What's New in My Specialty?
Cystic Fibrosis

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Cystic Fibrosis

- Autosomal recessive multi-system disease that requires cross-disciplinary care
- First genetic disease to be sequenced
- More than 1900 disease causing mutations
- About 25,000 living patients
- Over 10 million carriers in the US

CF Transmembrane Regulator (CFTR) Protein

- CFTR mutations lead to absent or decreased epithelial chloride transport
- Biochemical defect leads to thick mucus
- F508del is the most common mutation
- G551D, a missense mutation, leads to decreased chloride transport
- Disease causing mutations shorten life

Early Death in CF

Median age at death in 1938 was 6 months

Current median age at death is 27 years

Projected median age

- “The expectation of life at birth”
- 40 years (2014)

Causes of Death

Lung disease:	68%
Lung transplant related:	12%
Liver Disease:	3%
Suicide:	3%
Other:	8%

Improved survival

Better treatments

Organized centers for treatment

Better recognition and diagnosis of disease

Utah Neonatal Screening

Immunoreactive Trypsinogen

DNA screen for most common mutations

Sweat Chloride Test

Referral to the CF Center for guidance

Making a Diagnosis of CF

1) Clinical Syndrome
   - Unexplained chronic purulent lung disease
   - Malabsorption syndrome
2) Laboratory demonstration of CFTR defect
   - Sweat Chloride Test
   - Nasal Potential Difference
3) Identification of genetic mutation

So What's New?

Treatments that target the biochemical defect that leads to clinical manifestations of disease.

Ivacaftor

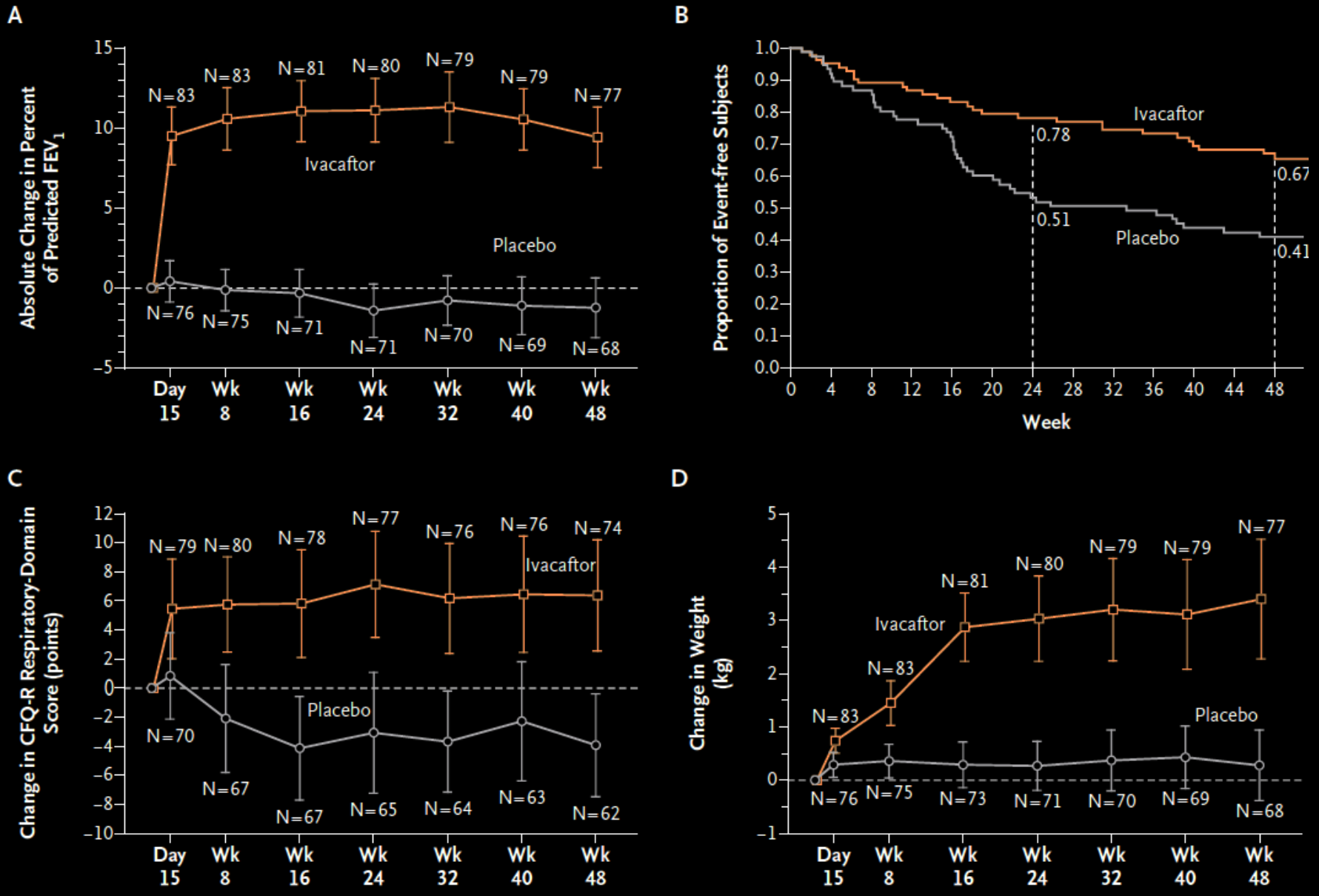
Small molecule “potentiator” of CFTR

Targets G551D mutation

Improves chloride transport

Dramatic results from RCT

Ramsey *et al NEJM* 2011;365:1663-1672



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Our Clinical Experience

- 18 adult patients with G551D mutations in Utah
- 2 have liver transplants without lung disease
  - Deferred treatment until lung disease starts
  - Protecting transplants from ivacaftor toxicities
- Adherent patients
  - Better lungs, arrested disease progression, few admissions
- Non-adherent patients
  - Non-sustained lung function improvement, progressive disease, more admissions

The Future

Ivacaftor/Lumacaftor combination therapy

Targets F508del/F508del—70% of patients

Press Release June 24, 2014

- 2.6-4.0 percentage point increase in FEV_1, $p \leq 0.0004$
- 30-39% drop in APE, $p \leq 0.0014$
- Well tolerated

Summary

CF shortens life by 40 years

Patients die primarily of lung disease

New treatments target the biochemical defect

These are exciting times in CF!