Workshop on endpoints for cystic fibrosis clinical trials

Agenda

27-28 September 2012
European Medicines Agency, London, United Kingdom
## Programme overview

### Scope

Clinical trials in cystic fibrosis (CF) investigate a widening array of novel therapeutics addressing the basic underlying defect in CF. Advances in symptomatic treatment options and patient care have resulted in great improvement of survival with the majority of young children with CF having spirometry within the normal range and rarely experiencing pulmonary exacerbations.

This success has created challenges to the development of future CF therapies: statistically significant changes in pulmonary function and exacerbation rate become more difficult to demonstrate as baseline population values improve. Disease-modifying drugs should ideally be administered prior to development of lung damage, adding to the challenges of designing and conducting clinical trials to evaluate the efficacy of such agents.

A systematic approach to outcome-measures development is needed to provide regulators with the tools necessary for evaluating new therapies.

### Workshop chair, panellists and other experts

**Chairperson**

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<tr>
<th>Chairperson</th>
<th>Institution</th>
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<tr>
<td>Irmgard Eichler</td>
<td>EMA</td>
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**Panellists, speakers:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
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<tr>
<td>Christiane De Boeck</td>
<td>European Cystic Fibrosis Society</td>
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<td>Stuart Elborn</td>
<td>European Cystic Fibrosis Society</td>
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<tr>
<td>Elmer Schabel</td>
<td>CHMP Gastroenterology guideline drafting group</td>
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<td>Steffen Thirstrup</td>
<td>CHMP Respiratory drafting group</td>
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<td>Paolo Siviero</td>
<td>Italian Medicines Agency (AIFA)</td>
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<td>Mair Powell</td>
<td>Infectious Disease Working Party / Scientific Advice Working Party (IDWP / SAWP)</td>
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<td>Birgit Dembski</td>
<td>Patient representative, CF Europe</td>
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<td>Emma Lake</td>
<td>Patient representative, CF Trust</td>
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<td>Johannes Taminiau</td>
<td>Paediatric Committee (PDCO)</td>
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<td>Laura Fregonese</td>
<td>EMA</td>
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<td>Michael Berntgen</td>
<td>EMA</td>
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<td>Marco Cavaleri</td>
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<td>Efthymios Manolis</td>
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<tr>
<td>Concepcion Prieto Yerro</td>
<td>Committee for Medicinal Products for Human Use (CHMP)</td>
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Other experts:

Patrick Salmon        CHMP
Jane Davies           Expert - European Cystic Fibrosis Society
Harm Tiddens          Expert - European Cystic Fibrosis Society
Matthias Griese      Expert - European Cystic Fibrosis Society
Isabelle Fajac        Expert - European Cystic Fibrosis Society
Janice Abbott         Expert - European Cystic Fibrosis Society
Juliet E. Foweraker   Expert - European Cystic Fibrosis Society
Felix Ratjen          Expert - European Cystic Fibrosis Society
Maria Jesús Fernández Cortizo  PDCO / IDWP
Irja Lutsar           PDCO / IDWP
Johan W. Mouton       Radboud University Nijmegen Medical Centre
Caroline Auriche      SAWP
Robert James Hemmings SAWP
Frank Bodewes         University Medical Center Groningen
Programme details

Thursday, 27 September 2012

08:00-08:50 Registration

09:00 Start of the Workshop

Room 2A Welcome, health & safety and declarations of interests

Participants will be welcomed, instructed about health and safety issues and asked to confirm that they have no conflicts of interests in relation to any of the issues, products or applications to be discussed during the meeting.

Introduction by workshop chairperson (10’)

Brief introduction of the objectives, topics and panel/participants of the workshop.

Presentations to set the scene for the break-out group discussions

Presentation 1 CF – update: changing demographics of patient population and evolving standards of care – implications for clinical-trial design and endpoints (15’)
Speaker: Stuart Elborn

Presentation 2 Difficulties/challenges encountered – look into the future: academia perspective (15’)
Speaker: Christiane De Boeck

Presentation 3 Difficulties/challenges encountered – look into the future: industry perspective (15’)
Speaker: David Waltz (Vertex Pharmaceuticals Incorporated)

Presentation 4 Difficulties/challenges encountered – look into the future: patient perspective (15’)
Speaker: Emma Lake

General discussion (20’)

10:30-10:45 Intermission

Presentation 5 Difficulties encountered – regulatory perspective: focus on endpoints used in clinical trials
- Orphan designation, speaker: Laura Fregonese (10’)
- Scientific advice, speaker: Efthymios Manolis (10’)
- Paediatric investigation plans, speaker: Irmgard Eichler (10’)
- Marketing authorisation, speaker: Concha Prieto Yerro (15’)
- Endpoints for added clinical benefit in view of HTA, speaker: Paolo Siviero (15’)

General discussion (30’)

Workshop on endpoints for cystic fibrosis clinical trials
EMA/895687/2011
12:15-13:30  Lunch break

Break-out sessions (180’ + 15’ intermission)

Participants will be pre-assigned to the following groups.

Room 2A  Session 1:

**Pulmonary disease** (Chairs: Christiane De Boeck – Steffen Thirstrup)

*Topic 1.1*  Clinical efficacy endpoints

*Topic 1.2*  Biomarkers

*Topic 1.3*  Surrogate endpoints

*Topic 1.4*  PRO

Room 2G  Session 2:

**Bronchopulmonary infection** (Chairs: Mair Powel – Stuart Elborn)

*Topic 2.1*  General microbiological issues

*Topic 2.2*  PK/PD studies – particular focus on inhaled antibiotics

*Topic 2.3*  Microbiological endpoints
  - Antibiotic eradication therapy
  - Chronic suppressive (pseudomonas) antibiotic treatment

*Topic 2.4*  Methodological issues
  - Study duration
  - Choice of comparator
  - Study design – inhaled antibiotics: on/off regime, alternating antibiotics

Room 3C  Session 3:

**Exocrine pancreatic insufficiency** (Chairs: Johannes Taminiau – Elmer Schabel)

*Topic 3.1*  (Novel) outcome measures
  - New pancreatic enzyme products
  - CFTR modifiers

15:00-15:15  Intermission

16:45  Close of day
Break-out sessions continue (90’)
Participants continue working in pre-assigned groups.

Room 2A  Session 1: Pulmonary disease
Room 4C  Session 2: Bronchopulmonary infection
Room 3C  Session 3: Exocrine pancreatic insufficiency

10:30-10:45  Intermission

Break-out sessions continue (90’)
Participants continue working in pre-assigned groups.

12:15-13:30  Lunch break

Room 2A  Presentation of outcomes to plenary from each group and discussion

Session 1:  Pulmonary disease, Christiane De Boeck – Steffen Thirstrup
Session 2:  Bronchopulmonary infection, Mair Powel – Stuart Elborn
Session 3:  Exocrine pancreatic insufficiency, Johannes Taminiau – Elmer Schabel

General discussion

Summary and conclusions

15:30  Close of workshop