

forum 2024



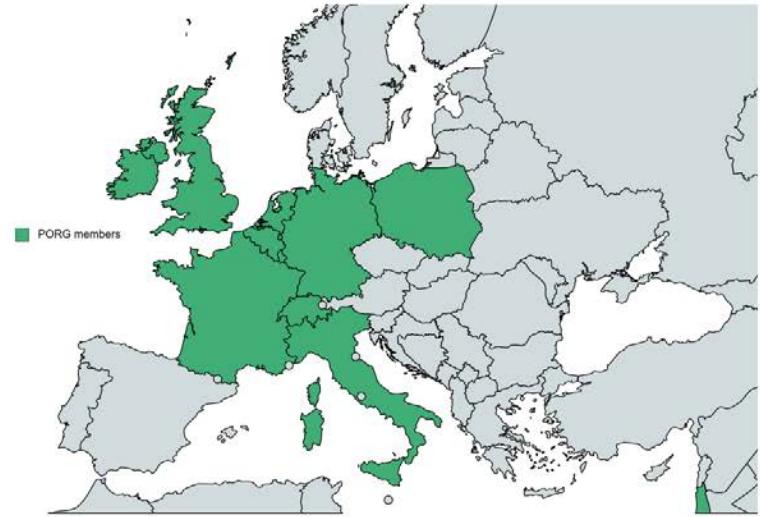
Aggiornamenti dagli ultimi Congressi scientifici internazionali

# Giuseppe F. Parisi

Pediatra

UOC Broncopneumologia Pediatrica e Fibrosi Cistica  
AOU Policlinico – San Marco – Catania  
Direttore: Prof. S. Leonardi

# Patient Organisations Research Group (PORG)



- L'obiettivo del PORG è quello di migliorare le partnership tra le organizzazioni europee associate, al fine di espandere la rete europea di ricerca sulla FC e accelerare l'accesso a nuovi farmaci per le persone con FC attraverso la ricerca.
- Il PORG conta attualmente 11 membri, tra cui Belgio, Francia, Germania, Irlanda, Israele, Italia, Lussemburgo, Paesi Bassi, Polonia, Svizzera e Regno Unito.



## Patient Organisations Research Group (PORG)

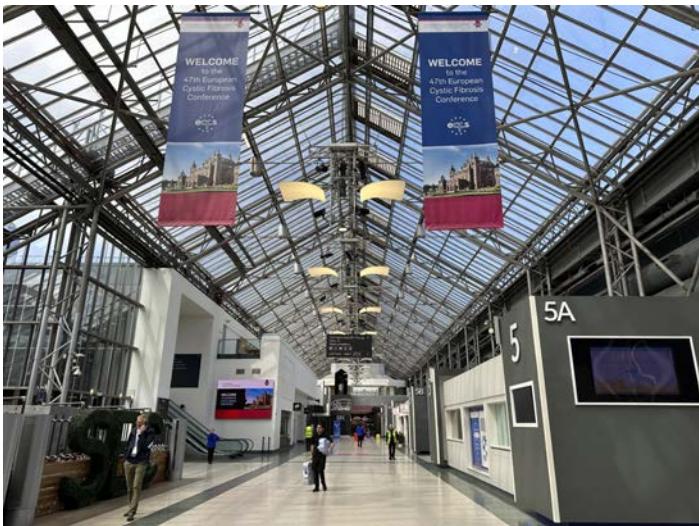
- Priorità di ricerca secondo i pazienti
- Collaborazione con ECFS Patient Registry
- Collaborazione con ECFS Clinical Trials Network
- Organizzazione dell'European CF Young Investigators Meeting (EYIM)
- Organizzazione dell'incontro pre-conferenza prima della ECFS Basic Science Conference
- Supporto finanziario (insieme a ECFS) di ricercatori postdoc

forum 2024



# 47th EUROPEAN CYSTIC FIBROSIS CONFERENCE

5 – 8 JUNE 2024 | GLASGOW, UNITED KINGDOM



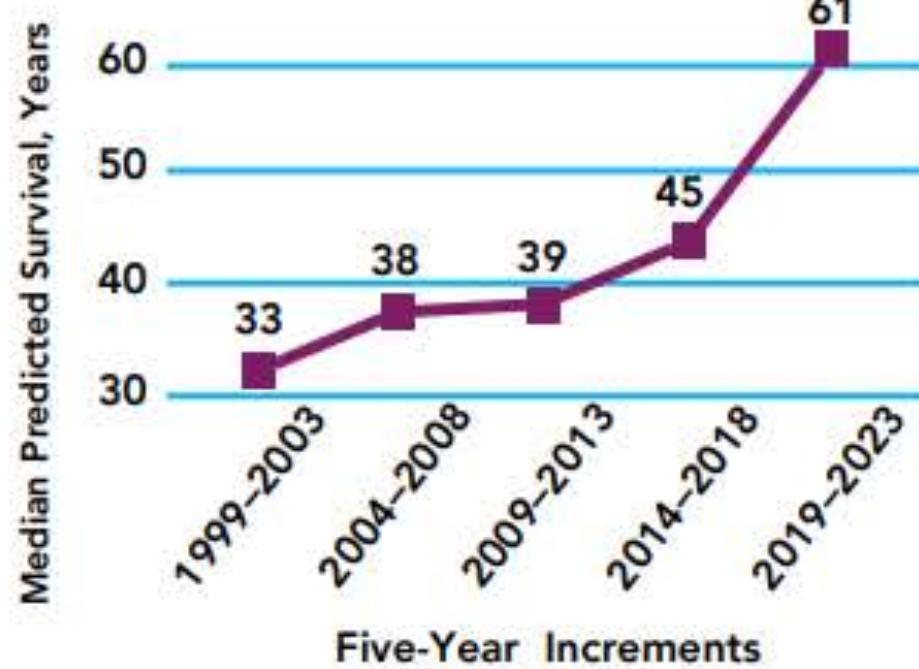
2023

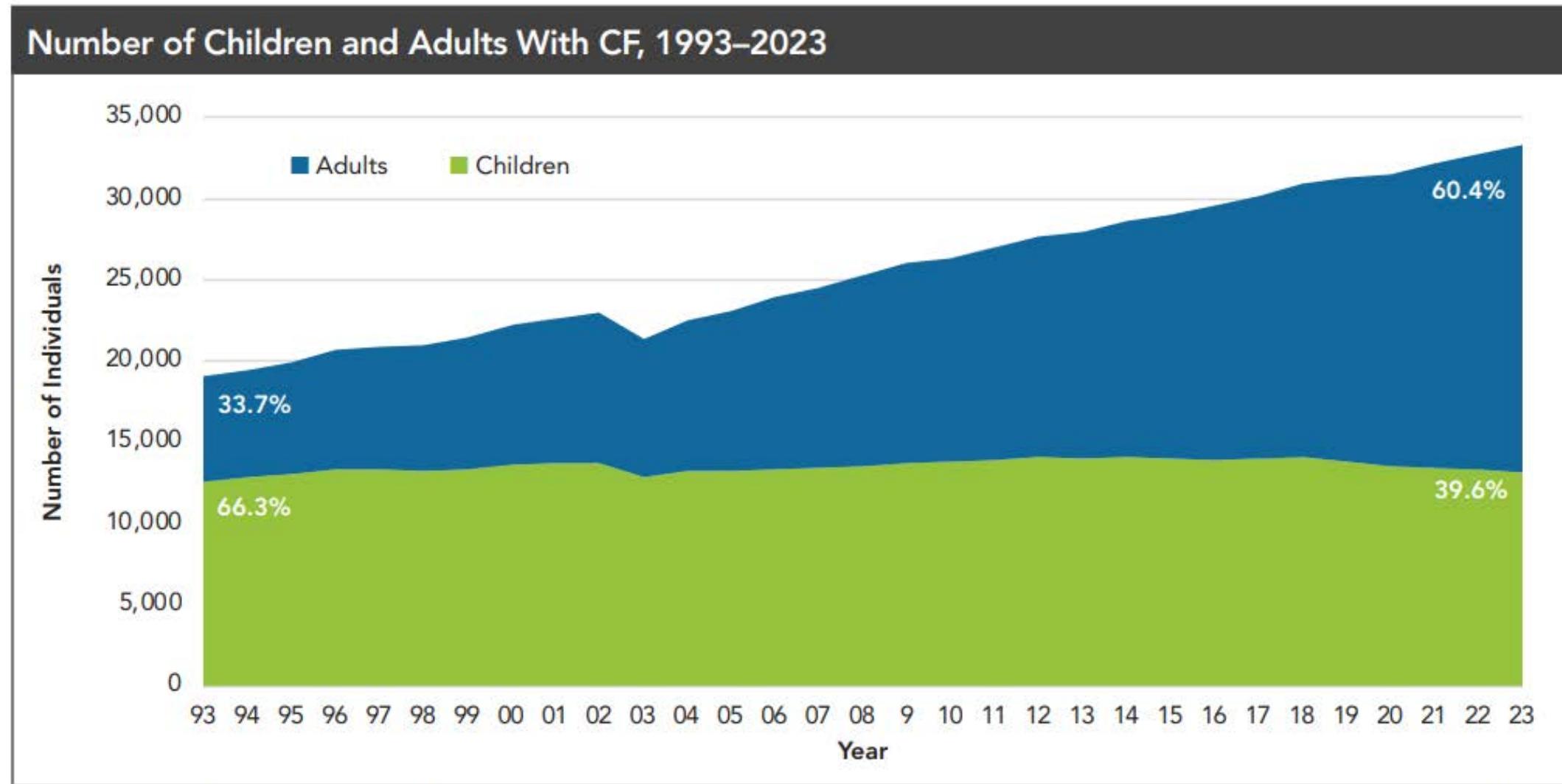
CYSTIC FIBROSIS FOUNDATION  
PATIENT REGISTRY HIGHLIGHTS

## SURVIVAL

61  
YEARS  
2019-2023

Among people with CF born 2019-2023, half are predicted to live to 61+ years. However, this does not reflect individual variability. The median survival is lower for those ineligible for modulators by possibly over a decade.





The decrease in the number of individuals reported in 2003 is due to a delay in obtaining informed consent forms before the close of the calendar year at some CF Care Centers.

# Transizione del paziente con fibrosi cistica

## Transition in cystic fibrosis

Giuseppe Fabio Parisi<sup>1</sup>, Salvatore Leonardi<sup>1</sup>, Manuela Goia<sup>2</sup>, Elisabetta Bignamini<sup>2</sup>

<sup>1</sup> UOC Broncopneumologia Pediatrica e Fibrosi Cistica, Presidio Ospedaliero San Marco, Azienda Ospedaliera Universitaria Policlinico di Catania, Catania; <sup>2</sup> SC Pneumologica Pediatrica, Centro Regionale di Riferimento: Fibrosi Cistica Piemonte-Valle d'Aosta, Insufficienza respiratoria cronica in età evolutiva, OIRM Città della Salute e della Scienza di Torino, Torino

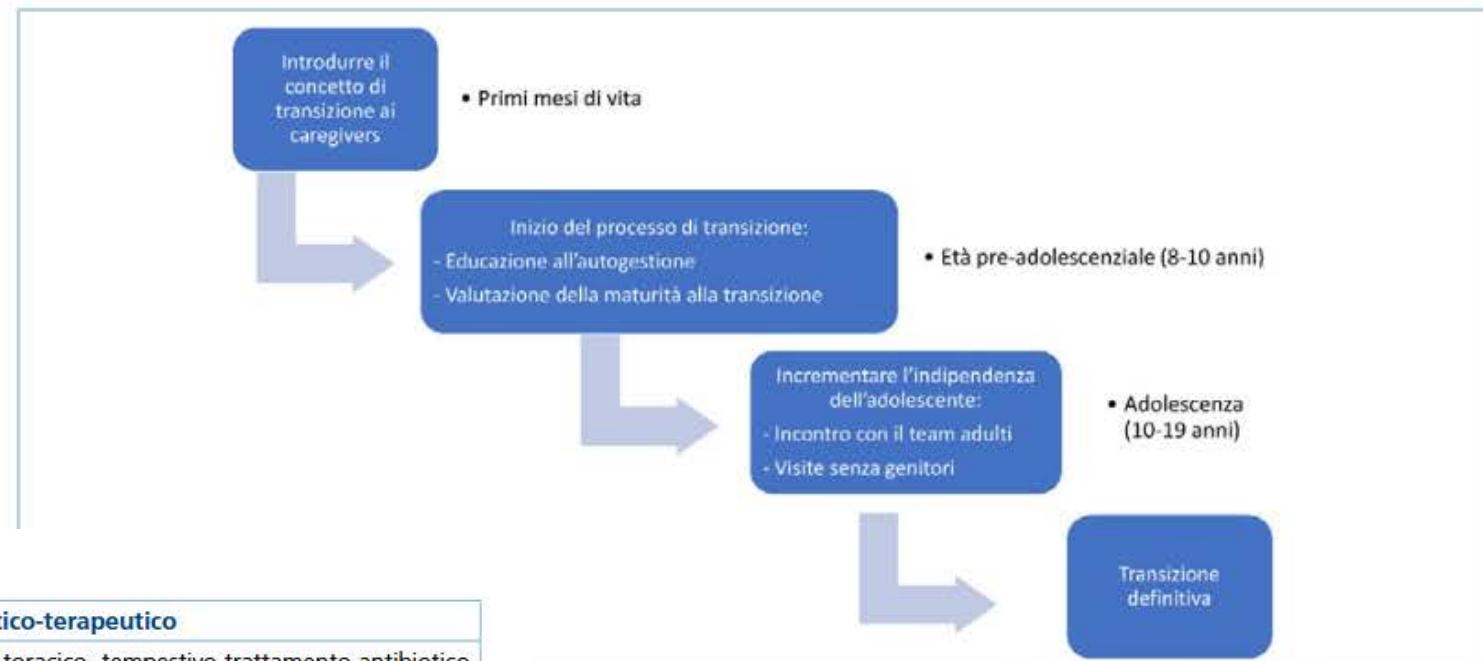


Tabella I. Caratteristiche cliniche del paziente in fase di transizione.

Presentazione clinica	Work-up diagnostico-terapeutico
Riacutizzazione respiratoria	Valutazione clinica, laboratoristica e di <i>imaging</i> toracico, tempestivo trattamento antibiotico con implementazione di quello mucolitico e fisioterapico
Emottisi	Valutazione se moderata, grave o recidivante, eventuale indicazione a embolizzazione delle arterie bronchiali
Pneumotorace	Eventuale posizionamento di drenaggio pleurico in base all'entità
Insufficienza respiratoria cronica	Prescrizione di O <sub>2</sub> terapia cronica ed eventuale utilizzo di NIV notturna in presenza di insufficienza respiratoria ipercapnica
Poliposi nasale/sinusite	Controlli periodici ORL/ <i>imaging</i> cranio-sinusale per eventuale intervento di chirurgia endoscopica nasale (FESS)
Epatopatia/pancreatiti ricorrenti/DIOS	Controlli gastroenterologici periodici e monitoraggio ecografico/doppler epatico e degli esami ematologici di funzionalità epatica
Malassorbimento	Controllo digestivo feci, vitamine liposolubili e visite nutrizionali
Diabete	Screening periodico con curva da carico di glucosio e, se alterata, valutazione diabetologica per impostazione di eventuale terapia insulinica
Osteoporosi	Controllo periodico delle vitamine liposolubili, MOC e valutazione endocrinologica per terapia con bifosfonati oltre a supplementazione
Infertilità maschile	Counselling pre-concepcional per impostazione di eventuali tecniche di fecondazione assistita
Stato ansioso depressivo	Valutazione psichiatrica per terapia specifica antidepressiva

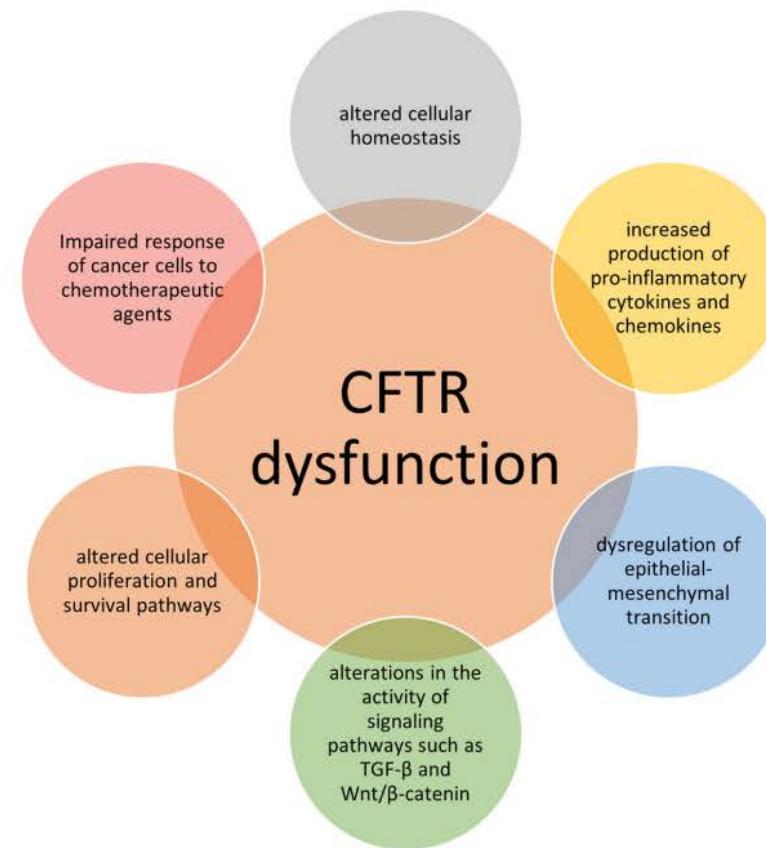
*Rassegna di Patologia dell'Apparato Respiratorio* 2023;38:166-173  
doi: 10.36166/2531-4920-712

Review

## Cystic Fibrosis and Cancer: Unraveling the Complex Role of CFTR Gene in Cancer Susceptibility

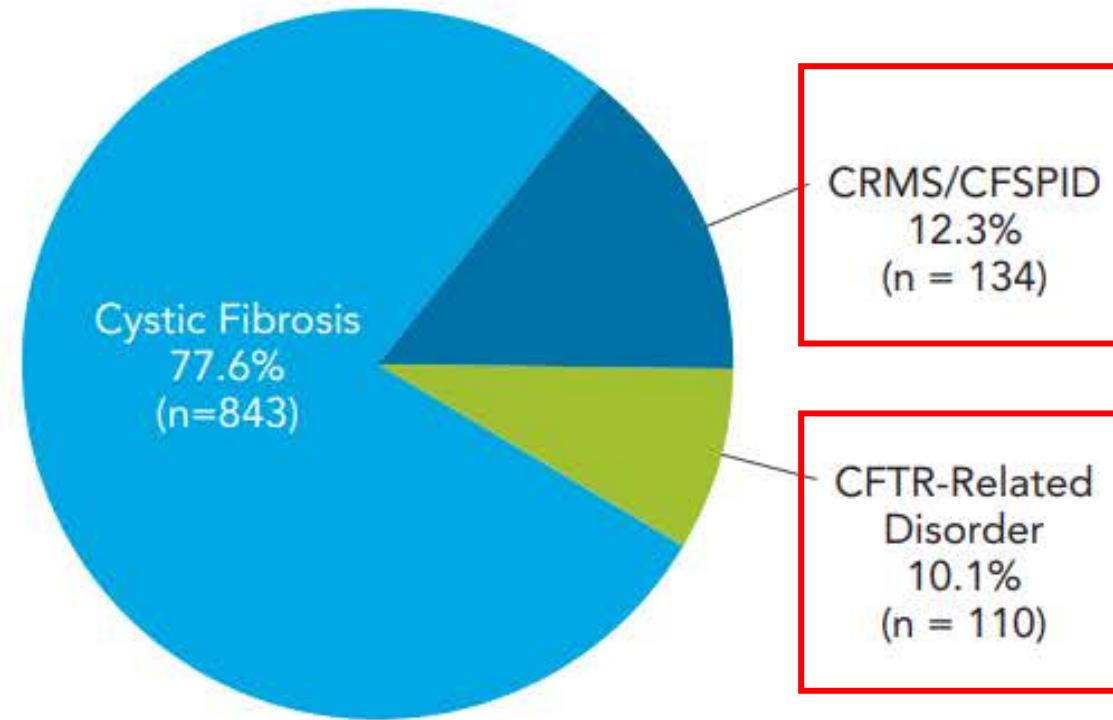
Giuseppe Fabio Parisi <sup>1,\*</sup>, Maria Papale <sup>1</sup>, Giulia Pecora <sup>1</sup>, Novella Rotolo <sup>1</sup>, Sara Manti <sup>2</sup>, Giovanna Russo <sup>3</sup> and Salvatore Leonardi <sup>1</sup>

Pancreatic cancer	<ul style="list-style-type: none"> <li>Chronic inflammation</li> <li>Altered bile flow</li> <li>Oxidative stress</li> </ul>	5–10
Liver cancer	<ul style="list-style-type: none"> <li>Chronic inflammation</li> <li>Altered bile flow</li> <li>Impaired liver regeneration</li> <li>Genetic variations in modifier genes, such as the Solute Carrier Organic Anion Transporter (SLCO) family</li> </ul>	1.5–2
Intestinal cancers	<ul style="list-style-type: none"> <li>Chronic inflammation</li> <li>Oxidative stress</li> <li>Altered composition of intestinal microbiota</li> <li>Genetic polymorphisms</li> <li>Implications of tumor suppressor genes</li> </ul>	6
Breast cancer	Hormonal imbalances, such as increased estrogen levels	not well-established
Lung cancer	Chronic inflammation Altered mucociliary clearance	not well-established



**Figure 1.** CFTR dysfunction and mechanisms related to predisposition to cancers. CFTR dysfunction in CF triggers chronic inflammation, impaired DNA repair, and hormonal imbalances. These mechanisms collectively predispose individuals to various cancers, highlighting the intricate interplay between CF and cancer susceptibility.

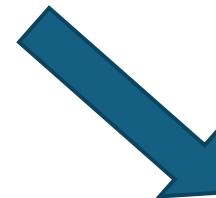
## CF, CRMS/CFSPID, and CFTR-Related Disorder New Diagnoses in 2023



# CFSPID

Cystic Fibrosis Screen Positive, Inconclusive Diagnosis

## Screening Neonatale Positivo



**Test del sudore negativo**  
(Cloro < 30 mmol/L)

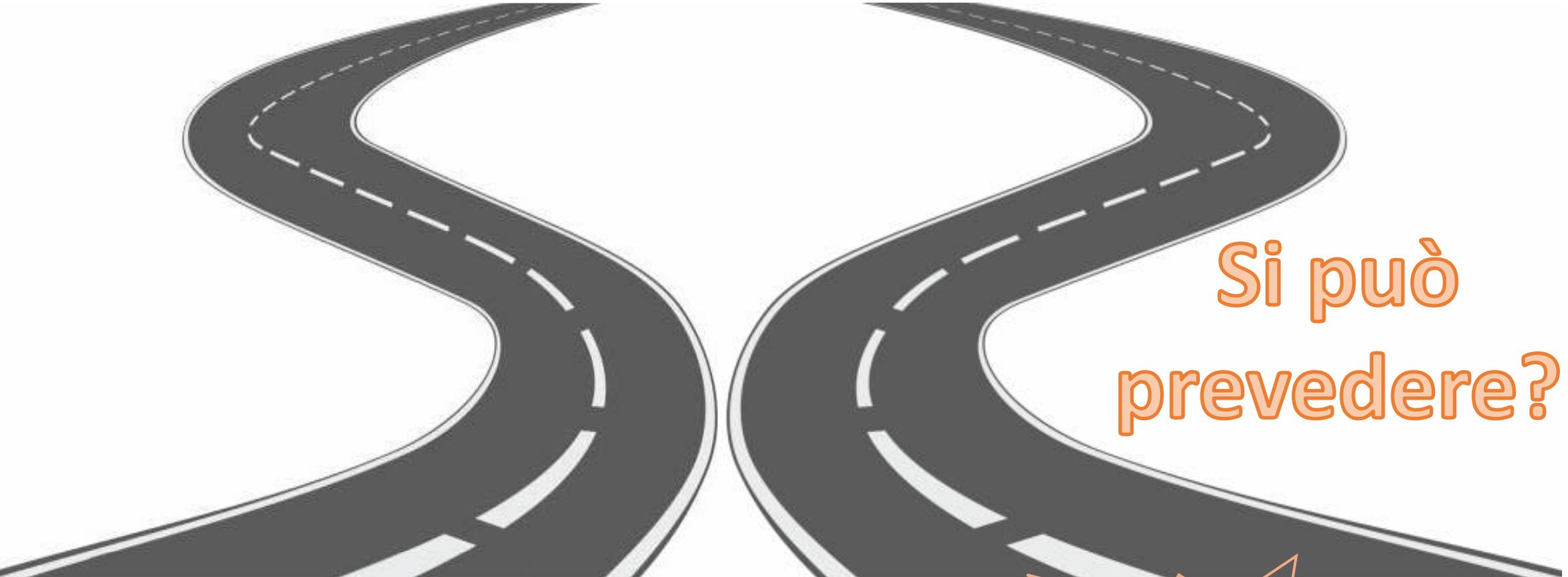
**2 mutazioni del CFTR,**  
di cui almeno una di significato  
patogenetico incerto

**Test del sudore dubbio**  
(Cloro 30 – 59 mmol/L)

**1 o nessuna mutazione  
del CFTR**

# CFSPID

forum 2024

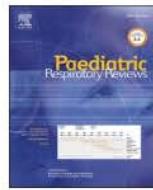
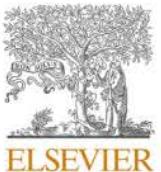


Si può  
prevedere?

A graphic of two grey asphalt roads with white dashed lines, curving from the left and right towards each other, eventually meeting at a central junction. This visual metaphor represents the convergence of different paths or perspectives.

# CFSPID





## Review

## Biochemical and genetic tools to predict the progression to Cystic Fibrosis in CRMS/CFSPID subjects: A systematic review



Vito Terlizzi<sup>a</sup>, Sara Manti<sup>b,\*</sup>, Federica D'Amico<sup>b</sup>, Giuseppe F. Parisi<sup>c</sup>, Elena Chiappini<sup>d,e</sup>,  
 Rita Padoan<sup>f</sup>

<sup>a</sup> Department of Pediatric Medicine, Meyer Children's Hospital IRCCS, Cystic Fibrosis Regional Reference Center, Florence, Italy

<sup>b</sup> Department of Human Pathology of Adult and Evolutive Age "Gaetano Barresi", University of Messina, Messina, Italy

<sup>c</sup> Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy

<sup>d</sup> Infectious Diseases Unit, Meyer Children's Hospital IRCCS, Florence, Italy

<sup>e</sup> Department of Health Sciences, University of Florence, Florence, Italy

<sup>f</sup> Italian Cystic Fibrosis Registry, Scientific Board, Rome, Italy

**Table 2**

Percentage of CFSPID > CF/CFSPID in the different populations.

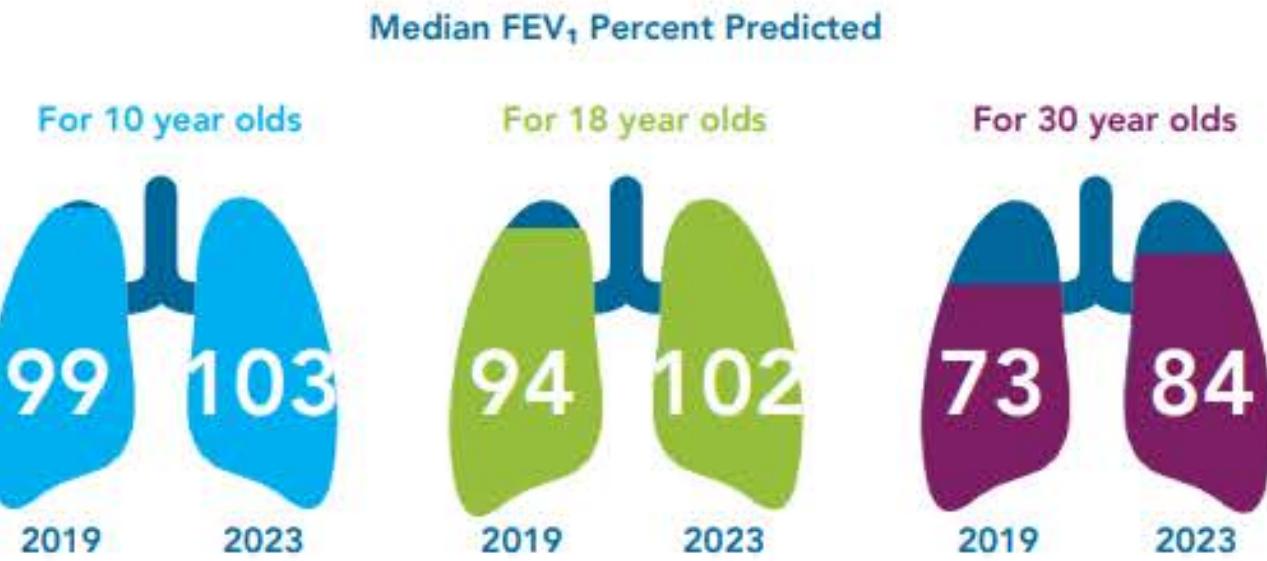
Authors	Year	CFSPID > CF/CFSPID	%	Ref.
Terlizzi V et al.	2021	18/336	5.3 %	[16]
Tosco A et al.	2022	6/58	10.3 %	[35]
Ooi CY et al.	2015	11/82	11.0 %	[25]
Ooi CY et al. <sup>§</sup>	2019	14/98	14.3 %	[26]
Gunnell MA et al.	2023	11/63	17.5 %	[34]
Salinas DB et al.	2022	12/59	20.3 %	[37]
Gonska T et al.	2021	24/115	21.0 %	[28]
Munck A et al.	2020	28/63	44.0 %	[30]
Groves T et al.	2015	14/29	48.0 %	[54]

<sup>§</sup> also includes patients from the same authors' 2015 paper.

## EDUCATIONAL AIM S

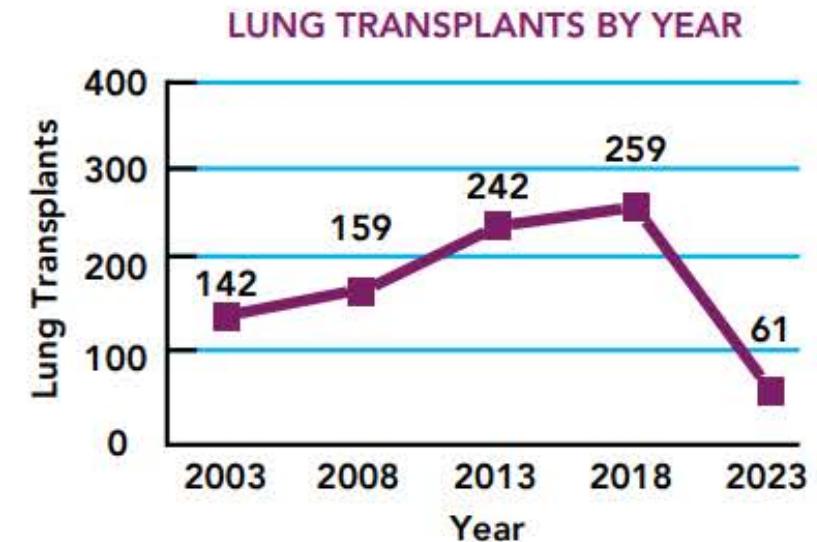
The reader will come to appreciate:

- An analysis of the characteristics of CFSPID individuals who evolve into CF.
- That the presence of one CF-causing CFTR variant, an initial sweat chloride (SC)  $\geq 40$  mmol/L or an increase of SC  $> 2.5$  mmol/L/year could allow identification of subjects at risk of progression to CF.
- That CFSPID individuals with a CF causing variant/VVCC genotype and first SC in the higher borderline range may require more frequent and prolonged clinical follow-up.



## TRANSPLANTATION

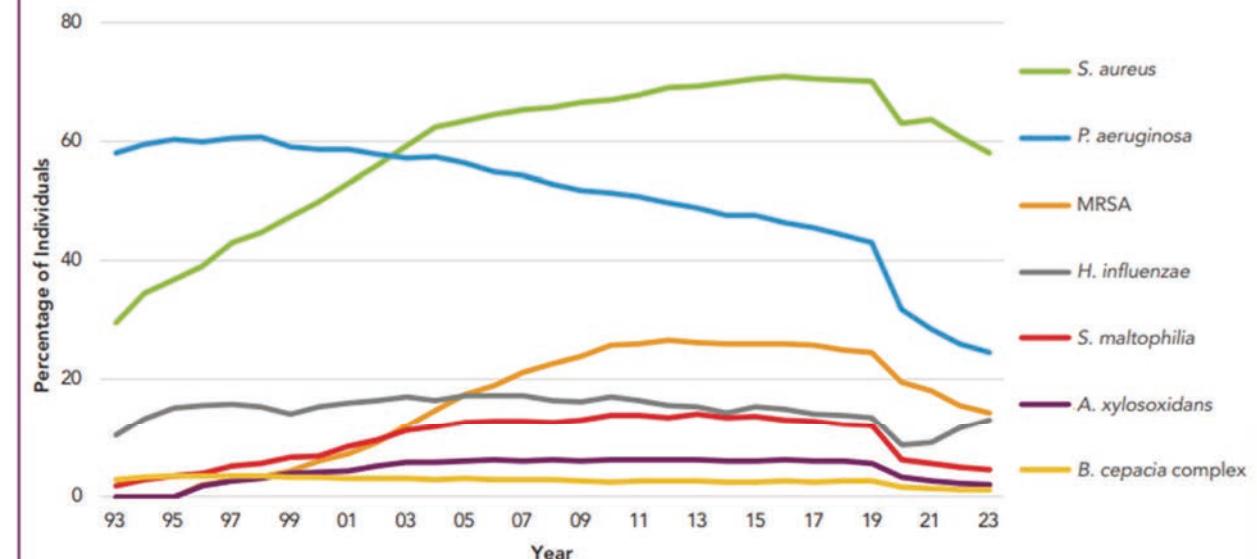
In the Registry, there has been a dramatic decrease in the number of lung transplants reported compared to the numbers prior to the adoption of elexacaftor/tezacaftor/ivacaftor. In 2023, there were 61 lung transplants reported.



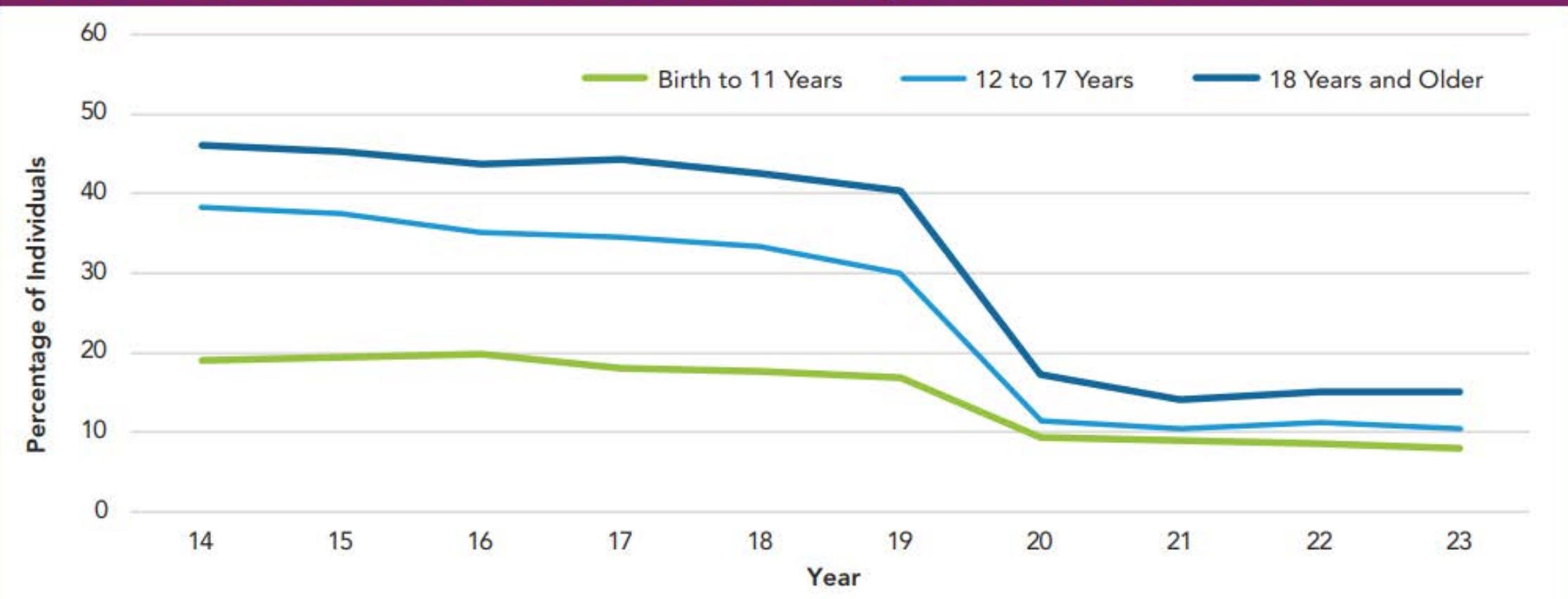
## MICROBIOLOGY

Bacteria	Percent With Infection	Median Age in Years at First Infection
 <i>Pseudomonas aeruginosa</i>	<b>25%</b>	<b>5</b>
 <i>Stenotrophomonas maltophilia</i>	<b>5%</b>	<b>9</b>
 <i>Methicillin-resistant Staphylococcus aureus</i>	<b>14%</b>	<b>10</b>
 <i>Achromobacter xylosoxidans</i>	<b>2%</b>	<b>14</b>
 <i>Burkholderia cepacia complex</i>	<b>1%</b>	<b>20</b>
 <i>Nontuberculous mycobacteria</i>	<b>10%</b>	<b>25</b>

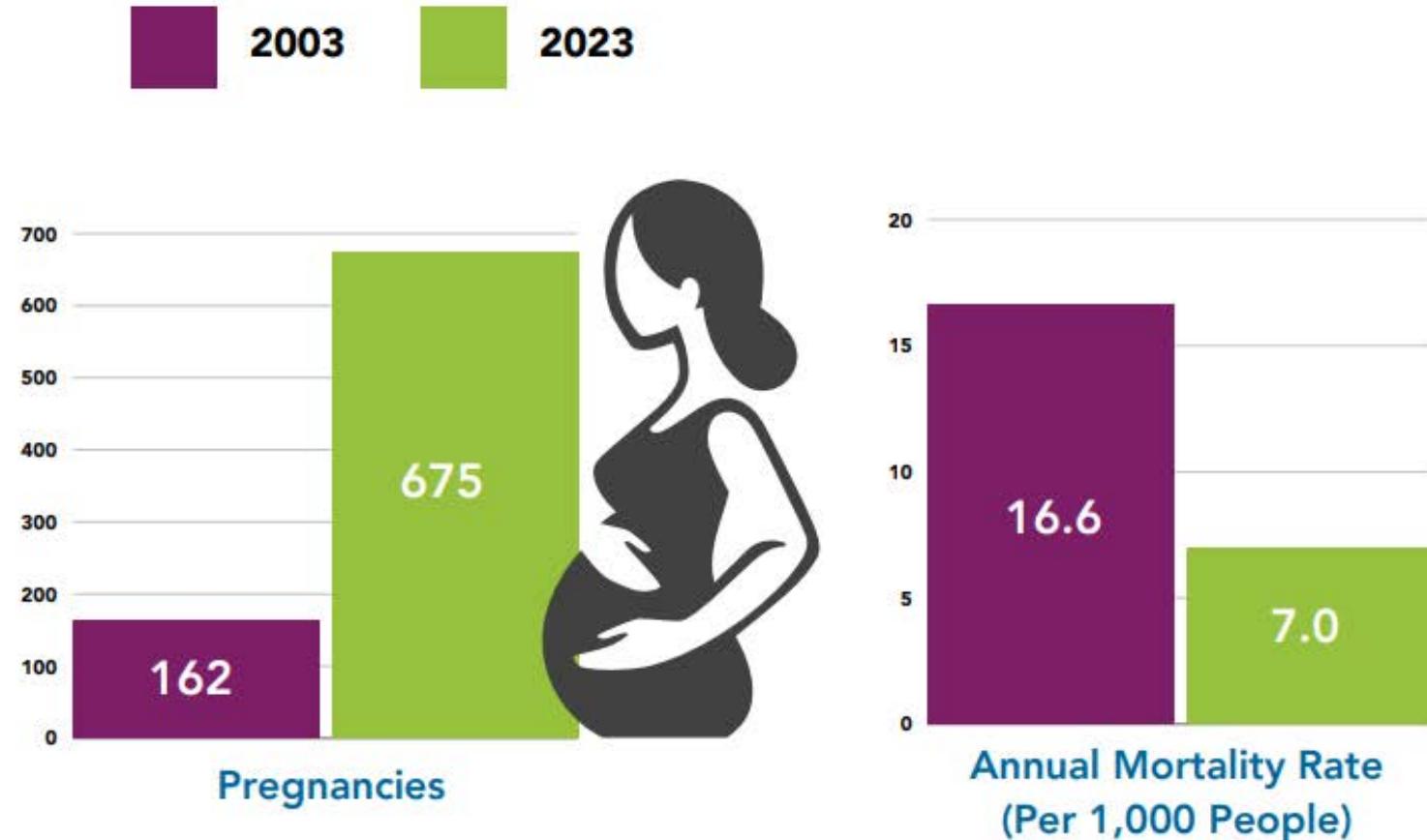
Prevalence of Respiratory Microorganisms, 1993–2023



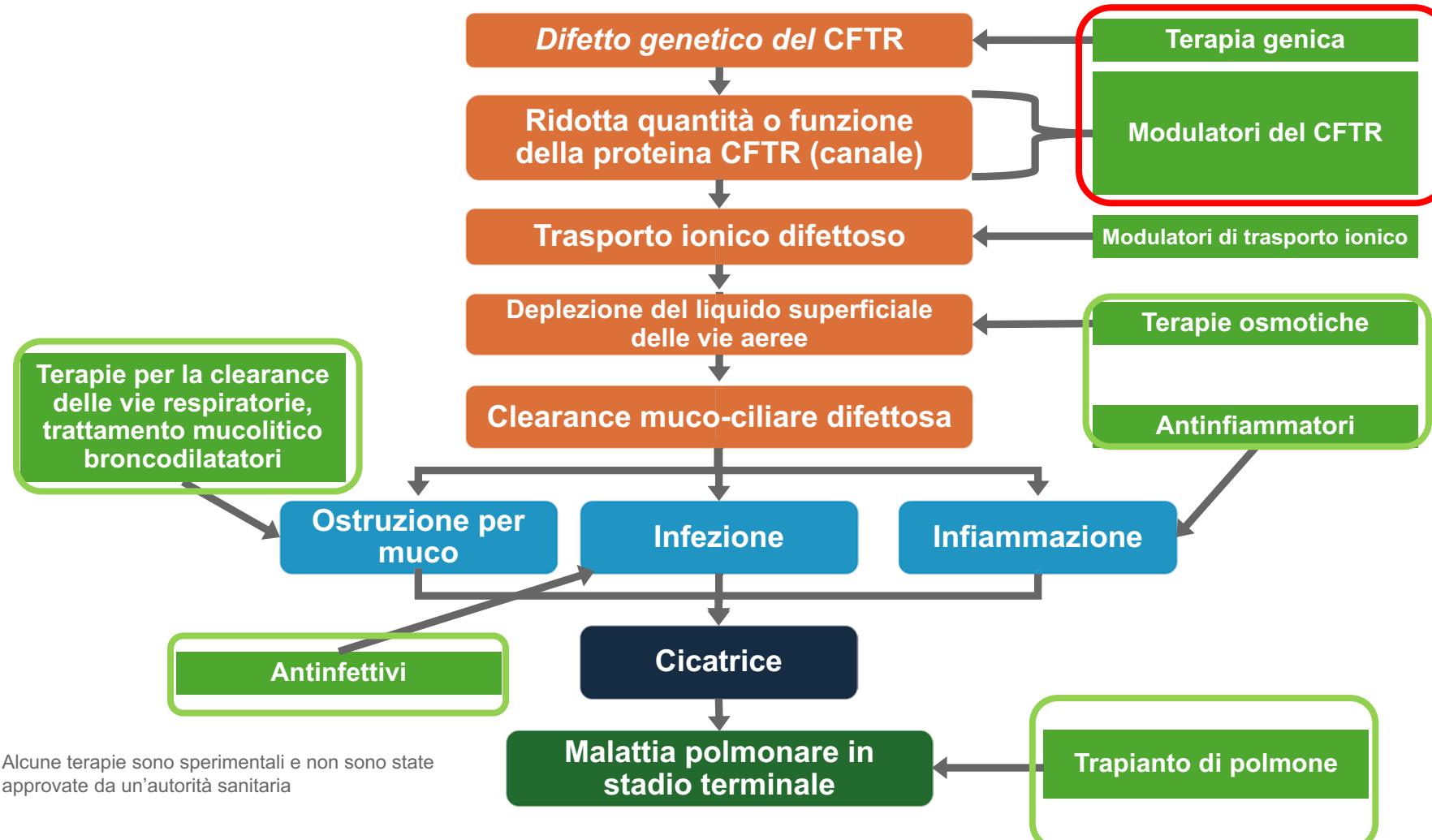
### Individuals Treated With IV Antibiotics for a Pulmonary Exacerbation, 2014–2023

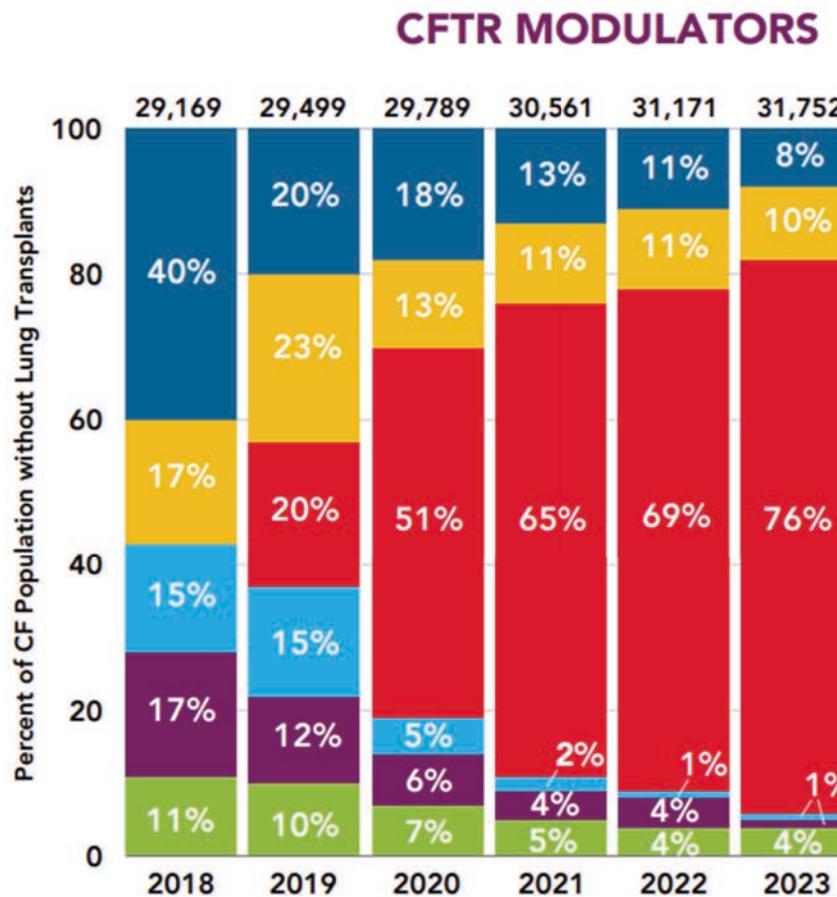


## 20 YEARS OF PROGRESS



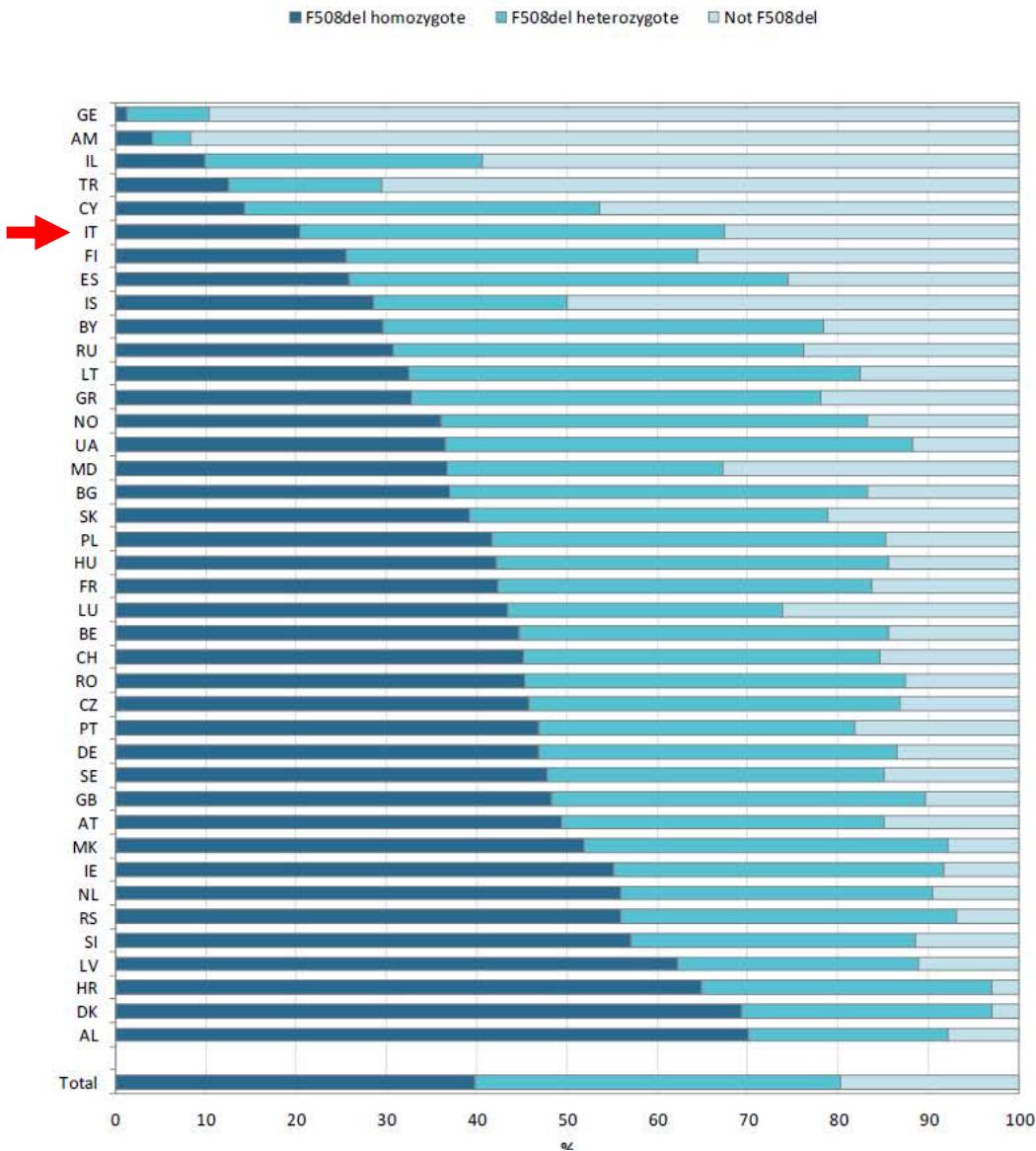
### Cascata patofisiologica della malattia polmonare nella FC<sup>1,2</sup>

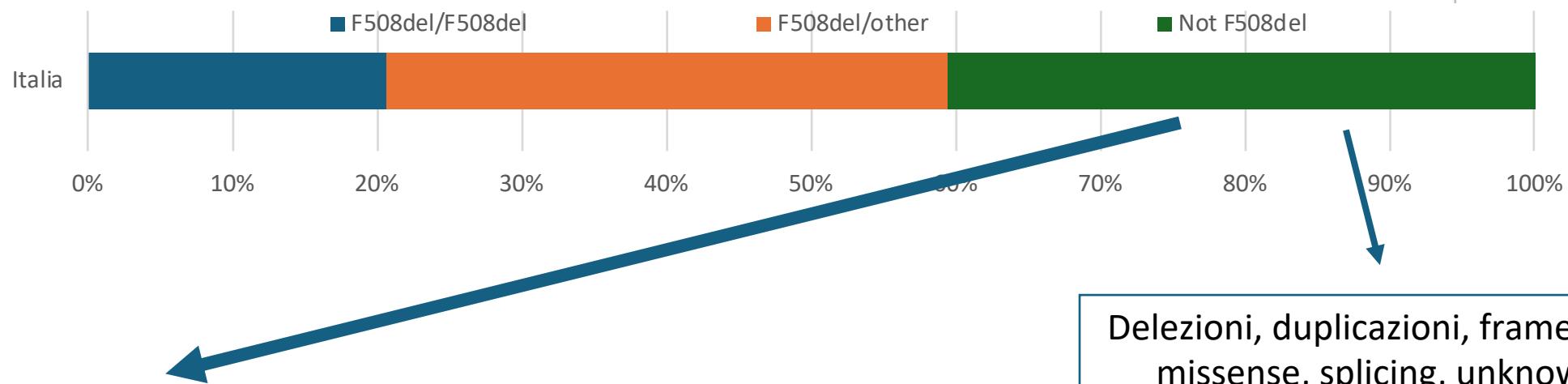




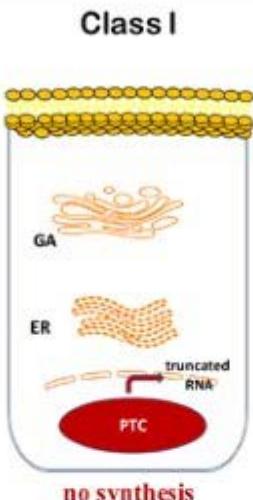
In 2023, 8% of the population was ineligible for a modulator based on their genotype.

- Ineligible by Age or Genotype
- Eligible, None Prescribed
- Elexa/Teza/Iva (Trikafta®)
- Teza/Iva (Symdeko®)
- Luma/Iva (Orkambi®)
- Iva (Kalydeco®)





Mutazioni non-sense (stop, classe I):  
Arresto prematuro della produzione di CFTR



MUTAZIONE TIPO "STOP"	2022	
	n.	%
G542X	528	8,7
W1282X	222	3,7
R553X	138	2,3
R1162X	129	2,1
E585X	54	0,9
R1158X	52	0,9
E831X	29	0,5
S1455X	22	0,4
Q1476X	13	0,2
R709X	11	0,2
L732X	10	0,2
Y849X	9	0,1
R785X	9	0,1
Q220X	8	0,1

NOTA: Omozigosi (mutazione stop/mutazione stop): 61

**Tabella 9.** Numero di pazienti portatori di almeno una delle mutazioni "non senso" (stop codon) (n. 1.234; 20,3%) con frequenza allelica  $\geq 0,1\%$  (n. 6.076). Anno 2022.

**Table 9.** Number of patients with at least one "non-sense" mutation (stop codon) (No. 1,234; 20.3%) with allelic frequency  $\geq 0.1\%$  (No. 6,076). Year 2022.

Delezioni, duplicazioni, frameshift,  
missense, splicing, unknown

GENOTIPO	2022	
	n.	%
F508del / Altro*	2.329	38,3
Altri genotipi	1.389	22,9
F508del / F508del	1.249	20,6
F508del / Funzione residua	548	9,0
Funzione residua/Altro*	502	8,3
Funzione residua/Funzione residua	59	1,0
F508del / Funzione Minima	1.545	25,4
Funzione Minima/ Funzione Minima	654	10,8
Funzione Minima / Altro**	2.490	41,0
Funzione Residua / Altro**	1.050	17,3
F508del / Gating	110	1,8
Gating / Altro**	198	3,3
F508del / Unknown	50	0,8

\*Include tutte le mutazioni non F508del e non funzione residua

\*\*Include tutte le altre mutazioni non F508del né funzione residua né funzione minima

**Tabella 8.** Prevalenza dei pazienti con mutazione F508del e funzione residua in omozigosi ed eterozigosi composta (n. 6.076). Anno 2022.

**Table 8.** Prevalence of homozygous and compound heterozygous patients F508del carriers and residual function carriers (No. 6,076). Year 2022.

## 2018 Priorities

- 1.What are the effective ways of simplifying the treatment burden of people with CF?**
- 2.How can we relieve gastro-intestinal symptoms, such as stomach pain, bloating and nausea?**
- 3.What is the best treatment for non-tuberculous mycobacterium (including when to start and what medication)?
- 4.Which therapies are effective in delaying or preventing progression of lung disease in early life?
- 5.Is there a way of preventing CF related diabetes?**
- 6.What effective ways of motivation, support and technologies help people with CF improve and sustain adherence to treatment?
- 7.Can exercise replace chest physiotherapy?
- 8.Which antibiotic combinations and dosing plans should be used for CF exacerbations and should antibiotic combinations be rotated?
- 9.Is there a way of reducing the negative effects of antibiotics e.g. resistance risk and adverse symptoms in people with CF?**
- 10.What is the best way of eradicating *Pseudomonas aeruginosa*?

## 2023 Priorities

- 1.What options are available for those not able to take current CFTR modulators (including rarer mutations, not eligible and unable to tolerate)?
- 2.What is the best way to diagnose lung infection when there is no sputum e.g. children and those on modulators?
- 3.How can we relieve gastro-intestinal symptoms, such as stomach pain, bloating and nausea?**
- 4.How do we manage an ageing population with CF?
- 5.Is there a way of reducing the negative effects of antibiotics e.g. resistance risk and adverse symptoms in people with CF?**
- 6.What are the long-term effects of medications (including CFTR modulators) in CF?
- 7.What are the effects of modulators on systems outside the lungs such as pancreatic function, liver disease, gastro-intestinal, bone density etc.?
- 8.What are the effective ways of simplifying the treatment burden of people with CF?**
- 9.Can genetic therapies (such as gene editing, stem cell and mRNA technology) be used as a treatment for CF?
- 10. Is there a way of preventing CF related diabetes (CFRD) in people with CF?**

Quali opzioni sono disponibili per coloro i quali non sono eleggibili al trattamento con modulatori CFTR?

Figure 2 The top 10 questions for research in cystic fibrosis in 2018 and 2023. Those marked in bold feature in both.

## THERATYPING

Sperimentazione, a livello cellulare, di farmaci già in uso clinico per la FC, su genotipi non precedentemente valutati e per i quali non erano progettati.



CrossMark

## Correction of CFTR function in intestinal organoids to guide treatment of cystic fibrosis

Anabela S. Ramalho<sup>1</sup>, Eva Fürstová<sup>2</sup>, Annelotte M. Vink<sup>3,4</sup>, Marc Ferrante<sup>5,6</sup>, Catherine Verfaillie<sup>7</sup>, Lieven Dupont<sup>8,9</sup>, Mieke Boon<sup>1,10</sup>, Marijke Proesmans<sup>1,10</sup>, Jeffrey M. Beekman<sup>3,4</sup>, Ifat Sarouk<sup>11</sup>, Carlos Vazquez Cordero<sup>12</sup>, Francois Vermeulen<sup>1,10</sup> and Kris De Boeck<sup>1,10</sup> on behalf of the Belgian Organoid Project<sup>13</sup>



Review

## Organoid Technology and Its Role for Therotyping Applications in Cystic Fibrosis

Jessica Conti<sup>1</sup>, Claudio Sorio<sup>1,\*</sup> and Paola Melotti<sup>2,\*</sup>



➤ J Physiol. 2022 Mar;600(6):1285-1286. doi: 10.1113/JP282586. Epub 2022 Jan 31.

## Nasal epithelial cells as a gold-standard predictive model for personalized medicine in cystic fibrosis

Nicoletta Pedemonte<sup>1</sup>

Affiliations + expand

PMID: 35038767 DOI: [10.1113/JP282586](https://doi.org/10.1113/JP282586)

Free article

<sup>1</sup> Department of Medicine, Division of General Pathology, University of Verona, 37134 Verona, Italy

<sup>2</sup> Cystic Fibrosis Centre, Azienda Ospedaliera Universitaria Integrata Verona, 37126 Verona, Italy

\* Correspondence: claudio.sorio@univr.it (C.S.); paola.melotti@aovr.veneto.it (P.M.)

# FDA Approves Expansion of Modulators for People With Certain Rare Mutations

The U.S. Food and Drug Administration (FDA) today expanded its approval of three CFTR modulators to include additional people with CF who have certain rare mutations. The approval enables more than 600 individuals with CF who were not previously eligible for modulators to access drugs that treat the underlying cause of their disease for the first time.

Dec. 21, 2020 | 3 min read

# forum 2024



**Table 6: List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to SYMDEKO**

546insCTA	E92K	G576A	L346P	R117G	S589N
711+3A→G*	E116K	G576A;R668C <sup>†</sup>	L967S	R117H	S737F
2789+5G→A*	E193K	G622D	L997F	R117L	S912L
3272-26A→G*	E403D	G970D	L1324P	R117P	S945L*
3849+10kbC→T*	E588V	G1069R	L1335P	R170H	S977F*
A120T	E822K	G1244E	L1480P	R258G	S1159F
A234D	E831X	G1249R	M152V	R334L	S1159P
A349V	F191V	G1349D	M265R	R334Q	S1251N
A455E*	F311del	H939R	M952I	R347H	S1255P
A554E	F508del*	F508C;SI251N <sup>†</sup>	M152V	R347L	T338I
A1006E	F1016S	F508del*	M265R	R347P	T1036N
A1067T	F1052V	F508del*	M952T	R352Q	T1053I
D110E	F1074L	F508del*	M1101K	R352W	V201M
D110H	F1099L	F508del*	P5L	R553Q	V232D
D192G	G27R	F508del*	P67L	R668C	V456A
D443Y	G85E	F508del*	P205S	R751L	V456F
D443Y;G576A;R668C <sup>†</sup>	G126D	F508del*	P574H	R792G	V562I
D579G	G178E	F508del*	I601F	R933G	V754M
D614G	G178R	F508del*	I618T	R1066H	V1153E
D836Y	G194R	F508del*	I807M	R1070Q	V1240G
D924N	G194V	F508del*	I980K	R1070W	V1293G
D979V	G314E	F508del*	I1027T	R1291R	R1162L
D1152H	G463V	F508del*	I1139V	R31L	W361R
D1270N	G480C	F508del*	I1269N	R74Q	W1282R
E56K	G551D	F508del*	I1366N	R74W	Y109N
E60K	G551S	F508del*	K1060T	R74W;D1270N <sup>†</sup>	S341P
E92K	G576A	F508del*	L15P	R74W;V201M <sup>†</sup>	Y161D
E116K	G576A;R668C <sup>†</sup>	F508del*	L165S	R74W;V201M;D1270N <sup>†</sup>	S364P
E193K	G622D	F508del*	L206W	R75Q	Y563N
E403D	G628R	F508del*	L320V	R117C	Y1014C
E474K	G970D	F508del*	R117G	S589N	Y1032C
E588V	G1061R	F508del*	R117H	S737F	

\* Clinical data for these mutations in Clinical Studies [see Clinical Studies (14.1 and 14.2)].

<sup>†</sup> A patient must have two copies of the F508del mutation or at least one copy of a responsive mutation presented in Table 6 to be indicated.

<sup>‡</sup> Complex/compound mutations where a single allele of the CFTR gene has multiple mutations; these exist independent of the presence of mutations on the other allele.

**Table 5: List of CFTR Gene Mutations that are Responsive to TRIKAFTA**

3141del9	E822K	G1069R	L967S	R117L	S912L
546insCTA	F191V	G1244E	L997F	R117P	S945L
A46D	F311del	G1249R	L1077P	R170H	S977F
A120T	F311L	G1349D	L1324P	R258G	S1159F
A234D	F508C	H139R	L1335P	R334L	S1159P
A349V	F508C;SI251N <sup>†</sup>	H199Y	L1480P	R334Q	S1251N
A455E	F508del*	H939R	M152V	R347H	S1255P
A554E	F575Y	H1054D	M265R	R347L	T338I
A1006E	F1016S	H1085P	M952I	R347P	T1036N
A1067T	F1052V	H1085R	M952T	R352Q	T1053I
D110E	F1074L	H1375P	M1101K	R352W	V201M
D110H	F1099L	H148T	P5L	R553Q	V232D
D192G	G27R	H175V	P5L	R74Q	W1282R
D443Y	G85E	H1366N	P205S	R75Q	Y1014C
D443Y;G576A;R668C <sup>†</sup>	G126D	H1375P	P574H	R792G	V562I
D579G	G178E	H1601F	P67L	R933G	V754M
D614G	G178R	H1618T	P67L	R1066H	V1153E
D836Y	G194R	H1807M	P67L	R1070Q	V1240G
D924N	G194V	H1980K	P67L	R1070W	V1293G
D979V	G314E	H1991R	P67L	R1162L	Y109N
D1152H*	G194V	K1060T	R74W;D1270N <sup>†</sup>	R1291R	Y161D
D1270N	G314E	L1027T	R74W;V201M;D1270N <sup>†</sup>	R1291R	S364P
E56K	G551D	L15P	R74W;V201M;D1270N <sup>†</sup>	R1291R	Y563N
E60K	G551S	L165S	R74W;V201M;D1270N <sup>†</sup>	R1291R	Y1014C
E60K	G551S	L206W	R75Q	S549N	Y1032C
E744K	G970D	L320V	R117C	S549R	
E588V	G1061R	L453S	R117H	S737F	

\* F508del is a responsive CFTR mutation based on both clinical and *in vitro* data [see Clinical Studies (14)].

<sup>†</sup> Complex/compound mutations where a single allele of the CFTR gene has multiple mutations; these exist independent of the presence of mutations on the other allele.

The FDA decision expands the labels for **Trikafta®** (elexacaftor/tezacaftor/ivacaftor), **Symdeko®** (tezacaftor/ivacaftor), and **Kalydeco®** (ivacaftor) to include additional rare mutations that were previously not approved for CFTR modulators. Trikafta is now approved for individuals who are 12 years and older with at least one of 177 newly-approved mutations; Symdeko is now approved for individuals who are 6 years and older with one of 127 additional mutations; and Kalydeco is now approved for individuals who are 4 months and older with one of 59 additional mutations.

## The French Compassionate Program of elexacaftor-tezacaftor-ivacaftor in people with cystic fibrosis with advanced lung disease and no F508del CFTR variant

Pierre-Régis Burgel, Isabelle Sermet-Gaudelus, Isabelle Durieu, Reem Kanaan, Julie Macey, Dominique Grenet, Michele Porzio, Nathalie Coolen-Allou, Raphael Chiron, Christophe Marguet, Benoit Douvry, Nadine Dufeu, Isabelle Danner-Boucher, Pierre Foucaud, Lydie Lemonnier, Emmanuelle Girodon, Jennifer Da Silva, Clémence Martin, on Behalf of the French CF Reference Network study group

### Metodi:

- Studio osservazionale sugli effetti di ETI su una popolazione di pazienti FC con patologia polmonare avanzata ( $\text{FEV}_1 < 40\%$ ), non eleggibili a ETI.
- Efficacia valutata da una commissione a 4-6 settimane in termini di manifestazioni cliniche, cloro sudorale,  $\text{FEV}_1\%$ .

### Results:

- Tra gli 84 pazienti con FC arruolati, ETI era efficace in 45 di essi.
- Tra i responders, 22/45 (49%) erano portatori di mutazioni non approvate dalla FDA.

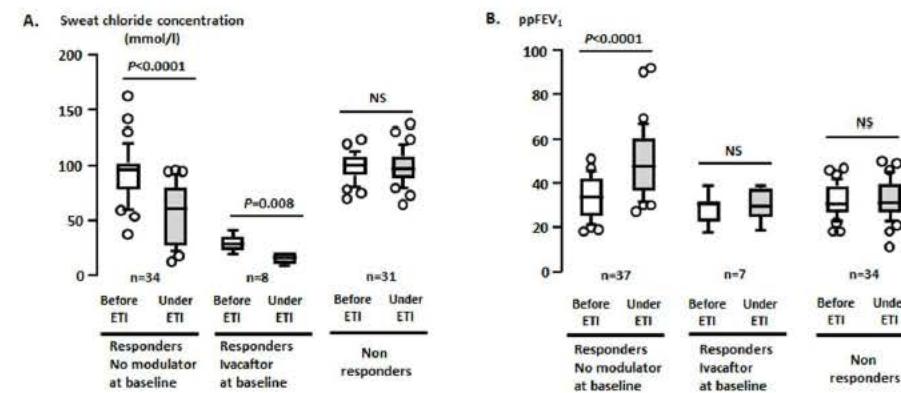
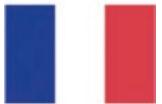


Figure 1. Comparison of sweat chloride concentration and ppFEV1 before ETI and under ETI according to responder status and ivacaftor at baseline. A. Sweat chloride concentration B. ppFEV1. Box plots: median [IQR] (error bars, 10-90 percentile) with outliers. Data were analyzed using the nonparametric Wilcoxon's test.



forum 2024



## Les médicaments et moi

Qui sommes-nous ?

Actualités

Bulletin officiel des actes,  
décisions et avis

Disponibilité des produits de  
santé

Vos démarches

Documents de référence

Informations de sécurité

Dossiers thématiques

Espace presse

Contactez-nous

Domaine médical ▾

Produit de santé ▾



< Retour

ACTUALITÉS > INNOVATION > ACCÈS COMPASSIONNEL > MUCOVISCIDOSE : DE NOUVEAUX PATIENTS VONT POUVOIR ...

PUBLIÉ LE 19/05/2022 - MIS À JOUR LE 01/06/2023



## Mucoviscidose : de nouveaux patients vont pouvoir bénéficier de l'association des comprimés pelliculés Kaftrio et Kalydeco

A+

A-



### Actualisation du 1<sup>er</sup> juin 2023

Depuis le 1<sup>er</sup> juin 2023, le [cadre de prescription compassionnelle \(CPC\)](#) associant les médicaments Kaftrio et Kalydeco s'étend aux patients atteints de mucoviscidose non porteurs d'une mutation F508del, dès l'âge de 6 ans et quel que soit le degré de sévérité de la maladie. Le traitement n'est pas indiqué chez les patients qui présentent 2 gènes mutés prédictifs de l'absence de synthèse de la protéine CFTR. L'élargissement du CPC prend en compte l'évolution des connaissances scientifiques.

Il est toujours recommandé que la prescription du traitement soit soumise à l'avis du centre coordinateur du centre de référence maladie rare (CRMR) mucoviscidose et affections liées à une anomalie de CFTR, selon la pratique clinique actuelle, et que les patients traités dans le cadre de ce CPC soient inscrits dans le registre français de la mucoviscidose.

Accédez au [protocole d'utilisation thérapeutique et de suivi des patients \(PUT-SP\)](#), qui détaille les modalités d'emploi de Kaftrio 75 mg/50 mg/100 mg comprimé pelliculé, Kaftrio 37,5 mg/25 mg/50 mg comprimé pelliculé, associés respectivement à Kalydeco 150 mg comprimé pelliculé et Kalydeco 75 mg comprimé pelliculé dans les conditions de ce CPC.

## Décision du 02/02/2024 - Modification du CPC Kaftrio (ivacaftor, tezacaftor, élexacaftor) et Kalydeco (ivacaftor)

**La directrice générale de l'ANSM,**

**Vu** le code de la santé publique, notamment les articles L. 5121-12-1 III, L. 5121-14-3 et R. 5121-76-9 ;

**Vu** le cadre de prescription compassionnelle (CPC) établi le 19/05/2022 et modifié le 01/06/2023 ;

**Vu** l'autorisation d'accès précoce (AAP) octroyée par la Haute autorité de santé le 07/09/2023 dans l'indication « en association dans le traitement des patients atteints de mucoviscidose âgés de 6 ans et plus, non porteurs d'une mutation F508del du gène CFTR (cystic fibrosis trans-membrane conductance regulator) et porteurs d'une mutation répondeuse à ivacaftor/tezacaftor/elexacaftor sur base de la données in vitro disponibles (voir rubrique 5.1 du RCP) ;

**Vu** les échanges intervenus entre l'Agence nationale de sécurité du médicament et des produits de santé (ANSM) et l'exploitant des autorisations de mise sur le marché (AMM) des spécialités concernées ;

**Considérant** que suite à l'octroi de l'AAP précitée, l'indication thérapeutique mentionnée dans le CPC doit être modifiée ;

**Considérant** que, dans l'intérêt des patients, il est nécessaire de maintenir un encadrement sécurisé de l'utilisation de Kaftrio et Kalydeco dans les autres indications couvertes par le CPC ;

**Considérant** que la modification apportée au CPC n'emporte pas de conséquence sur la durée de validité de celui-ci ;

**Décide :**

### **Article 1<sup>er</sup> :**

Le CPC précité est modifié comme suit en ce qui concerne le libellé de l'indication thérapeutique :

« Traitement de la mucoviscidose chez les patients âgés de 6 ans et plus non porteurs de la mutation F508del, hormis ceux présentant 2 gènes mutés prédictifs de l'absence de synthèse de protéine CFTR et ceux porteurs d'une mutation répondeuse à ivacaftor/tezacaftor/elexacaftor sur la base de données in vitro disponibles telles que définies dans le cadre de l'autorisation d'accès précoce ».

### **Article 2 :**

Le protocole d'utilisation thérapeutique et de suivi des patients joint à la présente décision remplace le protocole en vigueur.

*“Trattamento della fibrosi cistica in pazienti di età pari o superiore a 6 anni non portatori della mutazione F508del, ad eccezione di quelli con 2 geni mutati per cui è documentata la non responsività alla terapia, come definito nell'autorizzazione all'accesso anticipato”.*

# The expanded French compassionate programme for elexacaftor-tezacaftor-ivacaftor use in people with cystic fibrosis without a F508del CFTR variant: a real-world study

Pierre-Régis Burge, Isabelle Sermet-Gaudelus, Emmanuelle Girodon, Isabelle Durieu, Véronique Houdouin, Camille Audousset, Julie Macey, Dominique Grenet, Michele Porzio, Marlène Murris-Espin, Philippe Reix, Mélisande Baravalle, Chantal Belleguic, Laurent Mely, Juliette Verhille, Laurence Weiss, Martine Reynaud-Gaubert, Marie Mittaine, Rebecca Hamidfar, Sophie Ramel, Laure Cossion, Benoit Douvry, Isabelle Danner-Boucher, Pierre Foucaud, Charlotte Roy, Espérie Burnet, Caroline Raynal, Marie-Pierre Audrezet, Jennifer Da Silva, Clémence Martin, on behalf of the French Cystic Fibrosis Reference Network study group\*

**Interpretation** In France, over half of the population with cystic fibrosis without a F508del variant responded to elexacaftor-tezacaftor-ivacaftor, with most responders having no FDA-approved variant. The treatment period was relatively short and further research is warranted to describe the long-term safety and effectiveness of elexacaftor-tezacaftor-ivacaftor in this population.

37 variants were unequivocally non-responsive (always non-responsive in at least three non-responders), including I507del, L227R, E1104X, E585X, G542X, Q220X, R1162X, R553X, S466X, W1098X, W1282X, W846X, Y122X, 1078delT, 1677delTA, 2183AA>G, 3659delC, 394delTT, 1717-1G>A, 2622+1G>A, 3120+1G>A, 621+1G>T, 711+1G>T, CFTRdele17a-18, CFTRdele2-3, 1811+1.6kbA>G, and c.3469-1304C>G. In addition, 96 variants (two FDA-approved [I175V and M152V] and 94 non-FDA-approved) were probably non-responsive (always non-responsive in one or two non-responders).

Another 64 variants were present only in trans of known responsive variants and could therefore not be categorised.



# forum 2024

LIFC  
Lega Italiana  
Fibrosi Cistica

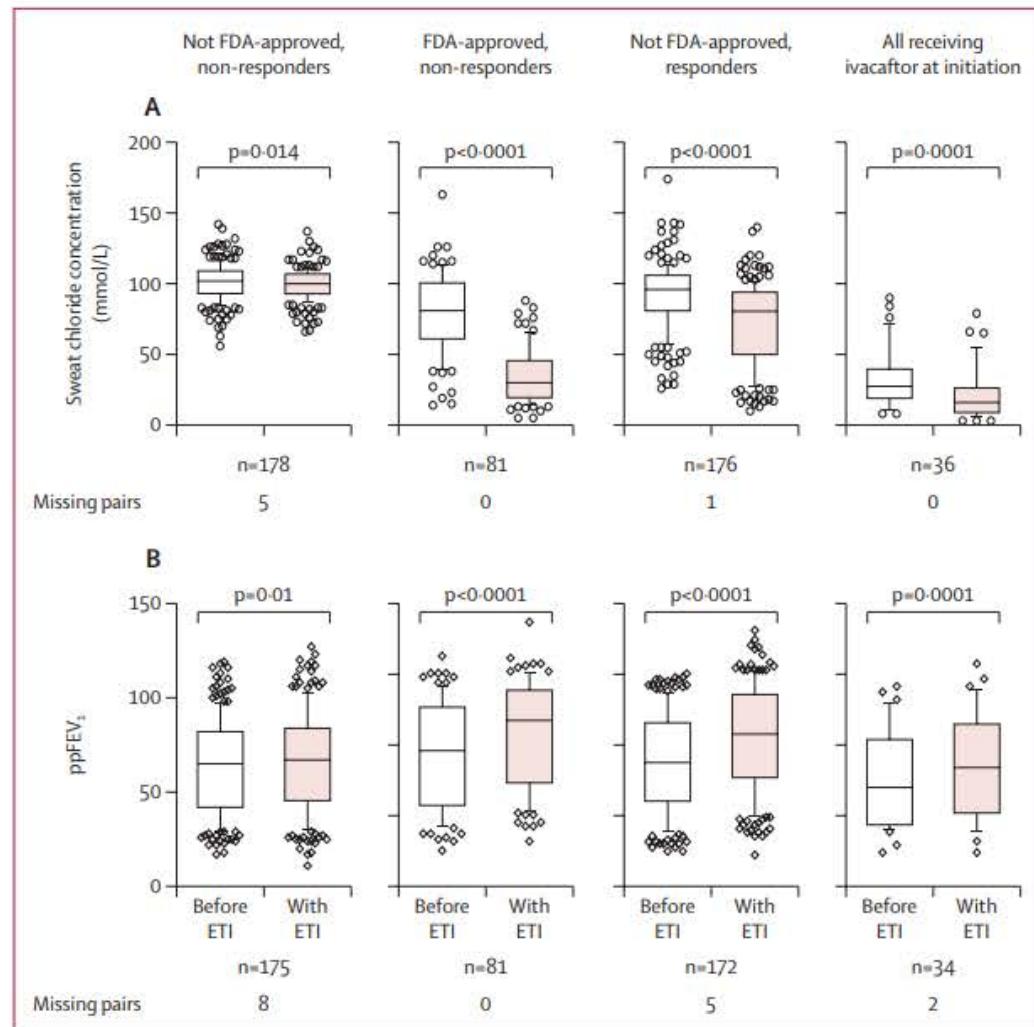


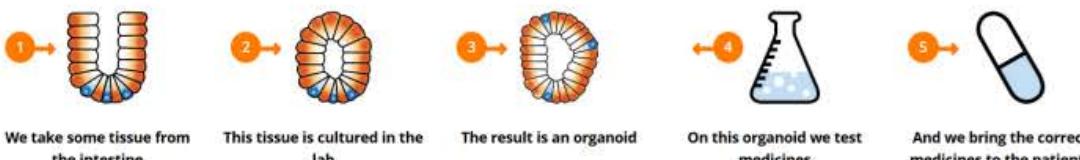
Figure 2: Comparison of (A) sweat chloride concentration and (B) ppFEV<sub>1</sub>, before ETI initiation and with ETI treatment

# Newsletter HIT-CF Europe

September 2018



HIT-CF Europe aims to evaluate the efficacy and safety of three drug candidates in patients with CF and rare mutations, pre-selected by their mini-intestines in the laboratory.



#### Organoid screening study

The first part of the HIT-CF project aims at enrolling 500 people with CF with two rare CFTR-mutations from across Europe. A biopsy from these people will be taken and organoids will be generated.

In each European participating country separately, approval has to be obtained from the local Ethical Committee before the biopsy can be taken.

#### This month, recruiting will start in several countries!

- We have received approval for the study in: Czech Republic, Portugal, Spain, Belgium, Israel and the Netherlands!
- In the following countries we hope to get approval very soon: Poland, Sweden, Germany, France and Austria
- The other countries that are initializing the study are the following: United Kingdom, Italy and Denmark

More detailed information on the countries and hospitals that are participating can be found on [www.hitcf.org](http://www.hitcf.org)

#### Testing organoids in different laboratories

All biopsies will be sent to HUB located in Utrecht, the Netherlands. HUB will generate organoids from biopsies and send the organoids to the organoid screening laboratories of University Medical Centre Utrecht, KU Leuven and Lisbon University.

Utrecht, Leuven, Lisbon and HUB have been working hard on preparing for the organoid screening phase, and we are confident we can start screening the first organoids in the months to come.

#### Do you want to participate, or do you want more info about the HIT-CF project?

Visit the website of HIT-CF or send an e-mail to [HITCF@umcutrecht.nl](mailto:HITCF@umcutrecht.nl)



# Newsletter HIT-CF Europe

September 2024

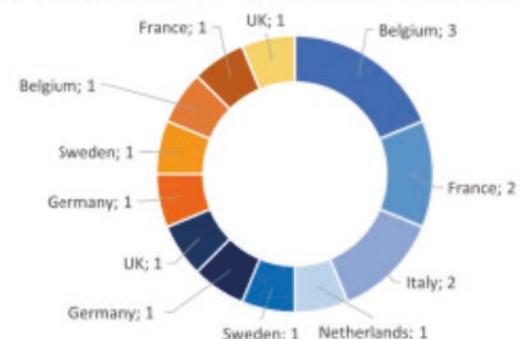
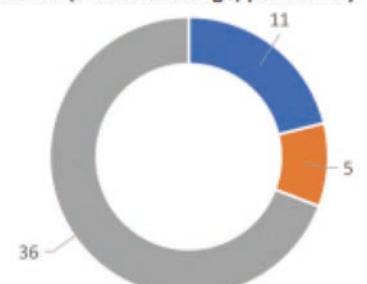


The HIT-CF Europe project aims to provide new treatment options to people with cystic fibrosis (CF) and ultra-rare genetic profiles. The project will evaluate the efficacy and safety of drug candidates provided by collaborating pharmaceutical companies in patients selected through preliminary tests in the laboratory on their mini-intestines – also called organoids.



#### Enrollment in the CHOICES trial is in full swing

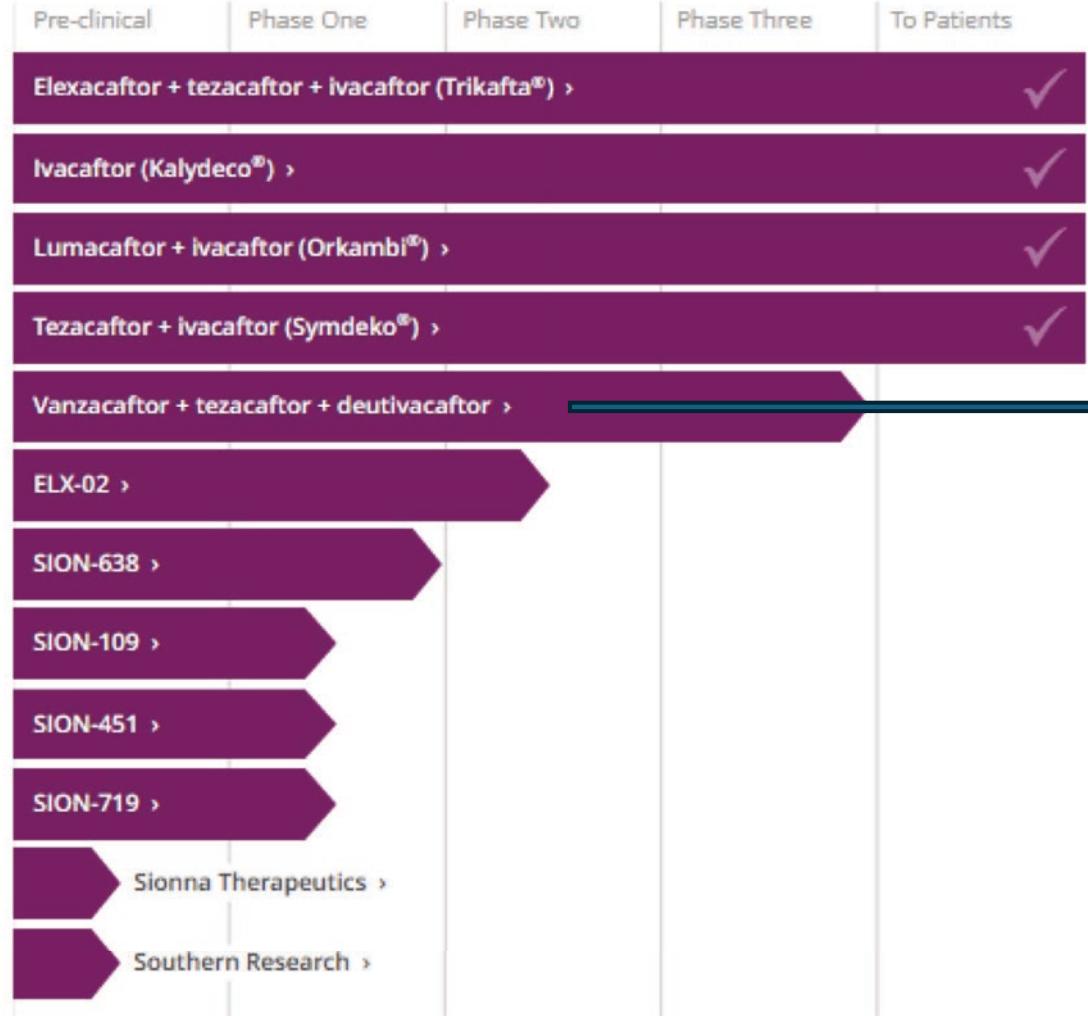
We hope you all enjoyed a relaxing summer and were able to spend time with your loved ones. During the summer months, the CHOICES study team and the staff at the local study sites have been hard at work. At this moment, 11 people have been enrolled in CHOICES. Enrolled means that they are taking the active drug or placebo. An additional 5 have been screened. Screened means that all necessary exams have been done and participants are ready to start the trial. The left graph, or "pie" represents all 52 people that need to be enrolled in CHOICES. In blue you see the ones that are already enrolled, in orange the ones that are screened to be enrolled, and in grey the participants that are expected, but not yet screened. CHOICES is currently running in 10 study sites in 7 countries: Belgium, France, Italy, the Netherlands, Germany, Sweden and the UK. On the right "pie" you see how many participants are enrolled (shades of blue) and screened (shades of orange) per country.



■ Enrolled ■ Screened ■ Expected

## Restore CFTR Protein | [Learn more >](#)

Modulators and nonsense readthrough therapies



**Poster #122**

### Safety and Efficacy of Vanzacaftor/Tezacaftor/Deutivacaftor (VNZ/TEZ/D-IVA) in Children 6 Through 11 Years of Age with Cystic Fibrosis

Jordana E. Hoppe,<sup>1</sup> Ajay S. Kasai,<sup>1</sup> Jessica E. Pittman,<sup>1</sup> Renee Jensen,<sup>1</sup> Lena Thia,<sup>1</sup> Phillip Robinson,<sup>2</sup> Ponnchit Tirakitsootorn,<sup>3</sup> Bonnie Ramsey,<sup>4</sup> Marcus Mall,<sup>5</sup> Jennifer L. Taylor-Cousar,<sup>1</sup> Edward McKone,<sup>6</sup> Elizabeth Tullis,<sup>7</sup> Daniell B. Salinas,<sup>8</sup> Jiaqiang Zhu,<sup>9</sup> Yih-Chieh Chen,<sup>10</sup> Patrick R. Scosby,<sup>11</sup> Gwyneth Davies<sup>12</sup>

<sup>1</sup>University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, Colorado, USA; <sup>2</sup>Emory University School of Medicine and Children's Healthcare of Atlanta, Atlanta, Georgia, USA; <sup>3</sup>Washington University School of Medicine, St. Louis, Missouri, USA; <sup>4</sup>The Hospital for Sick Children, Toronto, Ontario, Canada; <sup>5</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA; <sup>6</sup>Mayo Clinic, Rochester, Minnesota, USA; <sup>7</sup>University of Michigan Hospital, Ann Arbor, Michigan, USA; <sup>8</sup>Massachusetts General Hospital, Boston, Massachusetts, USA; <sup>9</sup>U.S. Food and Drug Administration, Bethesda, Maryland, USA; <sup>10</sup>U.S. Great Ormond Street Institute of Child Health and Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

<sup>11</sup>University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, Colorado, USA; <sup>12</sup>University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, Colorado, USA

**Background**

Vanzacaftor/tezacaftor/deutivacaftor (VNZ/TEZ/D-IVA) is an investigational next-generation, highly selective, triple oral CFTR modulator. It is designed to restore CFTR function to levels similar to those seen in patients with one normal allele (heterozygotes), which leads to near-normal levels of CFTR function.

**Objectives**

• Primary Endpoint: Safety of VNZ/TEZ/D-IVA.

**METHODS**

Figure 1. Phase 3 Open-Label Study in Children – HIGHLIGHT

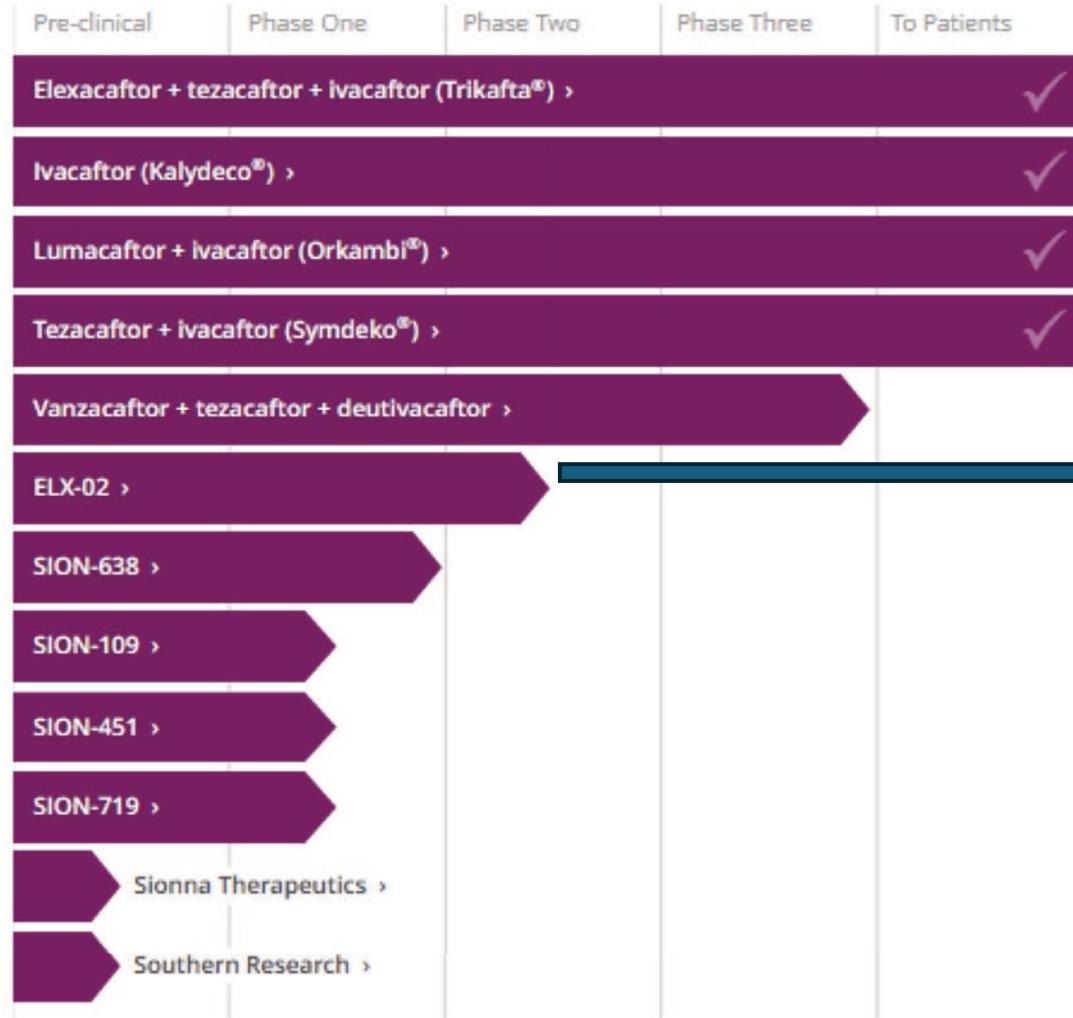
**Poster #120**

### Vanzacaftor/Tezacaftor/Deutivacaftor in Adolescents and Adults with Cystic Fibrosis: Results from Two Randomized, Active-Controlled Phase 3 Trials

Clare Keating,<sup>1</sup> Lael M. Yonker,<sup>2</sup> François Vermeulen,<sup>3</sup> Dario Prats,<sup>4</sup> Rachel W. Linnemann,<sup>5</sup> Aaron Trimble,<sup>6</sup> Tom Kotsimbos,<sup>7</sup> Joel Morris,<sup>8</sup> Andrew T. Braun,<sup>9</sup> Mark O'Carroll,<sup>10</sup> Ravinder Singh,<sup>11</sup> Sivaraman Subbarao,<sup>12</sup> Bonnie Ramsey,<sup>13</sup> Marcus A. Howell,<sup>14</sup> Jennifer L. Taylor-Cousar,<sup>15</sup> Edward P. McKone,<sup>16</sup> Elizabeth Tullis,<sup>17</sup> Peter McPhee,<sup>18</sup> Anna Lam,<sup>19</sup> Alexander Honig,<sup>20</sup> Michael D. Hwang,<sup>21</sup> Daniel J. O'Dell,<sup>22</sup> Daniel J. O'Dell,<sup>23</sup> Daniel J. O'Dell,<sup>24</sup> Daniel J. O'Dell,<sup>25</sup> Daniel J. O'Dell,<sup>26</sup> Daniel J. O'Dell,<sup>27</sup> Daniel J. O'Dell,<sup>28</sup> Daniel J. O'Dell,<sup>29</sup> Daniel J. O'Dell,<sup>30</sup> Daniel J. O'Dell,<sup>31</sup> Daniel J. O'Dell,<sup>32</sup> Daniel J. O'Dell,<sup>33</sup> Daniel J. O'Dell,<sup>34</sup> Daniel J. O'Dell,<sup>35</sup> Daniel J. O'Dell,<sup>36</sup> Daniel J. O'Dell,<sup>37</sup> Daniel J. O'Dell,<sup>38</sup> Daniel J. O'Dell,<sup>39</sup> Daniel J. O'Dell,<sup>40</sup> Daniel J. O'Dell,<sup>41</sup> Daniel J. O'Dell,<sup>42</sup> Daniel J. O'Dell,<sup>43</sup> Daniel J. O'Dell,<sup>44</sup> Daniel J. O'Dell,<sup>45</sup> Daniel J. O'Dell,<sup>46</sup> Daniel J. O'Dell,<sup>47</sup> Daniel J. O'Dell,<sup>48</sup> Daniel J. O'Dell,<sup>49</sup> Daniel J. O'Dell,<sup>50</sup> Daniel J. O'Dell,<sup>51</sup> Daniel J. O'Dell,<sup>52</sup> Daniel J. O'Dell,<sup>53</sup> Daniel J. O'Dell,<sup>54</sup> Daniel J. O'Dell,<sup>55</sup> Daniel J. O'Dell,<sup>56</sup> Daniel J. O'Dell,<sup>57</sup> Daniel J. O'Dell,<sup>58</sup> Daniel J. O'Dell,<sup>59</sup> Daniel J. O'Dell,<sup>60</sup> Daniel J. O'Dell,<sup>61</sup> Daniel J. O'Dell,<sup>62</sup> Daniel J. O'Dell,<sup>63</sup> Daniel J. O'Dell,<sup>64</sup> Daniel J. O'Dell,<sup>65</sup> Daniel J. O'Dell,<sup>66</sup> Daniel J. O'Dell,<sup>67</sup> Daniel J. O'Dell,<sup>68</sup> Daniel J. O'Dell,<sup>69</sup> Daniel J. O'Dell,<sup>70</sup> Daniel J. O'Dell,<sup>71</sup> Daniel J. O'Dell,<sup>72</sup> Daniel J. O'Dell,<sup>73</sup> Daniel J. O'Dell,<sup>74</sup> Daniel J. O'Dell,<sup>75</sup> Daniel J. O'Dell,<sup>76</sup> Daniel J. O'Dell,<sup>77</sup> Daniel J. O'Dell,<sup>78</sup> Daniel J. O'Dell,<sup>79</sup> Daniel J. O'Dell,<sup>80</sup> Daniel J. O'Dell,<sup>81</sup> Daniel J. O'Dell,<sup>82</sup> Daniel J. O'Dell,<sup>83</sup> Daniel J. O'Dell,<sup>84</sup> Daniel J. O'Dell,<sup>85</sup> Daniel J. O'Dell,<sup>86</sup> Daniel J. O'Dell,<sup>87</sup> Daniel J. O'Dell,<sup>88</sup> Daniel J. O'Dell,<sup>89</sup> Daniel J. O'Dell,<sup>90</sup> Daniel J. O'Dell,<sup>91</sup> Daniel J. O'Dell,<sup>92</sup> Daniel J. O'Dell,<sup>93</sup> Daniel J. O'Dell,<sup>94</sup> Daniel J. O'Dell,<sup>95</sup> Daniel J. O'Dell,<sup>96</sup> Daniel J. O'Dell,<sup>97</sup> Daniel J. O'Dell,<sup>98</sup> Daniel J. O'Dell,<sup>99</sup> Daniel J. O'Dell,<sup>100</sup> Daniel J. O'Dell,<sup>101</sup> Daniel J. O'Dell,<sup>102</sup> Daniel J. O'Dell,<sup>103</sup> Daniel J. O'Dell,<sup>104</sup> Daniel J. O'Dell,<sup>105</sup> Daniel J. O'Dell,<sup>106</sup> Daniel J. O'Dell,<sup>107</sup> Daniel J. O'Dell,<sup>108</sup> Daniel J. O'Dell,<sup>109</sup> Daniel J. O'Dell,<sup>110</sup> Daniel J. O'Dell,<sup>111</sup> Daniel J. O'Dell,<sup>112</sup> Daniel J. O'Dell,<sup>113</sup> Daniel J. O'Dell,<sup>114</sup> Daniel J. O'Dell,<sup>115</sup> Daniel J. O'Dell,<sup>116</sup> Daniel J. O'Dell,<sup>117</sup> Daniel J. O'Dell,<sup>118</sup> Daniel J. O'Dell,<sup>119</sup> Daniel J. O'Dell,<sup>120</sup> Daniel J. O'Dell,<sup>121</sup> Daniel J. O'Dell,<sup>122</sup> Daniel J. O'Dell,<sup>123</sup> Daniel J. O'Dell,<sup>124</sup> Daniel J. O'Dell,<sup>125</sup> Daniel J. O'Dell,<sup>126</sup> Daniel J. O'Dell,<sup>127</sup> Daniel J. O'Dell,<sup>128</sup> Daniel J. O'Dell,<sup>129</sup> Daniel J. O'Dell,<sup>130</sup> Daniel J. O'Dell,<sup>131</sup> Daniel J. O'Dell,<sup>132</sup> Daniel J. O'Dell,<sup>133</sup> Daniel J. O'Dell,<sup>134</sup> Daniel J. O'Dell,<sup>135</sup> Daniel J. O'Dell,<sup>136</sup> Daniel J. O'Dell,<sup>137</sup> Daniel J. O'Dell,<sup>138</sup> Daniel J. O'Dell,<sup>139</sup> Daniel J. O'Dell,<sup>140</sup> Daniel J. O'Dell,<sup>141</sup> Daniel J. O'Dell,<sup>142</sup> Daniel J. O'Dell,<sup>143</sup> Daniel J. O'Dell,<sup>144</sup> Daniel J. O'Dell,<sup>145</sup> Daniel J. O'Dell,<sup>146</sup> Daniel J. O'Dell,<sup>147</sup> Daniel J. O'Dell,<sup>148</sup> Daniel J. O'Dell,<sup>149</sup> Daniel J. O'Dell,<sup>150</sup> Daniel J. O'Dell,<sup>151</sup> Daniel J. O'Dell,<sup>152</sup> Daniel J. O'Dell,<sup>153</sup> Daniel J. O'Dell,<sup>154</sup> Daniel J. O'Dell,<sup>155</sup> Daniel J. O'Dell,<sup>156</sup> Daniel J. O'Dell,<sup>157</sup> Daniel J. O'Dell,<sup>158</sup> Daniel J. O'Dell,<sup>159</sup> Daniel J. O'Dell,<sup>160</sup> Daniel J. O'Dell,<sup>161</sup> Daniel J. O'Dell,<sup>162</sup> Daniel J. O'Dell,<sup>163</sup> Daniel J. O'Dell,<sup>164</sup> Daniel J. O'Dell,<sup>165</sup> Daniel J. O'Dell,<sup>166</sup> Daniel J. O'Dell,<sup>167</sup> Daniel J. O'Dell,<sup>168</sup> Daniel J. O'Dell,<sup>169</sup> Daniel J. O'Dell,<sup>170</sup> Daniel J. O'Dell,<sup>171</sup> Daniel J. O'Dell,<sup>172</sup> Daniel J. O'Dell,<sup>173</sup> Daniel J. O'Dell,<sup>174</sup> Daniel J. O'Dell,<sup>175</sup> Daniel J. O'Dell,<sup>176</sup> Daniel J. O'Dell,<sup>177</sup> Daniel J. O'Dell,<sup>178</sup> Daniel J. O'Dell,<sup>179</sup> Daniel J. O'Dell,<sup>180</sup> Daniel J. O'Dell,<sup>181</sup> Daniel J. O'Dell,<sup>182</sup> Daniel J. O'Dell,<sup>183</sup> Daniel J. O'Dell,<sup>184</sup> Daniel J. O'Dell,<sup>185</sup> Daniel J. O'Dell,<sup>186</sup> Daniel J. O'Dell,<sup>187</sup> Daniel J. O'Dell,<sup>188</sup> Daniel J. O'Dell,<sup>189</sup> Daniel J. O'Dell,<sup>190</sup> Daniel J. O'Dell,<sup>191</sup> Daniel J. O'Dell,<sup>192</sup> Daniel J. O'Dell,<sup>193</sup> Daniel J. O'Dell,<sup>194</sup> Daniel J. O'Dell,<sup>195</sup> Daniel J. O'Dell,<sup>196</sup> Daniel J. O'Dell,<sup>197</sup> Daniel J. O'Dell,<sup>198</sup> Daniel J. O'Dell,<sup>199</sup> Daniel J. O'Dell,<sup>200</sup> Daniel J. O'Dell,<sup>201</sup> Daniel J. O'Dell,<sup>202</sup> Daniel J. O'Dell,<sup>203</sup> Daniel J. O'Dell,<sup>204</sup> Daniel J. O'Dell,<sup>205</sup> Daniel J. O'Dell,<sup>206</sup> Daniel J. O'Dell,<sup>207</sup> Daniel J. O'Dell,<sup>208</sup> Daniel J. O'Dell,<sup>209</sup> Daniel J. O'Dell,<sup>210</sup> Daniel J. O'Dell,<sup>211</sup> Daniel J. O'Dell,<sup>212</sup> Daniel J. O'Dell,<sup>213</sup> Daniel J. O'Dell,<sup>214</sup> Daniel J. O'Dell,<sup>215</sup> Daniel J. O'Dell,<sup>216</sup> Daniel J. O'Dell,<sup>217</sup> Daniel J. O'Dell,<sup>218</sup> Daniel J. O'Dell,<sup>219</sup> Daniel J. O'Dell,<sup>220</sup> Daniel J. O'Dell,<sup>221</sup> Daniel J. O'Dell,<sup>222</sup> Daniel J. O'Dell,<sup>223</sup> Daniel J. O'Dell,<sup>224</sup> Daniel J. O'Dell,<sup>225</sup> Daniel J. O'Dell,<sup>226</sup> Daniel J. O'Dell,<sup>227</sup> Daniel J. O'Dell,<sup>228</sup> Daniel J. O'Dell,<sup>229</sup> Daniel J. O'Dell,<sup>230</sup> Daniel J. O'Dell,<sup>231</sup> Daniel J. O'Dell,<sup>232</sup> Daniel J. O'Dell,<sup>233</sup> Daniel J. O'Dell,<sup>234</sup> Daniel J. O'Dell,<sup>235</sup> Daniel J. O'Dell,<sup>236</sup> Daniel J. O'Dell,<sup>237</sup> Daniel J. O'Dell,<sup>238</sup> Daniel J. O'Dell,<sup>239</sup> Daniel J. O'Dell,<sup>240</sup> Daniel J. O'Dell,<sup>241</sup> Daniel J. O'Dell,<sup>242</sup> Daniel J. O'Dell,<sup>243</sup> Daniel J. O'Dell,<sup>244</sup> Daniel J. O'Dell,<sup>245</sup> Daniel J. O'Dell,<sup>246</sup> Daniel J. O'Dell,<sup>247</sup> Daniel J. O'Dell,<sup>248</sup> Daniel J. O'Dell,<sup>249</sup> Daniel J. O'Dell,<sup>250</sup> Daniel J. O'Dell,<sup>251</sup> Daniel J. O'Dell,<sup>252</sup> Daniel J. O'Dell,<sup>253</sup> Daniel J. O'Dell,<sup>254</sup> Daniel J. O'Dell,<sup>255</sup> Daniel J. O'Dell,<sup>256</sup> Daniel J. O'Dell,<sup>257</sup> Daniel J. O'Dell,<sup>258</sup> Daniel J. O'Dell,<sup>259</sup> Daniel J. O'Dell,<sup>260</sup> Daniel J. O'Dell,<sup>261</sup> Daniel J. O'Dell,<sup>262</sup> Daniel J. O'Dell,<sup>263</sup> Daniel J. O'Dell,<sup>264</sup> Daniel J. O'Dell,<sup>265</sup> Daniel J. O'Dell,<sup>266</sup> Daniel J. O'Dell,<sup>267</sup> Daniel J. O'Dell,<sup>268</sup> Daniel J. O'Dell,<sup>269</sup> Daniel J. O'Dell,<sup>270</sup> Daniel J. O'Dell,<sup>271</sup> Daniel J. O'Dell,<sup>272</sup> Daniel J. O'Dell,<sup>273</sup> Daniel J. O'Dell,<sup>274</sup> Daniel J. O'Dell,<sup>275</sup> Daniel J. O'Dell,<sup>276</sup> Daniel J. O'Dell,<sup>277</sup> Daniel J. O'Dell,<sup>278</sup> Daniel J. O'Dell,<sup>279</sup> Daniel J. O'Dell,<sup>280</sup> Daniel J. O'Dell,<sup>281</sup> Daniel J. O'Dell,<sup>282</sup> Daniel J. O'Dell,<sup>283</sup> Daniel J. O'Dell,<sup>284</sup> Daniel J. O'Dell,<sup>285</sup> Daniel J. O'Dell,<sup>286</sup> Daniel J. O'Dell,<sup>287</sup> Daniel J. O'Dell,<sup>288</sup> Daniel J. O'Dell,<sup>289</sup> Daniel J. O'Dell,<sup>290</sup> Daniel J. O'Dell,<sup>291</sup> Daniel J. O'Dell,<sup>292</sup> Daniel J. O'Dell,<sup>293</sup> Daniel J. O'Dell,<sup>294</sup> Daniel J. O'Dell,<sup>295</sup> Daniel J. O'Dell,<sup>296</sup> Daniel J. O'Dell,<sup>297</sup> Daniel J. O'Dell,<sup>298</sup> Daniel J. O'Dell,<sup>299</sup> Daniel J. O'Dell,<sup>300</sup> Daniel J. O'Dell,<sup>301</sup> Daniel J. O'Dell,<sup>302</sup> Daniel J. O'Dell,<sup>303</sup> Daniel J. O'Dell,<sup>304</sup> Daniel J. O'Dell,<sup>305</sup> Daniel J. O'Dell,<sup>306</sup> Daniel J. O'Dell,<sup>307</sup> Daniel J. O'Dell,<sup>308</sup> Daniel J. O'Dell,<sup>309</sup> Daniel J. O'Dell,<sup>310</sup> Daniel J. O'Dell,<sup>311</sup> Daniel J. O'Dell,<sup>312</sup> Daniel J. O'Dell,<sup>313</sup> Daniel J. O'Dell,<sup>314</sup> Daniel J. O'Dell,<sup>315</sup> Daniel J. O'Dell,<sup>316</sup> Daniel J. O'Dell,<sup>317</sup> Daniel J. O'Dell,<sup>318</sup> Daniel J. O'Dell,<sup>319</sup> Daniel J. O'Dell,<sup>320</sup> Daniel J. O'Dell,<sup>321</sup> Daniel J. O'Dell,<sup>322</sup> Daniel J. O'Dell,<sup>323</sup> Daniel J. O'Dell,<sup>324</sup> Daniel J. O'Dell,<sup>325</sup> Daniel J. O'Dell,<sup>326</sup> Daniel J. O'Dell,<sup>327</sup> Daniel J. O'Dell,<sup>328</sup> Daniel J. O'Dell,<sup>329</sup> Daniel J. O'Dell,<sup>330</sup> Daniel J. O'Dell,<sup>331</sup> Daniel J. O'Dell,<sup>332</sup> Daniel J. O'Dell,<sup>333</sup> Daniel J. O'Dell,<sup>334</sup> Daniel J. O'Dell,<sup>335</sup> Daniel J. O'Dell,<sup>336</sup> Daniel J. O'Dell,<sup>337</sup> Daniel J. O'Dell,<sup>338</sup> Daniel J. O'Dell,<sup>339</sup> Daniel J. O'Dell,<sup>340</sup> Daniel J. O'Dell,<sup>341</sup> Daniel J. O'Dell,<sup>342</sup> Daniel J. O'Dell,<sup>343</sup> Daniel J. O'Dell,<sup>344</sup> Daniel J. O'Dell,<sup>345</sup> Daniel J. O'Dell,<sup>346</sup> Daniel J. O'Dell,<sup>347</sup> Daniel J. O'Dell,<sup>348</sup> Daniel J. O'Dell,<sup>349</sup> Daniel J. O'Dell,<sup>350</sup> Daniel J. O'Dell,<sup>351</sup> Daniel J. O'Dell,<sup>352</sup> Daniel J. O'Dell,<sup>353</sup> Daniel J. O'Dell,<sup>354</sup> Daniel J. O'Dell,<sup>355</sup> Daniel J. O'Dell,<sup>356</sup> Daniel J. O'Dell,<sup>357</sup> Daniel J. O'Dell,<sup>358</sup> Daniel J. O'Dell,<sup>359</sup> Daniel J. O'Dell,<sup>360</sup> Daniel J. O'Dell,<sup>361</sup> Daniel J. O'Dell,<sup>362</sup> Daniel J. O'Dell,<sup>363</sup> Daniel J. O'Dell,<sup>364</sup> Daniel J. O'Dell,<sup>365</sup> Daniel J. O'Dell,<sup>366</sup> Daniel J. O'Dell,<sup>367</sup> Daniel J. O'Dell,<sup>368</sup> Daniel J. O'Dell,<sup>369</sup> Daniel J. O'Dell,<sup>370</sup> Daniel J. O'Dell,<sup>371</sup> Daniel J. O'Dell,<sup>372</sup> Daniel J. O'Dell,<sup>373</sup> Daniel J. O'Dell,<sup>374</sup> Daniel J. O'Dell,<sup>375</sup> Daniel J. O'Dell,<sup>376</sup> Daniel J. O'Dell,<sup>377</sup> Daniel J. O'Dell,<sup>378</sup> Daniel J. O'Dell,<sup>379</sup> Daniel J. O'Dell,<sup>380</sup> Daniel J. O'Dell,<sup>381</sup> Daniel J. O'Dell,<sup>382</sup> Daniel J. O'Dell,<sup>383</sup> Daniel J. O'Dell,<sup>384</sup> Daniel J. O'Dell,<sup>385</sup> Daniel J. O'Dell,<sup>386</sup> Daniel J. O'Dell,<sup>387</sup> Daniel J. O'Dell,<sup>388</sup> Daniel J. O'Dell,<sup>389</sup> Daniel J. O'Dell,<sup>390</sup> Daniel J. O'Dell,<sup>391</sup> Daniel J. O'Dell,<sup>392</sup> Daniel J. O'Dell,<sup>393</sup> Daniel J. O'Dell,<sup>394</sup> Daniel J. O'Dell,<sup>395</sup> Daniel J. O'Dell,<sup>396</sup> Daniel J. O'Dell,<sup>397</sup> Daniel J. O'Dell,<sup>398</sup> Daniel J. O'Dell,<sup>399</sup> Daniel J. O'Dell,<sup>400</sup> Daniel J. O'Dell,<sup>401</sup> Daniel J. O'Dell,<sup>402</sup> Daniel J. O'Dell,<sup>403</sup> Daniel J. O'Dell,<sup>404</sup> Daniel J. O'Dell,<sup>405</sup> Daniel J. O'Dell,<sup>406</sup> Daniel J. O'Dell,<sup>407</sup> Daniel J. O'Dell,<sup>408</sup> Daniel J. O'Dell,<sup>409</sup> Daniel J. O'Dell,<sup>410</sup> Daniel J. O'Dell,<sup>411</sup> Daniel J. O'Dell,<sup>412</sup> Daniel J. O'Dell,<sup>413</sup> Daniel J. O'Dell,<sup>414</sup> Daniel J. O'Dell,<sup>415</sup> Daniel J. O'Dell,<sup>416</sup> Daniel J. O'Dell,<sup>417</sup> Daniel J. O'Dell,<sup>418</sup> Daniel J. O'Dell,<sup>419</sup> Daniel J. O'Dell,<sup>420</sup> Daniel J. O'Dell,<sup>421</sup> Daniel J. O'Dell,<sup>422</sup> Daniel J. O'Dell,<sup>423</sup> Daniel J. O'Dell,<sup>424</sup> Daniel J. O'Dell,<sup>425</sup> Daniel J. O'Dell,<sup>426</sup> Daniel J. O'Dell,<sup>427</sup> Daniel J. O'Dell,<sup>428</sup> Daniel J. O'Dell,<sup>429</sup> Daniel J. O'Dell,<sup>430</sup> Daniel J. O'Dell,<sup>431</sup> Daniel J. O'Dell,<sup>432</sup> Daniel J. O'Dell,<sup>433</sup> Daniel J. O'Dell,<sup>434</sup> Daniel J. O'Dell,<sup>435</sup> Daniel J. O'Dell,<sup>436</sup> Daniel J. O'Dell,<sup>437</sup> Daniel J. O'Dell,<sup>438</sup> Daniel J. O'Dell,<sup>439</sup> Daniel J. O'Dell,<sup>440</sup> Daniel J. O'Dell,<sup>441</sup> Daniel J. O'Dell,<sup>442</sup> Daniel J. O'Dell,<sup>443</sup> Daniel J. O'Dell,<sup>444</sup> Daniel J. O'Dell,<sup>445</sup> Daniel J. O'Dell,<sup>446</sup> Daniel J. O'Dell,<sup>447</sup> Daniel J. O'Dell,<sup>448</sup> Daniel J. O'Dell,<sup>449</sup> Daniel J. O'Dell,<sup>450</sup> Daniel J. O'Dell,<sup>451</sup> Daniel J. O'Dell,<sup>452</sup> Daniel J. O'Dell,<sup>453</sup> Daniel J. O'Dell,<sup>454</sup> Daniel J. O'Dell,<sup>455</sup> Daniel J. O'Dell,<sup>456</sup> Daniel J. O'Dell,<sup>457</sup> Daniel J. O'Dell,<sup>458</sup> Daniel J. O'Dell,<sup>459</sup> Daniel J. O'Dell,<sup>460</sup> Daniel J. O'Dell,<sup>461</sup> Daniel J. O'Dell,<sup>462</sup> Daniel J. O'Dell,<sup>463</sup> Daniel J. O'Dell,<sup>464</sup> Daniel J. O'Dell,<sup>465</sup> Daniel J. O'Dell,<sup>466</sup> Daniel J. O'Dell,<sup>467</sup> Daniel J. O'Dell,<sup>468</sup> Daniel J. O'Dell,<sup>469</sup> Daniel J. O'Dell,<sup>470</sup> Daniel J. O'Dell,<sup>471</sup> Daniel J. O'Dell,<sup>472</sup> Daniel J. O'Dell,<sup>473</sup> Daniel J. O'Dell,<sup>474</sup> Daniel J. O'Dell,<sup>475</sup> Daniel J. O'Dell,<sup>476</sup> Daniel J. O'Dell,<sup>477</sup> Daniel J. O'Dell,<sup>478</sup> Daniel J. O'Dell,<sup>479</sup> Daniel J. O'Dell,<sup>480</sup> Daniel J. O'Dell,<sup>481</sup> Daniel J. O'Dell,<sup>482</sup> Daniel J. O'Dell,<sup>483</sup> Daniel J. O'Dell,<sup>484</sup> Daniel J. O'Dell,<sup>485</sup> Daniel J. O'Dell,<sup>486</sup> Daniel J. O'Dell,<sup>487</sup> Daniel J. O'Dell,<sup>488</sup> Daniel J. O'Dell,<sup>489</sup> Daniel J. O'Dell,<sup>490</sup> Daniel J. O'Dell,<sup>491</sup> Daniel J. O'Dell,<sup>492</sup> Daniel J. O'Dell,<sup>493</sup> Daniel J. O'Dell,<sup>494</sup> Daniel J. O'Dell,<sup>495</sup> Daniel J. O'Dell,<sup>496</sup> Daniel J. O'Dell,<sup>497</sup> Daniel J. O'Dell,<sup>498</sup> Daniel J. O'Dell,<sup>499</sup> Daniel J. O'Dell,<sup>500</sup> Daniel J. O'Dell,<sup>501</sup> Daniel J. O'Dell,<sup>502</sup> Daniel J. O'Dell,<sup>503</sup> Daniel J. O'Dell,<sup>504</sup> Daniel J. O'Dell,<sup>505</sup> Daniel J. O'Dell,<sup>506</sup> Daniel J. O'Dell,<sup>507</sup> Daniel J. O'Dell,<sup>508</sup> Daniel J. O'Dell,<sup>509</sup> Daniel J. O'Dell,<sup>510</sup> Daniel J. O'Dell,<sup>511</sup> Daniel J. O'Dell,<sup>512</sup> Daniel J. O'Dell,<sup>513</sup> Daniel J. O'Dell,<sup>514</sup> Daniel J. O'Dell,<sup>515</sup> Daniel J. O'Dell,<sup>516</sup> Daniel J. O'Dell,<sup>517</sup> Daniel J. O'Dell,<sup>518</sup> Daniel J. O'Dell,<sup>519</sup> Daniel J. O'Dell,<sup>520</sup> Daniel J. O'Dell,<sup>521</sup> Daniel J. O'Dell,<sup>522</sup> Daniel J. O'Dell,<sup>523</sup> Daniel J. O'Dell,<sup>524</sup> Daniel J. O'Dell,<sup>525</sup> Daniel J. O'Dell,<sup>526</sup> Daniel J. O'Dell,<sup>527</sup> Daniel J. O'Dell,<sup>528</sup> Daniel J. O'Dell,<sup>529</sup> Daniel J. O'Dell,<sup>530</sup> Daniel J. O'Dell,<sup>531</sup> Daniel J. O'Dell,<sup>532</sup> Daniel J. O'Dell,<sup>533</sup> Daniel J. O'Dell,<sup>534</sup> Daniel J. O'Dell,<sup>535</sup> Daniel J. O'Dell,<sup>536</sup> Daniel J. O'Dell,<sup>537</sup> Daniel J. O'Dell,<sup>538</sup> Daniel J. O'Dell,<sup>539</sup> Daniel J. O'Dell,<sup>540</sup> Daniel J. O'Dell,<sup>541</sup> Daniel J. O'Dell,<sup>542</sup> Daniel J. O'Dell,<sup>543</sup> Daniel J. O'Dell,<sup>544</sup> Daniel J. O'Dell,<sup>545</sup> Daniel J. O'Dell,<sup>546</sup> Daniel J. O'Dell,<sup>547</sup> Daniel J. O'Dell,<sup>548</sup> Daniel J. O'Dell,<sup>549</sup> Daniel J. O'Dell,<sup>550</sup> Daniel J. O'Dell,<sup>551</sup> Daniel J. O'Dell,<sup>552</sup> Daniel J. O'Dell,<sup>553</sup> Daniel J. O'Dell,<sup>554</sup> Daniel J. O'Dell,<sup>555</sup> Daniel J. O'Dell,<sup>556</sup> Daniel J. O'Dell,<sup>557</sup> Daniel J. O'Dell,<sup>558</sup> Daniel J. O'Dell,<sup>559</sup> Daniel J. O'Dell,<sup>560</sup> Daniel J. O'Dell,<sup>561</sup> Daniel J. O'Dell,<sup>562</sup> Daniel J. O'Dell,<sup>563</sup> Daniel J. O'Dell,<sup>564</sup> Daniel J. O'Dell,<sup>565</sup> Daniel J. O'Dell,<sup>566</sup> Daniel J. O'Dell,<sup>567</sup> Daniel J. O'Dell,<sup>568</sup> Daniel J. O'Dell,<sup>569</sup> Daniel J. O'Dell,<sup>570</sup> Daniel J. O'Dell,<sup>571</sup> Daniel J. O'Dell,<sup>572</sup> Daniel J. O'Dell,<sup>573</sup> Daniel J. O'Dell,<sup>574</sup> Daniel J. O'Dell,<sup>575</sup> Daniel J. O'Dell,<sup>576</sup> Daniel J. O'Dell,<sup>577</sup> Daniel J. O'Dell,<sup>578</sup> Daniel J. O'Dell,<sup>579</sup> Daniel J. O'Dell,<sup>580</sup> Daniel J. O'Dell,<sup>581</sup> Daniel J. O'Dell,<sup>582</sup> Daniel J. O'Dell,<sup>583</sup> Daniel J. O'Dell,<sup>584</sup> Daniel J. O'Dell,<sup>585</sup> Daniel J. O'Dell,<sup>586</sup> Daniel J. O'Dell,<sup>587</sup> Daniel J. O'Dell,<sup>588</sup> Daniel J. O'Dell,<sup>589</sup> Daniel J. O'Dell,<sup>590</sup> Daniel J. O'Dell,<sup>591</sup> Daniel J. O'Dell,<sup>592</sup> Daniel J. O'Dell,<sup>593</sup> Daniel J. O'Dell,<sup>594</sup> Daniel J. O'Dell,<sup>595</sup> Daniel J. O'Dell,<sup>596</sup> Daniel J. O'Dell,<sup>597</sup> Daniel J. O'Dell,<sup>598</sup> Daniel J. O'Dell,<sup>599</sup> Daniel J. O'Dell,<sup>600</sup> Daniel J. O'Dell,<sup>601</sup> Daniel J. O'Dell,<sup>602</sup> Daniel J. O'Dell,<sup>603</sup> Daniel J. O'Dell,<sup>604</sup> Daniel J. O'Dell,<sup>605</sup> Daniel J. O'Dell,<sup>606</sup> Daniel J. O'Dell,<sup>607</sup> Daniel J. O'Dell,<sup>608</sup> Daniel J. O'Dell,<sup>609</sup> Daniel J. O'Dell,<sup>610</sup> Daniel J. O'Dell,<sup>611</sup> Daniel J. O'Dell,<sup>612</sup> Daniel J. O'Dell,<sup>613</sup> Daniel J. O'Dell,<sup>614</sup> Daniel J. O'Dell,<sup>615</sup> Daniel J. O'Dell,<sup>616</sup> Daniel J. O'Dell,<sup>617</sup> Daniel J. O'Dell,<sup>618</sup> Daniel J. O'Dell,<sup>619</sup> Daniel J. O'Dell,<sup>620</sup> Daniel J. O'Dell,<sup>621</sup> Daniel J. O'Dell,<sup>622</sup> Daniel J. O'Dell,<sup>623</sup> Daniel J. O'Dell,<sup>624</sup> Daniel J. O'Dell,<sup>625</sup> Daniel J. O'Dell,<sup>626</sup> Daniel J. O'Dell,<sup>627</sup> Daniel J. O'Dell,<sup>628</sup> Daniel J. O'Dell,<sup>629</sup> Daniel J. O'Dell,<sup>630</sup> Daniel J. O'Dell,<sup>631</sup> Daniel J. O'Dell,<sup>632</sup> Daniel J. O'Dell,<sup>633</sup> Daniel J. O'Dell,<sup>634</sup> Daniel J. O'Dell,<sup>635</sup> Daniel J. O'Dell,<sup>636</sup> Daniel J. O'Dell,<sup>637</sup> Daniel J. O'Dell,<sup>638</sup> Daniel J. O'Dell,<sup>639</sup> Daniel J. O'Dell,<sup>640</sup> Daniel J. O'Dell,<sup>641</sup> Daniel J. O'Dell,<sup>642</sup> Daniel J. O'Dell,<sup>643</sup> Daniel J. O'Dell,<sup>644</sup> Daniel J. O'Dell,<sup>645</sup> Daniel J. O'Dell,<sup>646</sup> Daniel J. O'Dell,<sup>647</sup> Daniel J. O'Dell,<sup>648</sup> Daniel J. O'Dell,<sup>649</sup> Daniel J. O'Dell,<sup

## Restore CFTR Protein | [Learn more >](#)

Modulators and nonsense readthrough therapies



## Elox Pharmaceuticals, Inc. annuncia la valutazione dei dati finali dello studio clinico di Fase 2 di combinazione di ELX-02 nei pazienti di Fibrosi Cistica (FC) di Classe 1

14 giugno 2023 alle 22:53

 Condividi

Elox Pharmaceuticals, Inc. ha annunciato la valutazione finale dei dati dello studio clinico di Fase 2 di ELX-02 in combinazione con ivacaftor in pazienti FC di Classe 1 con almeno una mutazione nonsense. Nella valutazione finale, ELX-02 ha dimostrato un miglioramento clinicamente rilevante del ppFEV1. La valutazione finale dei dati include una rianalisi che utilizza la variazione di ppFEV1 dal Giorno 1 anziché dal basale, poiché diversi pazienti hanno avuto una progressione della malattia tra lo screening e il trattamento.

I risultati iniziali di questo studio sono stati comunicati nel settembre 2022. Valutazione finale dello studio di combinazione di fase 2 di ELX-02 in pazienti con FC di classe 1: Lo studio clinico di combinazione di Fase 2 di ELX-02 è stato progettato per valutare la sicurezza e l'attività biologica in pazienti con FC di Classe 1 con mutazione nonsense G542X, come monoterapia e in combinazione con ivacaftor dopo 5 settimane di trattamento. I risultati dell'analisi finale di 13 pazienti valutabili, rispetto agli 11 al momento della valutazione iniziale, sono riassunti di seguito: 6 dei 13 pazienti sono entrati nello studio dal braccio di monoterapia (dopo una media di 463 giorni) e hanno avuto una diminuzione della funzione polmonare (riduzione annualizzata del -4,26% del ppFEV1) a causa della progressione della malattia.

Il trattamento con ELX-02 ha stabilitizzato la malattia nel complesso e ha determinato un aumento clinicamente rilevante del ppFEV1 in sei dei tredici pazienti, in base alla variazione del ppFEV1 alla fine del trattamento, al Giorno 35, rispetto all'inizio del trattamento, al Giorno 1. I dati topline precedenti hanno confermato l'attività biologica.

## Genetic Therapy | [Learn more >](#)

Gene therapy, RNA therapy, gene editing, and antisense oligonucleotides (ASOs)

Pre-clinical | Phase One | Phase Two | Phase Three | To Patients

SPL84 >

VX-522 mRNA >

4D-710 >

ARCT-032 (LUNAR<sup>®</sup>-CF) >

RCT2100 >

SP-101 >

Carbon Biosciences >

Carmine Therapeutics >

Gensaic >

Nanite >

Pioneering Medicines >

Prime Medicine >

# forum 2024

## Terapia genica

fornisce all'organismo una copia corretta di un gene difettoso o un altro gene che possa compensarne il malfunzionamento

## mRNA

fornisce alla cellula le informazioni corrette per sintetizzare la proteina CFTR normale

## Editing genomico

manipolazione genetica in cui si procede alla delezione, all'inserimento, alla sostituzione o alla modifica del DNA genomico di un organismo vivente

## Oligonucleotidi antisenso

piccoli pezzi di DNA o RNA che si legano alla molecola di RNA e correggono queste istruzioni in modo da poter produrre una proteina CFTR a lunghezza intera

[← Back to the Drug Development Pipeline](#)

## SPL84

[Email](#) | [Print](#)

**STATUS**  
Phase Two

**THERAPEUTIC APPROACH**  
Genetic Therapy

This program is working to develop a potential therapy for people with CF who have splicing mutations. Splicing is an essential process in which RNA is cut into pieces and then stitched back together in a specific way. Splicing mutations in the CFTR gene cause the RNA to be cut or stitched incorrectly, leading to a mutated CFTR protein. SPL84 is a short nucleotide, or a small piece of genetic material, that is designed to bind to RNA and change its properties in specific ways. In the case of a splicing mutation, the short nucleotide is designed to ensure that the RNA is cut and stitched correctly, allowing functional CFTR protein to be made.

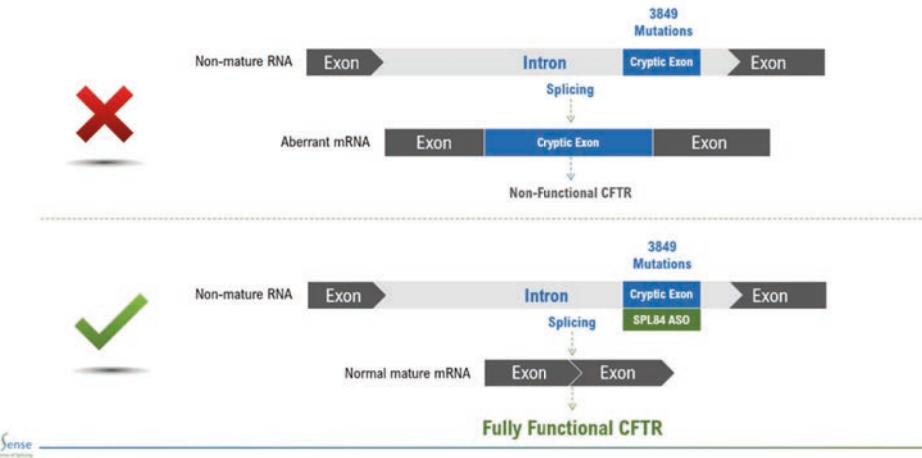
### Recent SPL84 Studies

#### ENROLLING

Study to evaluate SPL84 in adults with cystic fibrosis carrying the 3849 + 10 Kb C>T mutation (SpliSense SPL84-002)

[View all SPL84 studies >](#)

### SPL84 Produces Mature and Functioning WT CFTR



- Mutazioni splicing.
- Lo splicing è un processo essenziale in cui l'RNA viene tagliato in pezzi e poi ricucito insieme in un modo specifico.
- Le mutazioni di splicing nel gene CFTR causano un taglio o una ricucitura errata dell'RNA, che porta a una proteina CFTR mutata.
- SPL84 è un breve nucleotide, o un piccolo pezzo di materiale genetico, progettato per legarsi all'RNA e modificarne le proprietà in modi specifici. Nel caso di una mutazione di splicing, il nucleotide è progettato per garantire che l'RNA venga tagliato e ricucito correttamente, consentendo la produzione di una proteina CFTR funzionale.

## VX-522 mRNA

Email  | Print 

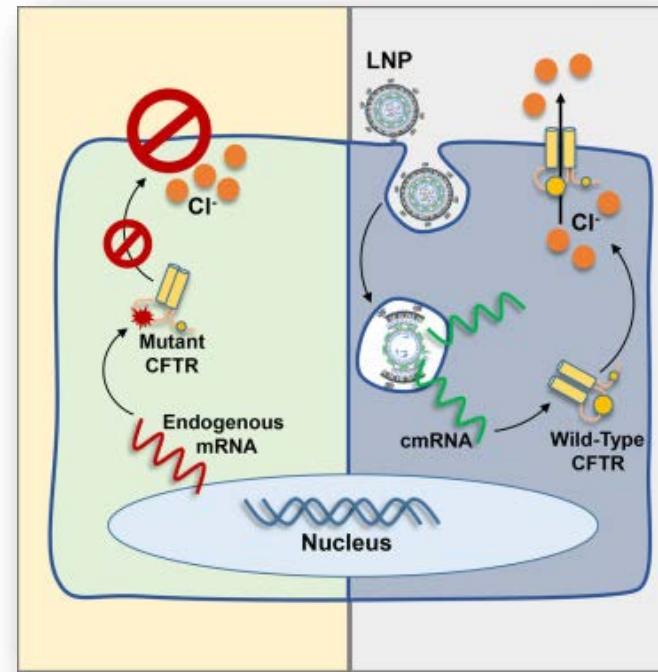
STATUS

Phase Two

THERAPEUTIC APPROACH

Genetic Therapy

VX-522 is an inhaled messenger RNA (mRNA) therapy. It aims to deliver a full-length copy of CFTR mRNA to lung cells using a lipid nanoparticle. Lung cells would then use the instructions in the mRNA to create functional CFTR protein. This type of therapy could work for any person with CF, including those with nonsense (also known as "x" or "stop") and other rare mutations that do not respond to CFTR modulators.



- L'obiettivo è fornire una copia a lunghezza intera del CFTR mRNA alle cellule polmonari utilizzando come vettore una nanoparticella lipidica.
- Le cellule polmonari userebbero quindi le istruzioni contenute nel mRNA per creare la proteina CFTR funzionale.
- Questa terapia potrebbe funzionare per qualsiasi persona con FC, indipendentemente dalle sue mutazioni CFTR.

[← Back to the Drug Development Pipeline](#)

## LUNAR®-CF

[Email](#)  [Print](#) 

STATUS	THERAPEUTIC APPROACH
Phase One	Genetic Therapy

This program is developing a potential inhaled therapy to deliver normal CFTR messenger RNA (mRNA) to the lungs. Lung cells would then use the instructions in the mRNA to create functional CFTR protein. This type of therapy could work for any person with CF, regardless of their CFTR mutations.

### Status

A Phase 1 study to test the safety and tolerability of this potential therapy is currently underway in New Zealand. The study initially enrolled healthy volunteers and is planned to expand to adults with CF later this year.

### Sponsor

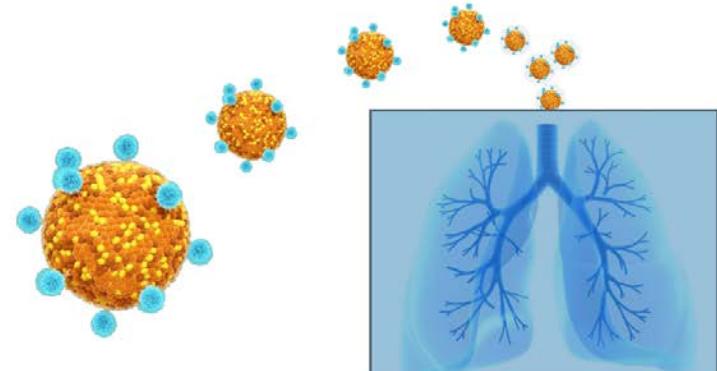
This program is sponsored by Arcturus Therapeutics and is partially funded by the Cystic Fibrosis Foundation.

### mRNA Replacement



Cargo: hCFTR mRNA

### LUNAR®- CF Therapy



Delivery vehicle: LUNAR®

Delivery format: Aerosol

Mutation agnostic treatment for CF lung disease

- LUNAR®-CF è una terapia sostitutiva dell'mRNA, per aerosol per il trattamento della malattia polmonare nella fibrosi cistica ed è indipendente dal genotipo.
- un mRNA CFTR umano incapsulato in LUNAR®, una nanoparticella lipidica, è stato sviluppato per fornire l'mRNA nell'epitelio delle vie aeree. Le proprietà fisicochimiche di LUNAR® erano stabili dopo l'aerosol.

[← Back to the Drug Development Pipeline](#)

## 4D-710

[Email](#) | [Print](#)

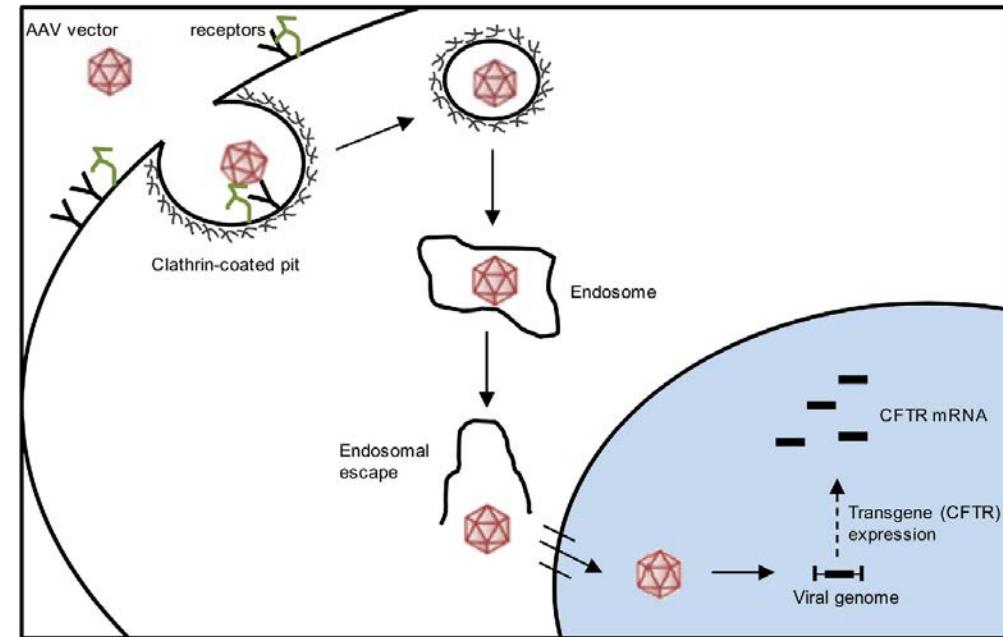
**STATUS**  
**Phase One**

**THERAPEUTIC APPROACH**  
**Genetic Therapy**

This program is working to advance a gene delivery vehicle that targets cells in the lung. 4D-710 is a customized adeno-associated virus (AAV) vector designed to deliver a healthy CFTR gene specifically to cells in the lungs of people with CF. This would allow the lung cells to create normally functioning CFTR protein, regardless of an individual's specific CFTR gene mutation.

**Status**

A Phase 1 study to test the safety of 4D-710 in adults with CF is underway.



- Terapia genica con vettore adenovirus associato
- Ridotta immunogenicità rispetto ai vettori adenovirali «classici»

## TERAPIA GENICA *NUOVI VETTORI VIRALI*

- Vettori Adenovirus Associati (AAV) – 4DMT / SPIROVANT
- Herpes Simplex (HSV) – KRYSTAL BIO
- Bocavirus – CARBON BIOSCIENCE
- Lentivirus – BOEHRINGER INGELHEIM



