Emerging Networks: Learning from Successful Networks

Tim Lee
European Cystic Fibrosis Society Clinical Trials Network

Enpr-EMA Annual Workshop March 22nd 2012

Parental permission obtained

Thorax 2007;**62:**723-732

Cystic Fibrosis

- Rare:
  0.74 per 10,000
  30,000 in EU
- Median survival 26-28 years
- Heavy burden of treatment to stay well
- Patients need better treatments that are easier to take

Clinical Trials Network

Abnormal Gene

Abnormal CFTR

Abnormal sodium chloride & water movement through cell

Abnormally thick and dry mucous

Bronchial airway obstruction

Infection

Inflammation

Lung damage

Thickened mucous

Release of protease & DNA

VICIOUS CIRCLE

Gene replacement

CFTR corrector, potentiator
Gene read through therapy

Ion Channel modulations
Restore airway surface liquid

Mucolytic drugs

Mucous clearance techniques

Antimicrobials

Anti-inflammatory agents

Lung transplant

Image adapted from Johns Hopkins Medicine CME "Ahead of the Curve"

ecfs ctn Clinical Trials Network

Clinical Trials in CF: What are the problems?

- Sample size
- Inappropriate inclusion and exclusion criteria
- Inappropriate / unreliable outcome measures
- Proposed new therapies not necessarily focussed on patient priorities
- Pharmaceutical companies have had difficulty accessing appropriate expert advice

Too many CF trials are underpowered

The number of controlled trials and sample size for interventions in cystic fibrosis, from 1961–1997 and 1998–2002

Intervention	1961–1997			1998–2002		
	No. of trials[a] (%)	Median sample size	Range	No. of trials[b] (%)	Median sample size	Range
Antibiotic	128 (24)	24	5–190	43 (17)	31	5–520
Physiotherapy	84 (16)	16	2–67	59 (21)	20	5–80
Mucolytic	60 (11)	20	4–968	30 (12.5)	24	7–474
Pancreatic enzyme	54 (10)	16.5	6–48	13 (5)	27	8–74
Nutrition	45 (8)	18	1–108	20 (8)	21	6–73
Gastro and liver	39 (7)	15	3–63	6 (2)	17	6–41
Anti-inflammatory	20 (4)	23.5	7–285	18 (7)	27	8–145
Bronchodilator	27 (6)	14	9–42	9 (4)	18	9–36
Gene therapy	8 (1)	12	6–16	10 (5)	13	6–44
Other[c]	64 (12)	16.5	5–397	46 (18)	19	3–749
Screening	8 (1)	1846.5	309–65,0341	1 (0.5)	109	109
Total	537			255		

[a] Excludes 7 trials where sample size was not stated.

[b] Excludes 6 trials where sample size was not stated.

[c] The intervention group 'other' includes aerosol delivery, oxygen therapy, vaccines, endocrine studies, complementary therapies and psychological studies. Note that aerosol delivery trials compare delivery devices, not pharmacological effectiveness of a drug being delivered. Thus whilst the drugs delivered may have been antibiotics or bronchodilators, if the focus of the study was aerosol delivery, not pharmacology, trials were coded as aerosol delivery trials i.e. other.

Briggs et al 2006, *J Cyst Fibros*

US Initiative: Cystic Fibrosis Foundation Therapeutics Development Network

- Established to accelerate the process of clinical research for new therapeutics
  - – Outcome measures, study design, key observational studies
- Originally 7 sites (1998), now with 77 network sites
- Industry sponsored (75%) and investigator-initiated studies (NIH, foundation funded)
- Over 200 clinical studies conducted in past 6 years (tracked)
- Network cohesion
  - – Annual in-person meeting (NACFC), quarterly newsletter, PI and RC calls
- Database to track site metrics (accessed through website)
  - – Studies conducted, start-up times, enrollment data
  - – Annual report to each site with their rank compared to peers
- Quality improvement in clinical research
  - – New web-based program built on work done over the past 5 years

Establishing a European Cystic Fibrosis Clinical Trial Network

- 2006: European CF Society priority
- A work-package titled ‘Coordination of Clinical Research’ was included in the FP6 funded European Coordination Action for Research in CF (EuroCareCF) project in 2006
- ECFS-Clinical Trials Network (ECFS-CTN) created
- 2007: Site selection survey (95 sites caring for >100 patients each)

ecfs ctn Clinical Trials Network

ECFS-CTN Site Selection

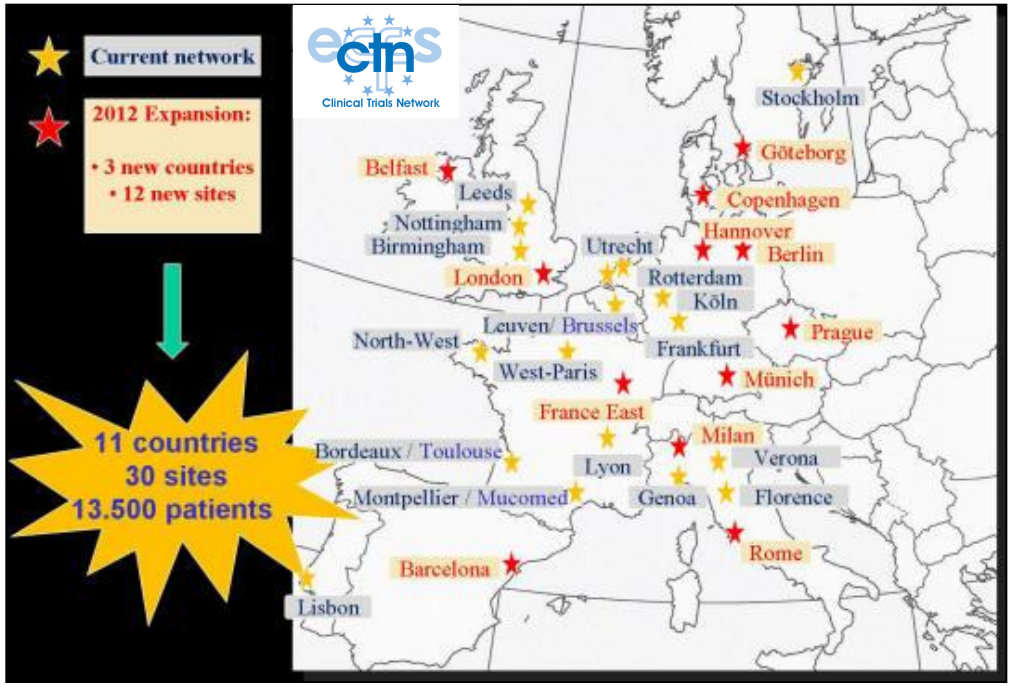
- Patient potential according to different age classes;
- Meeting the ECFS standards for standard of care;
- Experience of site director and staff in conducting clinical trials;
- Good clinical practice (GCP) accreditation of staff;
- Availability of specific measurement techniques, staff and infrastructure;
- Presence of interactive patient database;
- Proof of institutional support.

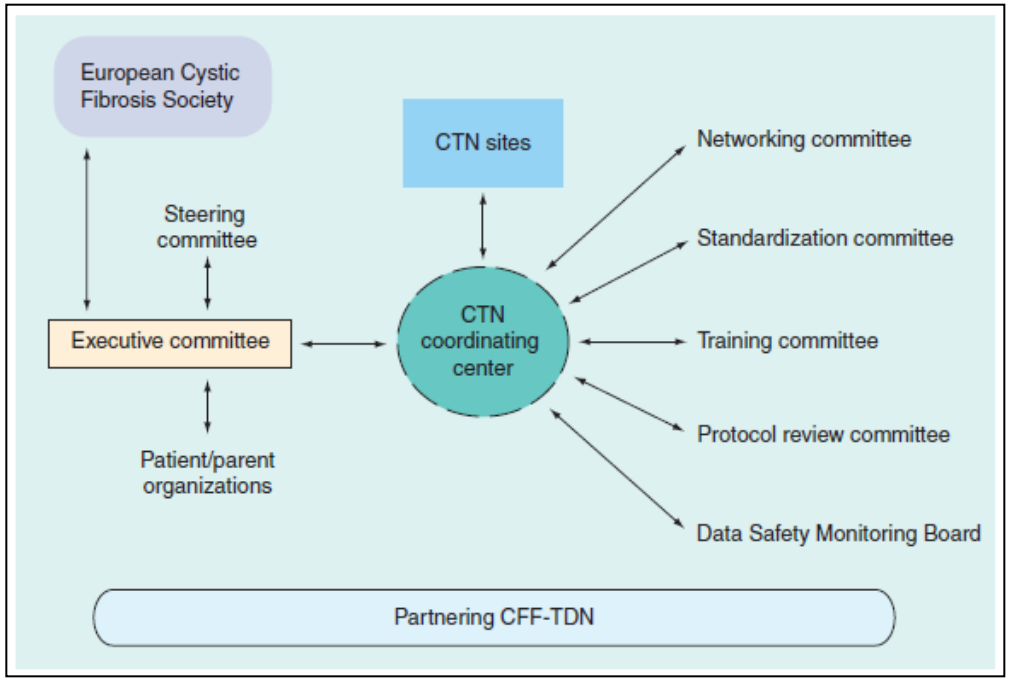
→ 18 Initial sites established in 2008, with expansion to 30 sites in 2012

ecfs ctn Clinical Trials Network

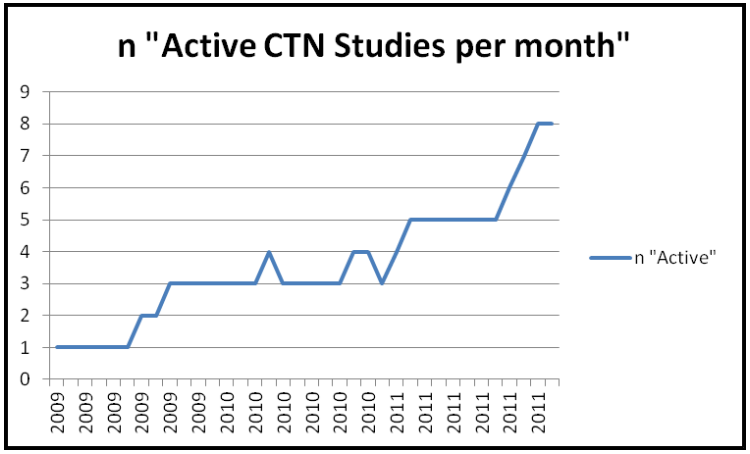
ECFS-CTN

- Close liaison with patient organisations (represented on Executive Committee and Steering Committee)
- CTN sites relay approaches re Trials to co-ordinating center
- CTN co-ordinates feasibility
- CTN protocol review process (co-ordinated with CFF-TDN)
- CTN sites run studies that are reviewed and approved by CTN
- Standardisation of outcome measures
- Co-operation with ECFS Patient Registry

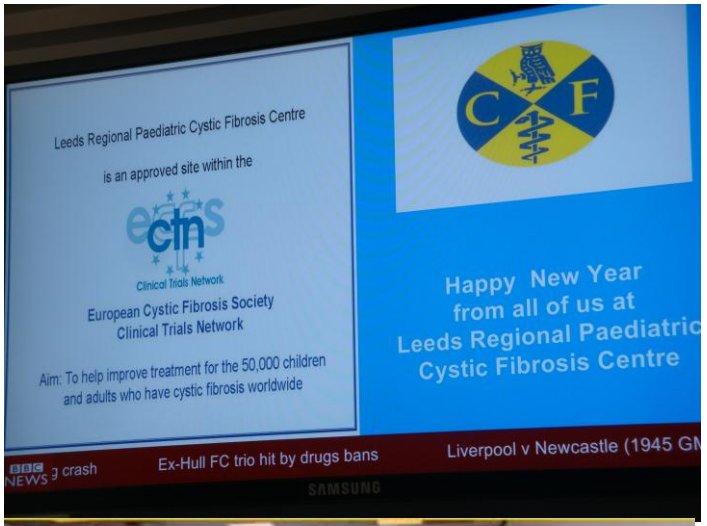




How are we doing?



- Enrollment into studies at CTN sites is greater than at non-CTN sites
- Regular meetings and training
- Patient involvement
- Quality Improvement
- Study prioritisation



Future Goals

- Aim to be involved as early as possible in protocol development (main challenge)
- Facilitating access of Pharmaceutical companies to paediatric clinical study centres and experts
- Contributing to bringing better more convenient treatments to patients

Parental permission obtained

Clinical Trials Network