EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Workshop on endpoints - cystic fibrosis clinical trials

London, 27 & 28 September 2012

Challenges: Design of clinical studies

- Advances in symptomatic treatments and patient care → great improvement of survival
- Majority of (young) children: spirometry within normal range, few pulmonary exacerbations
- Difficult to demonstrate significant changes in lung function and exacerbation rate as baseline population values improve

EMA Guideline on CF
Pulmonary disease efficacy data

Because up to now, there is no available systemic therapy to correct CFTR, the goal of therapy is to improve / maintain respiratory function, therefore delaying disease progression and increasing life expectancy.

- Clinical endpoint : assessment of respiratory function
- FEV1 is the recommended primary endpoint

Spirometry - FEV1
prime surrogate for lung disease severity in CF

- demonstrated to correlate with survival
- clinical predictor of mortality
- repeatable, reproducible results
- easy to measure
- standardised
- safe

Corey et al, J Pediatr 1997; Hayllar et al, Thorax 1997;
Belkin et al, Am J Respir Crit Care Med 2006;

Challenges for CF Drug Development : Opportunity costs

- Drug development pipeline: 25 medicinal products currently in clinical development

  http://www.cff.org/research/DrugDevelopmentPipeline

- Patient pool available for clinical trials limited
- Mutation targeted/personalized medicine development
- Need for large clinical trials of one product may hinder enrollment of patients into other trials, thus affecting opportunities to study another product

Challenges for CF Drug Development: Outcome measure

- Lung damage starting at early age
- Disease modifying drugs ideally to be administered before lung damage
- Spirometry not optimal for evaluating novel therapies aimed at earliest stages of CF lung disease

→ new measures of early lung damage are needed

- must be safe and feasible for serial testing in very young
- sensitive to meaningful changes in patient's health
- reflect meaningful clinical patient benefit

Aim of the workshop

Discuss and compile scientific evidence on outcome measures for evaluating medicines targeting

- CF lung disease
- Bronchopulmonary infection
- Exocrine pancreatic insufficiency

Expected deliverables

- Answers to list of questions
- Summarize available evidence on potential novel outcome measures
  - To lay ground for revising current EMA guideline on CF
  - To define a “core outcome set”
- Identify gaps of knowledge/need for further research
  - “To do list” for academia and/or industry to establish validity of available biomarkers as candidate surrogate endpoints

I wish us all a very successful and constructive workshop