

# Registries do have potential to be used in clinical trials



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Executive Committee, European CF Patient Registry

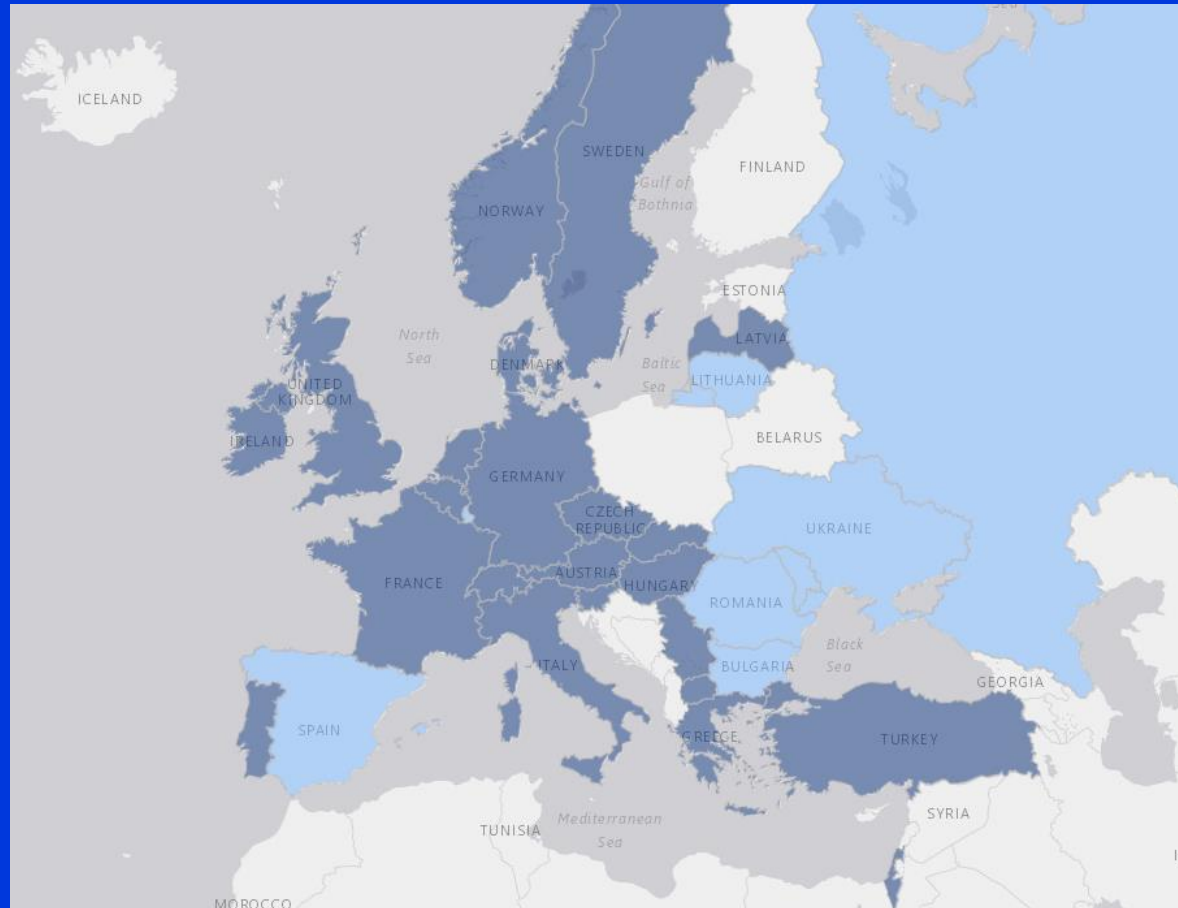
**Asterix Symposium, Zaandam NL, September 18 2017**

# Cystic Fibrosis

- Hereditary rare disease
- Intensive treatment
- High impact on QOL
- Decreased life expectancy
- 85.000 people worldwide registered
- > 2000 mutations, including ultrarare

# ECFS Patient Registry

- 31 Countries
- >42,000 pts
- 17 National Registries
- 81 centers using ECFS Registry Software



# Variables Collected by ECFSPR

## Demographic

Age, Gender, Status of patient, Date and cause of death

## Diagnosis

Age at diagnosis, Sweat test, Meconium Ileus, Neonatal screening

## Genetics

CFTR Genotype

## Growth/Lung function

FEV1 & FVC, height and weight

## Microbiology

Pseudomonas aeruginosa, Staphylococcus aureus, B. cepacia, NTM, MRSA

## Complications

Exacerbations (IVs, hospitalisations), Diabetes, Liver disease, Pancreatic status

## Therapy

Antibiotics, Bronchodilators, Mucolytics, Oxygen therapy, Pancreatic enzymes, CFTR Correctors

## Transplant

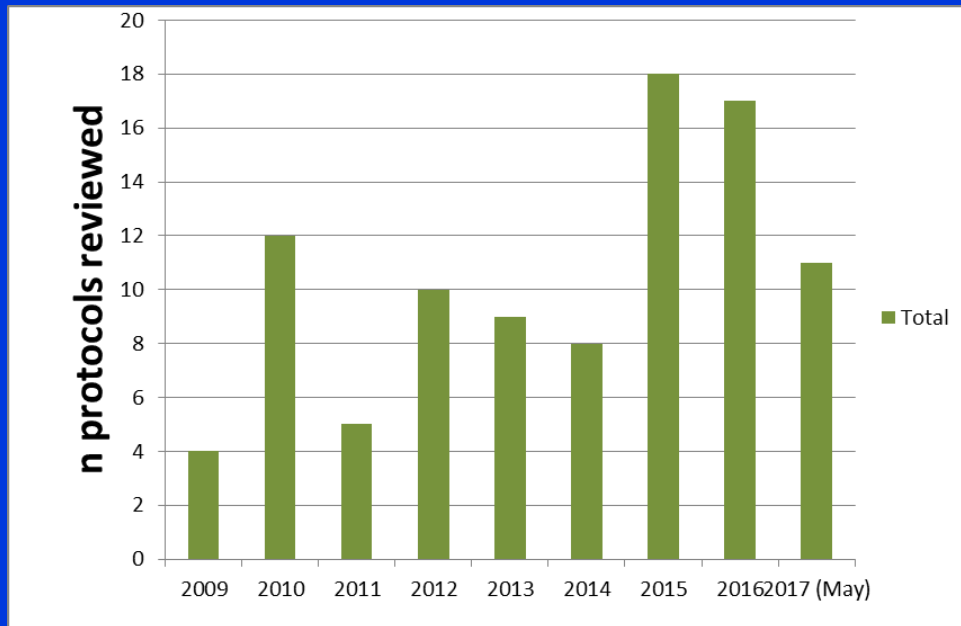
Lung/Liver transplant

# Registry Uses:

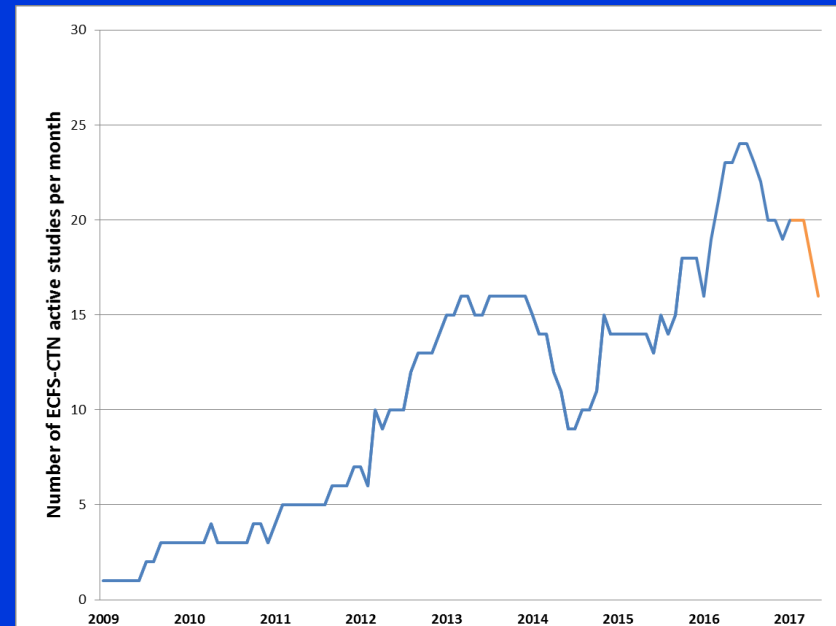


# Need for Novel Approaches to Clinical Trials: The ECFS Clinical Trial Network

## Increase in Protocols reviewed by CTN



## CTN Increase in Active Studies



# Registries and Clinical Trials

## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 24, 2013 VOL. 369 NO. 17

### Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

#### ORIGINAL ARTICLE

### Effectiveness of Fluticasone Furoate–Vilanterol for COPD in Clinical Practice

Jørgen Vestbo, D.M.Sc., David Leather, M.B., Ch.B., Nawar Diar Bakerly, M.D., John New, M.B., B.S., J. Martin Gibson, Ph.D., Sheila McCorkindale, M.B., Ch.B., Susan Collier, M.B., Ch.B., Jodie Crawford, M.Sc., Lucy Frith, M.Sc., Catherine Harvey, D.Phil., Henrik Svedsater, Ph.D., and Ashley Woodcock, M.D., for the Salford Lung Study Investigators\*

JACC: CARDIOVASCULAR INTERVENTIONS  
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PUBLISHED BY ELSEVIER INC. VOL. 7, NO. 8, 2014  
ISSN 1556-0384/14.00  
http://dx.doi.org/10.1016/j.jcin.2014.04.007

### A Registry-Based Randomized Trial Comparing Radial and Femoral Approaches in Women Undergoing Percutaneous Coronary Intervention The SAFE-PCI for Women (Study of Access Site for Enhancement of PCI for Women) Trial

Stéphane V. Rao, MD,\* Connie N. Hawn, MD, MHS,\* Brian Barbeau, BA,\* Lasse H. Abeler, BS,PHI,\* Kevin J. Anstrom, PhD,\* Rajesh B. Patel, MD,† James P. Janssens, MD,‡ Ryan M. L. Mazzaferri, Jr., MD,§ Sergio S. Jolly, MD,|| Alice Jacobs, MD,¶ L. Kristin Newby, MD,\* C. Michael Gibson, MD,§ David F. Kerei, MD,\* Rossana Mehran, MD,†† Ron Wadman, MD,†† Ian C. Gilchrist, MD,|| Brian J. McCosker,\* John C. Messenger, MD,|| Eric D. Peterson, MD, MSc,‡

### Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE trial). A multicenter, prospective, randomized, controlled clinical registry trial based on the Swedish angiography and angioplasty registry (SCAAR) platform. Study design and rationale

Ole Frøbert, MD, PhD,<sup>a</sup> Bo Lagerqvist, MD, PhD,<sup>b</sup> Thórarinn Guðnason, MD, PhD, FESC,<sup>c</sup> Leif Thuesen, MD, PhD,<sup>d</sup> Roger Svensson, MSc,<sup>e</sup> Göran K. Olivecrona, MD, PhD,<sup>f</sup> and Stefan K. James, MD, PhD<sup>b</sup> Örebro, Uppsala and

## The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research?

Michael S. Lauer, M.D., and Ralph B. D'Agostino, Sr., Ph.D.

Related article, p. 1587

Frøbert et al. Am H J 2010  
Frøbert et al. NEJM 2014  
Lauer & D'Agostini NEJM 2014

# Interaction

- EMA
- Pharma
- Clinicians
- Epidemiologists / Statisticians
- Patients

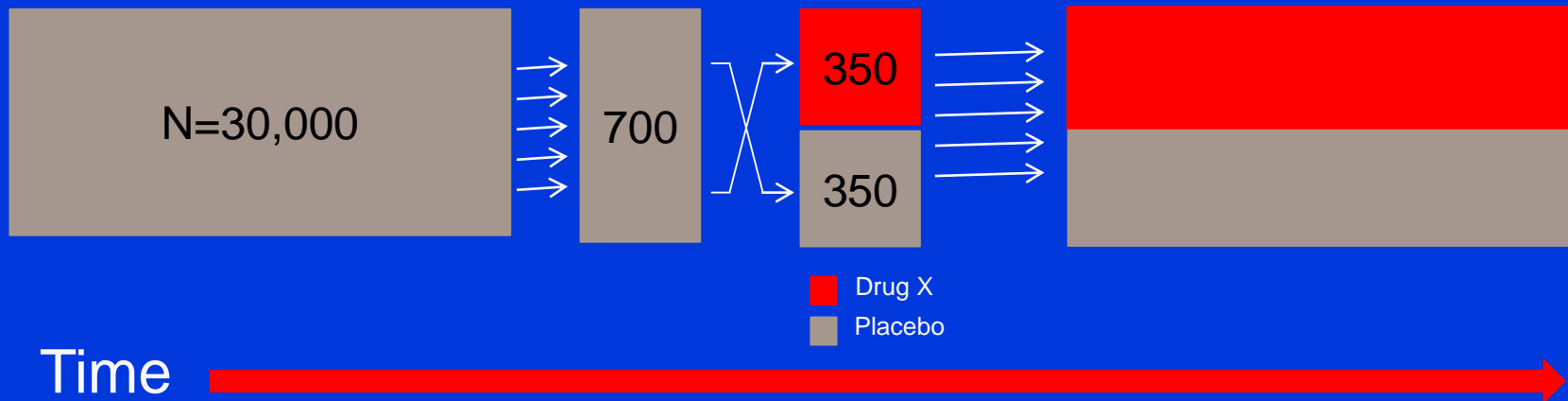


# The Multicenter, Prospective, Randomised, Controlled Clinical Registry Trial

Clinical registry with  
measures of patient  
baseline  
characteristics

Patient  
Subgroup  
Selection &  
Randomization

Follow-up of Patient  
Outcomes using  
Patient Registry



# The Multicenter, Prospective, Randomised, Controlled Clinical Registry Trial

## Advantages

- Considerable savings
  - TASTE \$50 per patient
- Increases ability to study more medications
- Supports & Promotes use and value of Registries
- Real-world assessments of baseline characteristics
- Opportunity to study populations difficult to recruit into RCT

## Disadvantages

- Missing data fields
- Quality of data
- Choice of population to study
- Blinding?
- Standardization of measures and outcomes

# Requirements for Using Registries for Clinical Trials



CLINICAL  
TRIALS  
**TRANSFORMATION**  
INITIATIVE

Public-Private Partnership  
Co-founded by Duke University & FDA  
Involves all stakeholders  
80+ members

**MISSION:** To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials



# Requirements for Using Registries for Clinical Trials



# Requirements for Using Registries for Clinical Trials

1. RELEVANCE

2. ROBUSTNESS

3. RELIABILITY

4. PATIENT PRIVACY

# Post-approval Phase IV Studies and CF Registries

## OPTIONS

1. Extension studies to RCT - “Open label study”
2. New Drug Safety/Efficacy Phase IV Product Specific Registry developed and maintained by Industry
3. Use of Existing Clinical Registries

# The “Hybrid” Phase IV/Registry Trial

- Registry Software can be adapted to include modules suitable for monitoring new drug safety and efficacy
  - Need early discussion between Industry/Registries regarding feasibility
  - Contains PRO, specific ADRs (ECG/LFTs etc.)
  - Can be used within the structures of a monitored post-approval trial

The screenshot displays the ECFSTracker software interface. The top navigation bar shows 'Centre1 > Patient Encounters > [100] 100 > Encounter History > Jan 6, 2014'. The patient information section includes '[100] 100', 'Jul, 1993 (20.9yr)', 'Male', and mutations 'p.Ser912X' and 'unknown'. The encounter is dated 'Jan 6, 2014 at Centre1 - Sarah Bloggs'. The 'Pharmacovigilanc' tab is selected, showing a table of vital signs and clinical data. A red arrow points to the 'Pharmacovigilanc' tab.

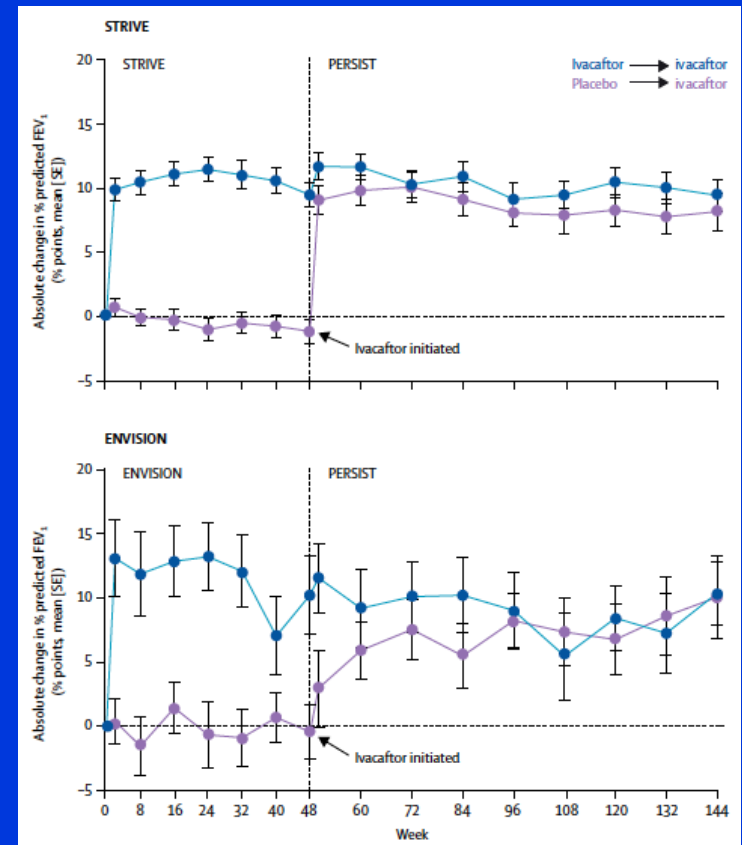
| Date | Respiration / Nutrition   | Therapy | Exacerbation History | Microbiology | Complications of CF | Vital Status / Transplant | Pharmacovigilanc  |
|------|---|---------|----------------------|--------------|---------------------|---------------------------|---|
|      | Weight (kg) 75.0 kg   |         |                      |              |                     |                           | Age (decimal) 20.48<br>FEV1 % of predicted 70.32<br>FVC % of predicted 77.38<br>FEV1 / FVC 0.76<br>Height z-score 0.58<br>Weight z-score 0.36<br>Body Mass Index 22.89<br>BMI z-score -0.05 |
|      | Height (cm) 181.0 cm  |         |                      |              |                     |                           |   |
|      | FEV1 in litres 3.4 litres   |         |                      |              |                     |                           |   |
|      | FVC in litres 4.5 litres  |         |                      |              |                     |                           |   |
|      | Seen by Physiotherapist <input type="radio"/> No <input checked="" type="radio"/> Unknown <input type="radio"/> Yes |         |                      |              |                     |                           |   |
|      | Seen by Dietician <input type="radio"/> No <input checked="" type="radio"/> Unknown <input type="radio"/> Yes       |         |                      |              |                     |                           |   |

# Real World Registry Studies

## How well do they work?

### Example - Ivacaftor Open Label Trail

- Open-Label - 144 weeks
- Lung Function Sustained over 144 weeks
  - ~9% increase
- Exacerbation frequency remained lower than placebo
  - ~0.5-0.7 per year v 1.3



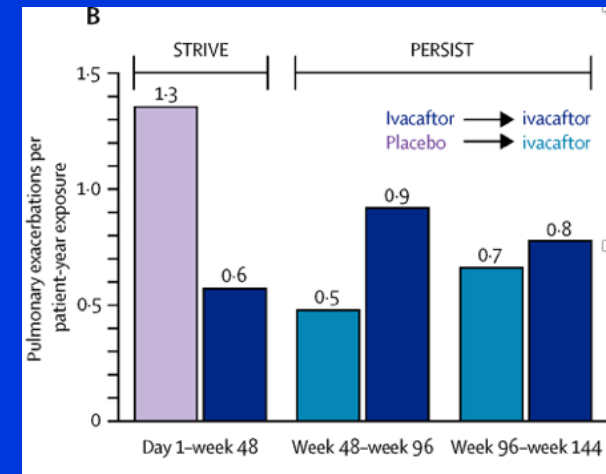
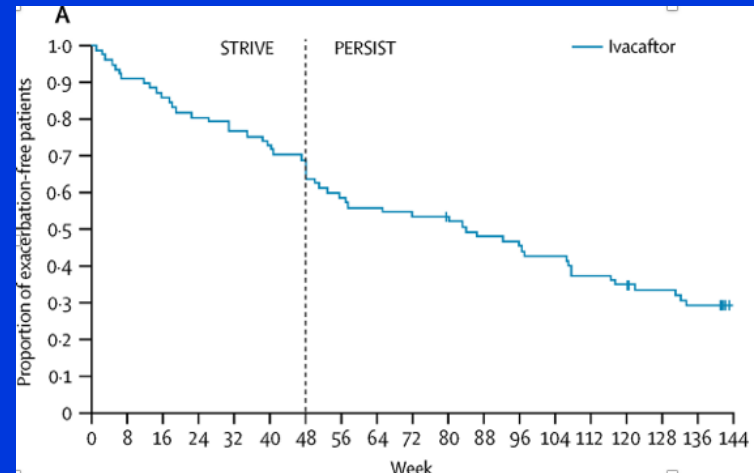


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# Conclusions

- CF registries have great potential and value for:
  - post-approval studies of newly approved CF therapies
  - phase III clinical trials
  - n=1 trial designs
- Early interaction with all stakeholders is essential to maximise effective use of registries for phase III and post-approval pharmacovigilance studies