Kalydeco – A new era in the treatment of Cystic Fibrosis

The Patient Experience

Katie Murphy, Research & Development Officer, Cystic Fibrosis Ireland

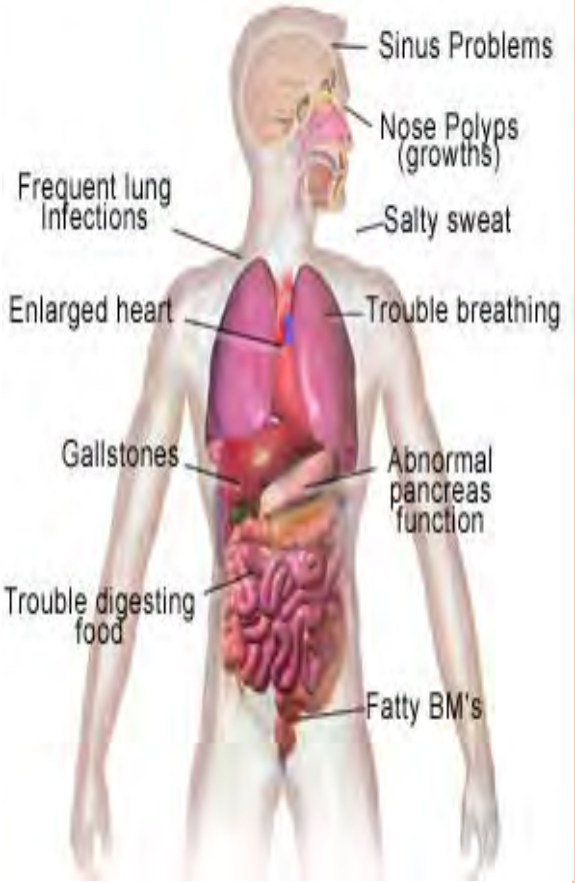
What is Cystic Fibrosis?

- **Cystic Fibrosis** is a genetic condition which primarily effects the lungs and digestive system.
- A defective gene and its protein product cause the body to produce unusually thick, sticky mucus that:

- *clogs the lungs and leads to life-threatening lung infections*
- *obstructs the pancreas and stops natural enzymes from helping the body break down and absorb food*

- The most common symptom associated with CF is recurrent chest infection, which result in lung damage, with the majority of death's occurring though respiratory failure.

- Other medical issues associated with CF include; CF related diabetes, osteoporosis, malnutrition, liver disease and infertility



Genetics of Cystic Fibrosis

- CF is the most common genetic condition effecting the lungs in Caucasians.
- 70,000 worldwide with 1,200 patients in Ireland and 5,000 in the UK

Ethnic Origin	Carrier Frequency	Newborns with CF
Ireland	1 in 19	1 in 1,400
UK – Caucasian	1 in 25	1 in 2,500
US – Caucasian	1 in 29	1 in 3,200
US – African Origin	1 in 65	1 in 17,000
US – Asian	1 in 90	1 in 31,000

- **When two 'carriers' of the mutated CF gene have a child, there is a 1 in 4 chance the baby will have CF**

How does CF effect the body?

- Genetic condition caused by mutations in the CFTR gene
- CFTR gene codes for CFTR protein
- Mutations in CFTR that severely reduce CFTR function cause CF
- The prevention/limitation of chloride getting to cell surface results in build up of mucus

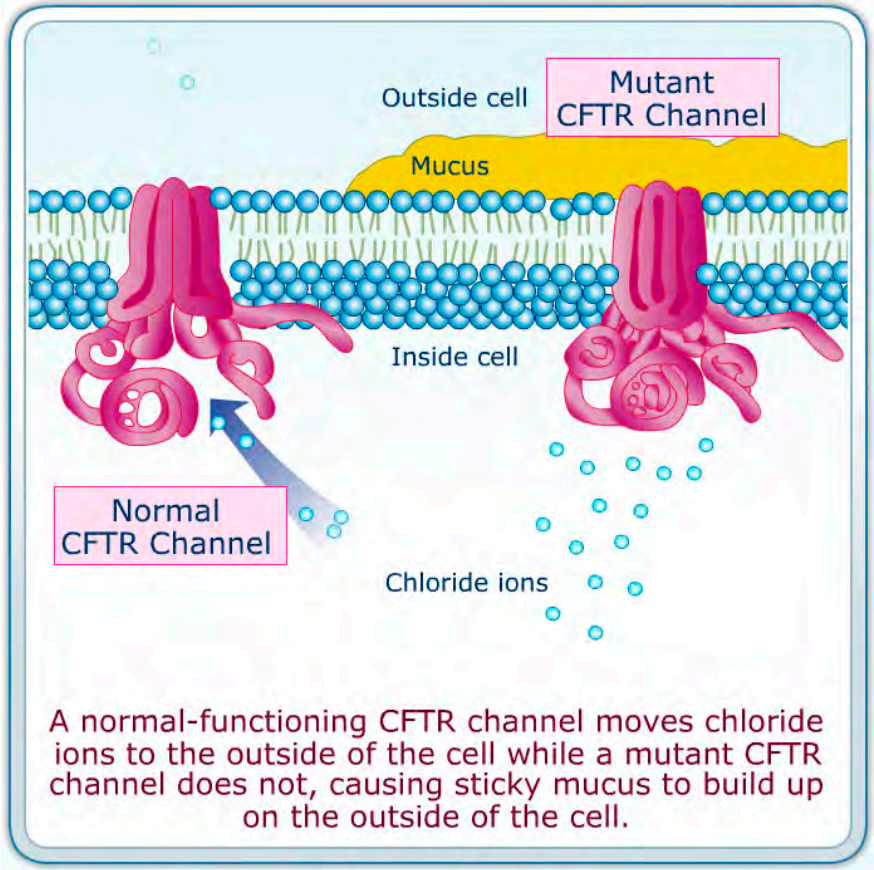


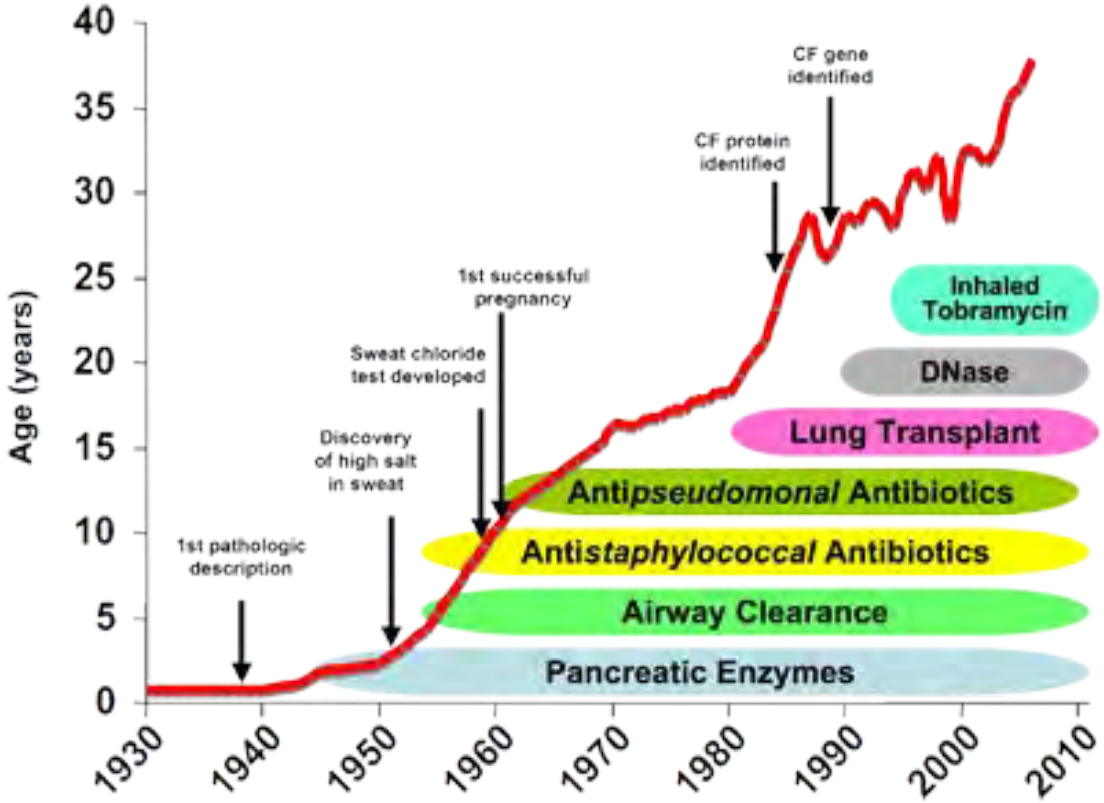
Image sourced from : http://prep-pg.blogspot.ie/2012/04/revolution-in-management-of-cystic.html

CFTR MUTATIONS CAN BE GROUPED TOGETHER BASED ON FUNCTION

Mutation	What's gone wrong	
Class I	Stop signal in CF gene occurs too soon; no CFTR is made	'Severe'
Class II	CFTR is misfolded keeping it from reaching the right place: affects 80% of PWCF	
Class III	CFR is made & in right place, but does not function normally	
Class IV	Opening in CFTR is faulty	'Milder'
Class V	CFTR is made in smaller than normal quantities	

- Significant differences in survival and median age at death between the cohorts.
- McKone et al. (2006) predicted these variations in survival based on mutation classification
- Median Survival
  - 37 years with "Severe"
  - 56 years with "Milder"

Improved prognosis in CF



Graph sourced from :
http://www.nationaljewish.org/healthinfo/conditions/cysticfibrosis/life-expectancy/

Patient group takes action!

- 1998 Cystic Fibrosis Foundation (CFF) approached Aurora Biosciences, a small biotec in San Diego looking at small molecule high-throughput screening
- 2000 $45 million to Aurora to screen for potential drug candidates for CF
- 2001 Aurora acquired by Vertex Pharmaceuticals $75 million to Vertex from CFF for R&D

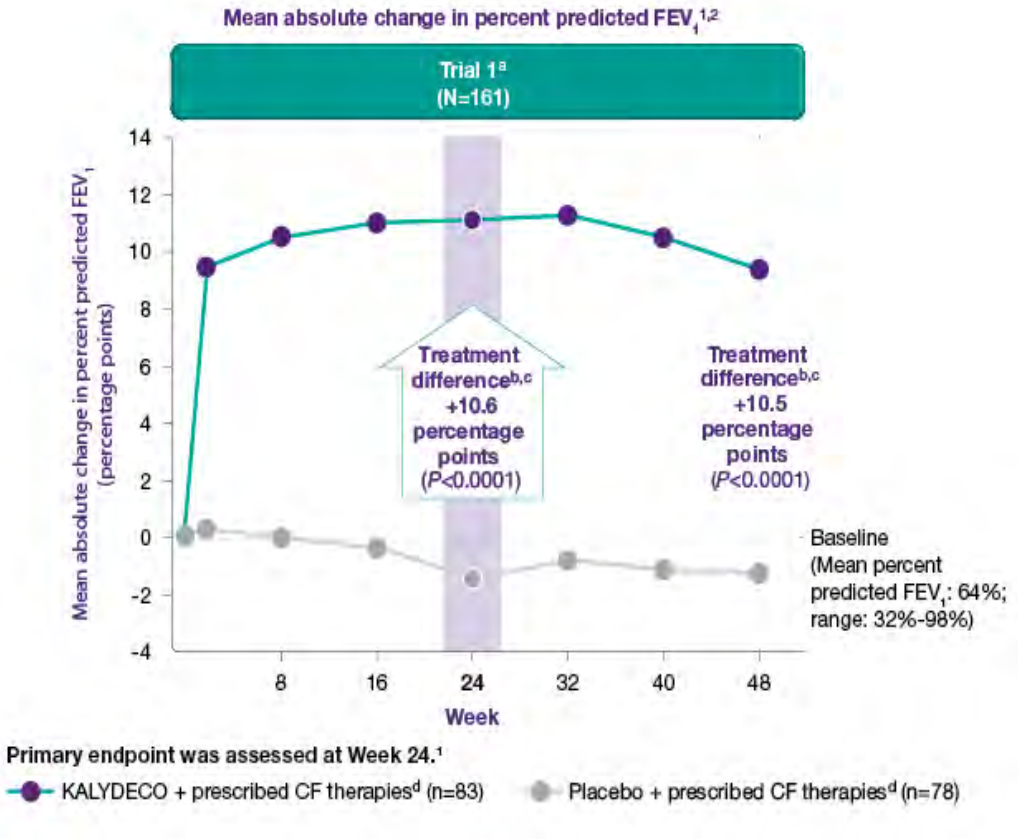
What was the outcome of this Philanthropic venture?

KALYDECO – THE CLINICAL BENEFITS

- *A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of VX-770 in Subjects with Cystic Fibrosis and the G551D Mutation*

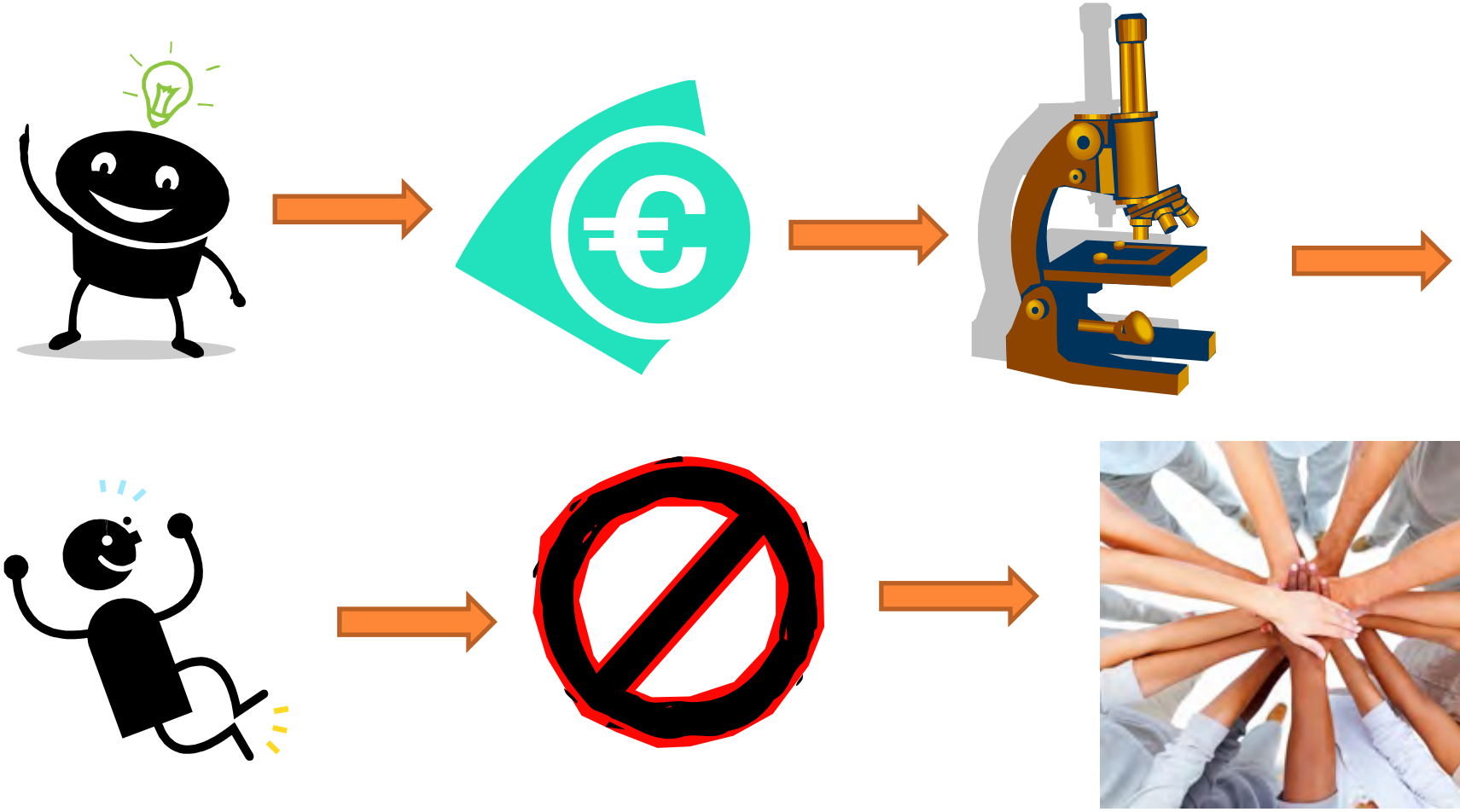
Results of trials:

- Increase in lung function by 10.6%, p<0.0001
- Increase in body weight by 2.8kg, p<0.0001
- 54% decrease in risk of first pulmonary exacerbation throughout the 48 week trial
- statistically significant improvement in relevant CF respiratory symptom score – measuring symptoms such as cough, sputum production, and difficulty breathing



The Research Process in general

Limited patient involvement



KALYDECO – NOT 'COST-EFFECTIVE'

Crunch talks to cut price of CF 'miracle' drug

Negotiations underway over new CF drug deemed 'too expensive'

Irish health authorities will negotiate the price of a "groundbreaking" new treatment for cystic fibrosis, which would currently cost the State more than €28 million annually.

Provide cystic fibrosis patients with the drug Kalydeco

Video: 'I prepared for the worst but I still cried'

CF drug may cost €230k per patient

Pressure on Health Minister to approve and supply new cystic fibrosis drug

The Minister and the HSE have been called upon to approve and supply a revolutionary new treatment for certain sufferers of cystic fibrosis.

13. In view of the very high drug acquisition cost, the significant budget impact, the absence of long term clinical data and the fact that the company has failed to demonstrate the cost-effectiveness of ivacaftor we cannot recommend reimbursement of ivacaftor at the submitted price of €234,804 per patient per annum. A mechanism such as a performance based risk sharing scheme and/or a significant reduction in price could facilitate access to ivacaftor treatment for cystic fibrosis patients with the G551D CFTR mutation.

How was Kalydeco approved in Ireland?

K-Day Arrives

- On the **1st of March 2013** Kalydeco was made available to people over the age of 6 years, who had the genetic mutation G551D
- Changes within one week!!!
- Increased lung function (22%)
- Normal sweat chloride
- Changes in CT scans

First Anniversary on Kalydeco
Patient Testimonial

- It is now a year later that I have been on Kalydeco, and the effects it has had are amazing. My lung function has improved about 40%, seeing to maintain around the 120% region now. My weight has increased by over 10kg and my overall happiness and well-being has improved hugely. It has been a good four years since I was admitted to hospital for IV antibiotics and to express how I feel would have no words.
- Kalydeco, I was told, was not a cure. And sure, it isn't. I continue to take my medication I was taking ten years ago, but the change my body has made is overwhelming for me, at times. I continue to grow more and more everyday, and feel a sense of relief at times, not having to go through what I did as a child, knowing that if I continue the way I do, CF won't hinder my life.
- Cystic Fibrosis has been hard to live with, yes. However, it has given me more and more a reason to be happier each and every day I continue to live. I will continue to be happy, no matter what. Right now, I'm the happiest person in the world.

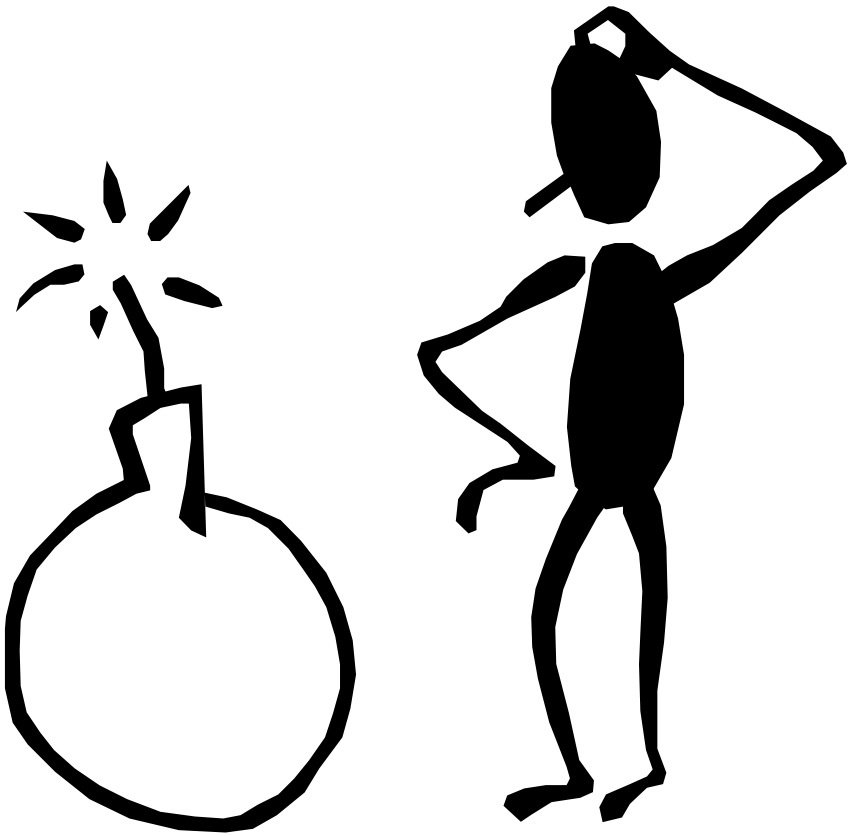
PWCF, Male, age 17

Health Economics & its' limitations for rare disease assessments

- Lack of comparators in the Health Technology Assessment
- The utilitarian view – "the greatest good for the **greatest number**"
- Various limitations with the QALY – no consideration for wider, long-term savings to be made (joining the workforce, prevention of other treatments being needed, etc).
- 'Lack of long term data on safety and effectiveness – often rare diseases not benefited from decades of research
- Presumption that health economics can accurately value the quality of a person's life
- Placing a price on a person's life is degrading for people living with illness
- Lack of understanding of implications of living with a particular illness – such as QoL, levels of suffering, etc.

Reference: *Hyri, H.I., Stren, A.D., Cox, T.M., & Roos, J.C.B (2014). Limits on use of health economic assessments for rare diseases. Q J Med; 107: 241-245*

What Next??



Thank You

Any Questions

Cystic Fibrosis Ireland