ASHP Best Practices Award

Making CF-MAGIC: Creation of a genomics-based clinical decision support program improves time to initiation and optimization of CFTR modulator therapies

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Authors of this presentation disclose the following relationships with commercial interests related to the subject of this poster:

Authors have nothing to disclose.

Introduction

UNC Health – Medical Center

- 850 bed facility, serving more than 37,000 patients per year; not-for profit medical system
  - North Carolina Memorial Hospital
  - North Carolina Children's Hospital
  - North Carolina Neurosciences Hospital
  - North Carolina Woman's Hospital
  - North Carolina Cancer Hospital
  - North Carolina Surgical Hospital

Department of Pharmacy

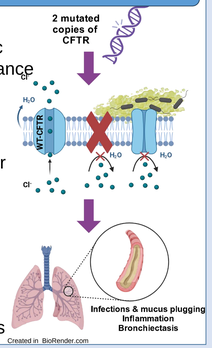
- Inpatient medicine, oncology, surgical, and pediatric services
- Outpatient clinics as Clinical Pharmacist Practitioners (CPPs)
- Emergency Medicine
- Retail/Outpatient Pharmacies
- URAC-accredited Specialty Pharmacy

Pediatric Cystic Fibrosis (CF) Center

- Cystic Fibrosis Foundation-accredited care center
- Multidisciplinary team including physicians, pharmacists, nurses, social workers, respiratory therapists, dietitians, and psychologist

Cystic Fibrosis

- A life-shortening genetic disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene
- CFTR encodes for a chloride channel, and in people with CF (PwCF), CFTR is either absent or does not function appropriately
- This disrupts the usual osmotic gradient, resulting in viscous secretions impacting multiple organ systems
- There are over 1,900 identified disease-causing CFTR mutations



CFTR Modulators

- Prior medications only treated **SYMPTOMS** of CF
- CFTR modulators (CFTRm) correct the underlying defective CFTR protein
- Eligibility is based on mutation type and age
- CFTR modulators have dramatically altered the CF disease course
- Median life expectancy is now **61 years**
- Earlier initiation of CFTRm results in increased and preserved lung function, and potential reversal or delay of extrapulmonary complications of CF

Ivacaftor 1st approved in 2012. Now approved down to 1 month of age for 97 mutations	**Lumacaftor/Ivacaftor** 1st approved in 2015. Now approved down to 1 year of age with two copies of F508del
Tezacaftor/Ivacaftor 1st approved in 2018. Now approved down to 6 years of age for 128 mutations	**Elexacaftor/ Tezacaftor/Ivacaftor** 1st approved in 2019. Now approved down to 2 years of age for 178 mutations

Description of the Program

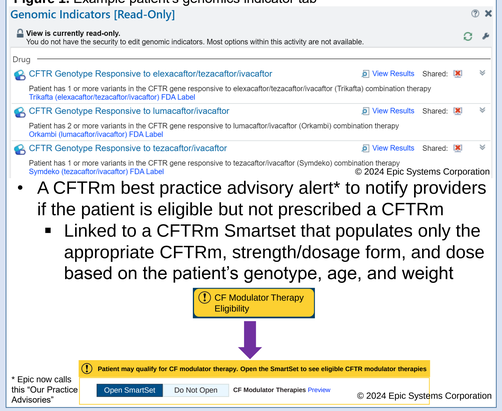
Goals of CF- MAGIC (CFTR ModulAtor PharmacoGenomICs)

1) Streamline the care of people with CF (PwCF)
2) Readily identify PwCF with qualifying CFTR mutations to ensure timely initiation of CFTRms
3) Revolutionize proactive decision support to expediently identify pediatric PwCF requiring dose optimization based on age and/or weight

PHASE I: The Build

- Genomic indicators were programmed for the CFTRms
  - Custom flags that denote which CFTRm(s) a patient is eligible for based on their CFTR variants
  - Foundational for additional clinical decision support (CDS) in the electronic health record (EHR)

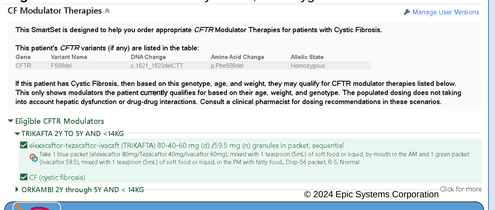
Figure 1. Example patient's genomics indicator tab



- A CFTRm best practice advisory alert* to notify providers if the patient is eligible but not prescribed a CFTRm
  - Linked to a CFTRm Smartset that populates only the appropriate CFTRm, strength/dosage form, and dose based on the patient's genotype, age, and weight

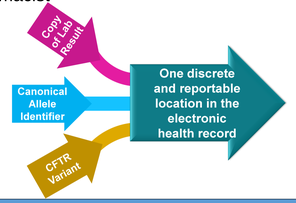
* Epic now calls this "Our Practice Advisories"

Figure 2. SmartSet order for a 4-year-old, homozygous F508del PwCF



PHASE II: The Input

- Entered each patient's individual CFTR variants into the electronic health record's genomics module
- Each patient's genomic indicator flags were validated by the pharmacist



PHASE III: The Magic

- A biweekly, prospective report was created, notifying providers of:
  - PwCF with upcoming CFTRm eligibility based on age
    - Within 3 months of their qualifying birthday
  - Pediatric PwCF on the cusp of dose adjustment based on age or weight
    - Within 1 week of their birthday or within 1 kg of dose adjustment weight threshold, respectively

Experience with the Program

- CFTR variants for 239 patients were entered

Table 1. CFTR Variant Entry Characteristics

Prior efforts to maintain a comprehensive patient list including each patient's CFTR variants	
Number of patients with CFTR variants listed in their problem list*, n (%)	180 (75)
Number correct, n (%)	172 (95.5)
Number incorrect, n (%)	5 (2.8)†
Number of patients missing from pharmacist maintained list, n (%)	5 (2.1%)
Baseline CFTR Source Laboratory Results	
Patients with no CFTR genotype lab result found within EHR, n (%)	59 (25)
CFTR genotype lab results found on external computer drive, n (%)	40 (16.7)
CFTR genotype lab results obtained by contacting our state's NBS lab, n (%)	6 (10.2)‡
CFTR genotype lab results obtained by contacting parents or external institution/ lab, n (%)	5 (8.5)
Unable to locate CFTR genotype results, n (%)	4 (1.7)
Patients with CFTR genotype lab found within the EHR's Media tab, n (%)	176 (75)
Results labeled in a readily identifiable manner, n (%)	47 (27)
Results not labeled in a readily identifiable manner, n (%)	88 (50)
Results found in other scanned notes, n (%)	16 (9.1)
Results found elsewhere in the EHR, n (%)	25 (14.2)
Patients with CFTR genotypes successfully entered into genomics module with corresponding lab result as a result of CF-MAGIC Phase 1	234 (98%)^

NBS = newborn screening; *From a prior quality improvement project; †Results not found for 4 patients to confirm accuracy of variants listed in problem list; ‡Requested results for 10 patients; only 6 were available
^Awaiting repeat CFTR genotyping or obtaining a copy of original CFTR genotype result for 5 patients

Program Validation and Results

- When compared to historical CFTRm reports for new approvals/label expansion, CF-MAGIC accurately identified all PwCF with CFTRm-eligible mutations
  - CF-MAGIC also identified a patient that was missed on the prior report used to identify ETI-eligible PwCF
- Historically, 24% of LUM/IVA-eligible and 63% of ETI-eligible PwCF had their 1st prescription sent within 1 month of the FDA approval date.
  - 48.4% and 73% of LUM/IVA-eligible and ETI-eligible PwCF had a first prescription sent in within 1 month of their eligible birthday. Three PwCF's first ETI prescription was delayed due to a missed birthday
  - Mean time to dose adjustments based on weight was 1.4 months for LUM/IVA and 5.24 months for ETI

Table 3. Prospective Reporting Results

CF-MAGIC Identified patients to date	n
Patients with upcoming eligibility for a modulator that were previously not identified	3 (ETI)
Patients with a missed weight adjustment	1 (LUM/IVA)
Patients receiving the improper dosage form for age	3 (ETI)
Patients with upcoming weight adjustment	11 (ETI)

ETI = elexacaftor/tezacaftor/ivacaftor; LUM/IVA = lumacaftor/ivacaftor

Discussion / Conclusion

CF-MAGIC is a novel utilization of CDS in the EHR that optimizes care of PwCF

- With an expected ETI label expansion in November 2024 and a new CFTR modulator coming to market by January 2025, CF-MAGIC will be incredibly useful in identifying PwCF who will newly qualify for CFTRm therapy
  - The adult UNC CF program is implementing CF-MAGIC in anticipation of these approvals

CF- MAGIC is a powerful tool to help pharmacists navigate the ever-evolving CF landscape, and care for their patients more efficiently and effectively.

Acknowledgements

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