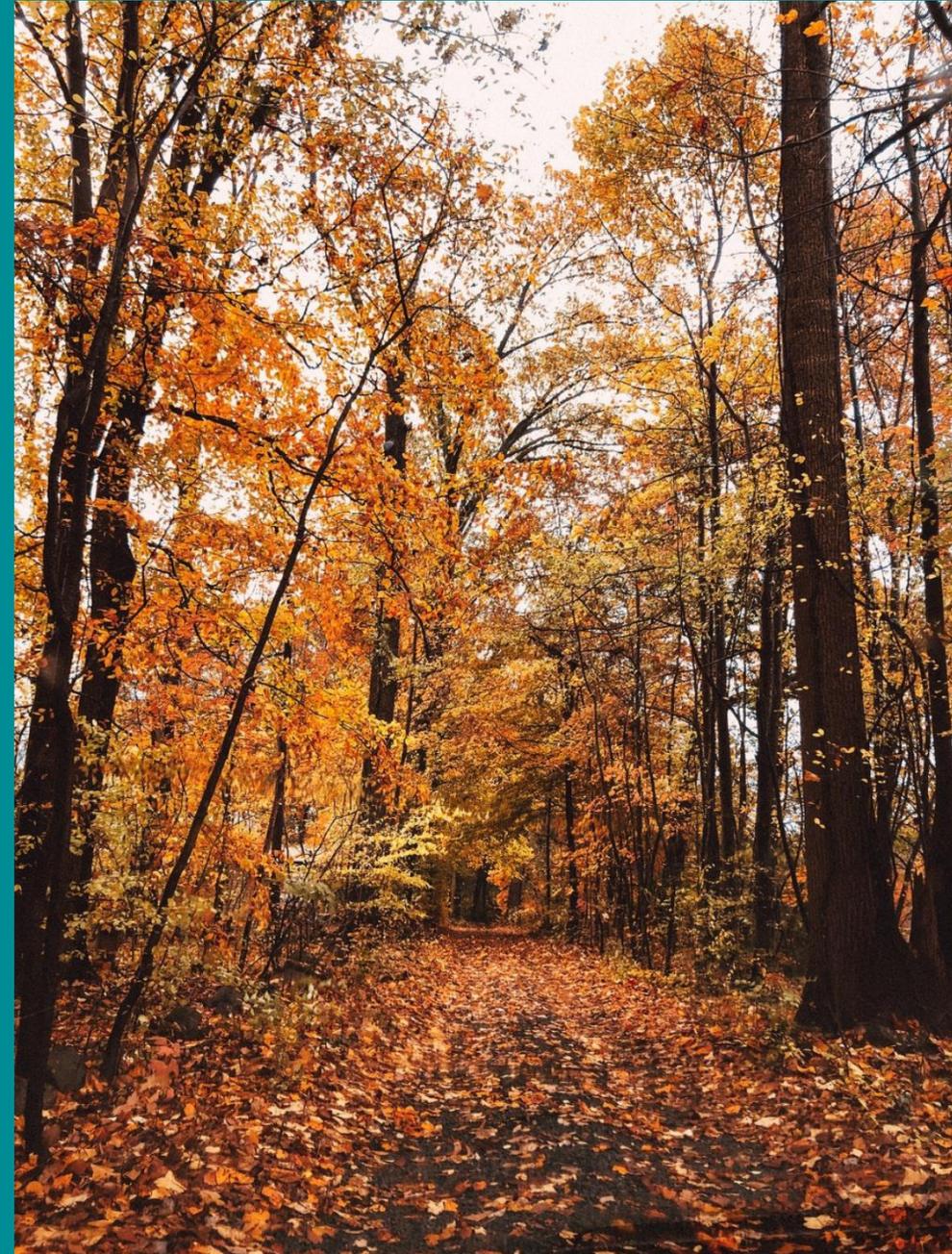
Atrium Health
Levine Children's

NACFC and Modulator Update 2021

Center & Program Director:
Dennis E Schellhase, MD

What's new from NACFC and with CFTR modulators?

- NACFC surprises
- What else is new
- Our presentations
- Modulators are still game changers



- **Diagnosis of CF** is not always straightforward
 - **CF** = 2 disease-causing mutations, SwCl \geq 60 mmol/L, > 1 manifestation of CF
 - **CRMS or CFSPID** = NBS positive: 1 disease-causing mutation and/or 1 mutation of unclear significance, SwCl 30-59 mmol/L, no manifestations of CF
 - **CFTR-RD** = no mutations or 1 disease-causing mutation and/or 1 mutation of unclear significance, SwCl \geq 30 mmol/L, only 1 manifestation of CF
 - Positive or indeterminate sweat test with normal genetics and no manifestations is not CF
 - Two positive sweat test with > 1 manifestation of CF and normal genetics is CF (at least in US)

- **Modulators** and liver function abnormalities
 - Modulators often bump up LFTs
 - Important to have a well-thought-out process (pathway) to evaluate LFT and bilirubin elevations
 - When benefits of modulator outweighs risks, equally important to have a well-thought-out process (pathway) to restart modulator after above evaluation

Something we will be working on in the next few months

- **Modulators and Nutrition Health**
 - Modulators improve several aspects of pancreatic and intestinal function
 - Starting modulators earlier in life may restore pancreatic function
 - May be increased risk of acute pancreatitis but not clear
 - Body composition should not just be assessed by BMI; patients on modulators may become overweight or obese; BMI > 85th percentile are not associated with increased lung function
 - CF Nutrition Guidelines particularly for pts on modulators are changing to age-appropriate individualized healthy diet, healthy fats, supplementing if needed with energy and/or protein-dense foods/supplements
 - Malnutrition remains bad!

• Interesting Demographics

- 15-20% of CF patients are *African, Latin or Asian-American*
CFF is listening to these communities and working on initiatives to decrease health disparities
- Median predicted survival of child born in 2020 with no new therapies is *59 years* (range 56-65 years)
- 57% of all CF patients are *18 years of age or older*
- For the first time ever, *FEV1 percent predicted is increasing* for all age groups and birth cohorts, most likely because of the introduction of Trikafta
- There are almost *1300 individuals with CF who have advanced lung disease* (85 children, ~1200 adults)

Therapies in Development:

- **Restoring CFTR Function**

- New corrector and potentiator modulators
- Small molecules to correct nonsense and splicing mutations
- CFTR-encoded mRNA delivered to lung cells
- Gene editing: CRISPR, insertion of superexons
- mRNA and gene delivery to lung cells

} Many technical challenges

- **Anti-Infective**

- New inhaled medications
- Novel therapies

- **Anti-inflammatory**

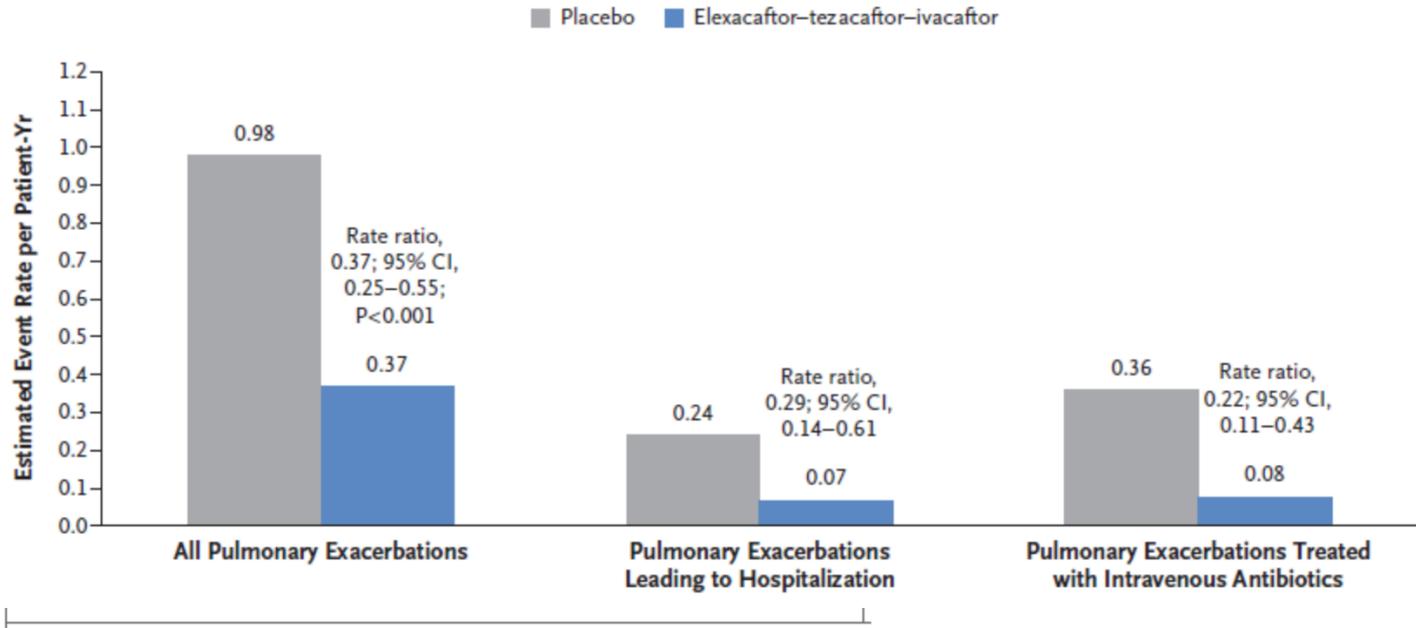
- Blocking neutrophil elastase and other mediators of inflammation

- **Nutritional-GI**

- Non-animal derived pancreatic enzyme

Two Poster Presentations:

- Beth Jorgensen, LSCW: Creating a virtual CF support group for adolescents during the COVID-19 pandemic. Poster #274
- Andrea Westmoreland, CCLS III: Implementation of “Pick Me Up” basket for CF patients and their families to decrease boredom and improve coping during extended hospitalizations. Poster #132



function & outcomes

Sustained significant improvement of 14.3% in FEV1 percent predicted
 NEJM 2019; Nov 7

Significant reduction in pul exacerbations, hospitalizations, IV antibiotic usage
 NEJM 2019; Nov 7

Trikafta rarely has concerning side effects:

- **Headaches**

- 17% active vs 15% in placebo arm
- Tx: flip am/pm Trikafta doses, OTC pain relievers, dose reduction
- Usually resolves after 7-14 days

- **Psychiatric and mental status changes**

- Not reported in clinical trials
- Tx: dose reduction with titration vs drug interruption, MH professional

- **Liver injury**

- 11% active vs 4% placebo arm
- Can be serious, at least one case report of pt needing liver transplant
- Pathway for evaluation, assessing benefits vs risks and restarting modulator recommended, should include Liver Specialist

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