

The Innovative Medicines Initiative (IMI)



2008 Respiratory Calls:

COPD Patient Reported Outcomes
Understanding Severe Asthma

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Strategic Research Agenda (SRA): COPD, Asthma, Rhinitis



- SRA identified three priority respiratory diseases based on medical need: COPD, Asthma and Rhinitis
- For each disease key bottlenecks fall into three main areas:
 - **Disease understanding:** Epidemiology, diagnosis, assessment of severity, phenotyping, biochemical and genomic markers
 - **Translational models:** Identification and validation of new preclinical and clinical models to facilitate translational research
 - **Measuring outcomes:** Selection and validation of Patient Reported Outcome (PRO) tools that can be used to generate data to evaluate the effects of pharmacological interventions from a patients perspective. Such data can inform regulatory and payer evaluations of treatment benefit.
- Objective is to build a European Network or “Centre of Excellence” for each disease area through the life of IMI, starting with 2008 calls
 - 2008 calls will be focused on ‘Disease Understanding’ for Severe Asthma and ‘Measuring Outcomes’ for COPD
 - Calls for 2009 and beyond will speak to other bottlenecks for the three diseases

What is COPD?

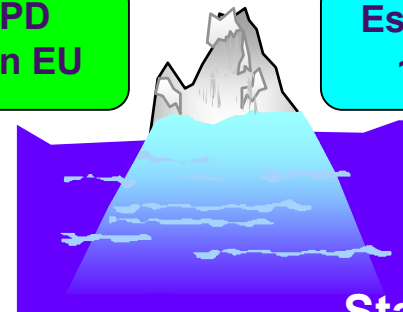


- A disease with distinct pathologies
 - Bronchitis
 - Emphysema
 - Small airway remodeling
 - Vascular remodeling
 - Systemic disease
 - Infection
- Mortality still increasing
- Causes significant disability and use of health-care resources, resulting from patients experience of daily symptoms and exacerbations
- High prevalence but under-diagnosed
 - The Fourth most common Chronic Disease
- Preventable disease
 - Caused by smoking!!!!

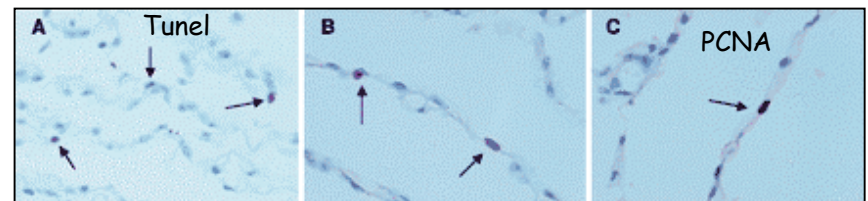


**Diagnosed COPD
~ 2.4 - 7 million in EU**

**Estimated total COPD
~ 16 million in EU**



Lung Alveoli in Emphysema



Extensive apoptosis and cell division

2008 COPD Patient Reported Outcomes (PRO) call: Background



- Evaluation of efficacy of new therapies has relied on the demonstration of reduction of airflow obstruction.
 - This does not capture the potential benefits that the patients experiences
 - Capturing the COPD patients' experience of the disease and effects of treatment is key to evaluating treatments for COPD
 - European Regulatory guidelines recommend the use of symptom endpoints, in addition to lung function measurements, for evaluating treatments for COPD
- A PRO is any report coming directly from patients, without interpretation by physicians or others, about how they function or feel in relation to a health condition and its therapy. PRO Measurement tools should be generated with adequate patient input.

Important aspects to measure when evaluating outcomes of treatments for COPD.



- A patient with COPD experiences a variety of symptoms including dyspnoea (shortness of breath).
 - Symptoms of COPD restrict patients' ability to perform daily activity and also results in psychological consequences resulting in significant impairments to overall health status.
- COPD patients also experience acute worsening of their symptoms- exacerbations- that often require a change in their treatment, sometimes even requiring hospitalization.
- There is a need for scientifically developed and validated PRO measures that capture symptoms, exacerbations and their impact on patients
 - Enable solid evidence on outcomes that reflect the patients' perspective on product label claims.

COPD call: What are we trying to solve?



- **Objectives**

- Understanding of the patients' experience of COPD to inform the **strategy to measure outcomes** that are relevant to patients for assessing treatment benefit
- Selection and/or Development of measures with good measurement properties that capture the COPD patients' experience of the disease and effects of treatment
 - To inform the definition of exacerbation
 - Understand day-to-day experience of symptoms
 - Evaluate impact of these symptoms

- **Scope**

- To build **consensus on the measurement strategy, especially PRO tools**, by working with the key consumers of the information on treatment benefit:
 - Clinical practitioners, academic clinical & health outcomes researchers, patients and payers

COPD call: What are we expecting and going to do?



Deliverables

- A measurement strategy that includes specific PRO tools:
 - Developed using robust psychometric methods
 - With input from and review by the major customer groups
 - Validated for use in treatment evaluations across Europe that can link to global efforts
 - Using appropriate prospective studies
 - Developed or adapted for capturing data using electronic data capture (EDC) devices for daily recording at home

COPD call: What are we expecting and going to do?



Project plan outline

- Planned in two phases :
 - **Phase A**: Develop a framework to understand the Patients experience of COPD, especially in the European context, to inform strategies to measure outcomes meaningful to patients in global clinical trials
 - **Phase B**: Develop/select and validate PRO measurement tools, to use in clinical trials evaluating treatments for the disease

COPD call:

What is expected from a public Consortium?



A Consortium or 'Centre of Excellence'

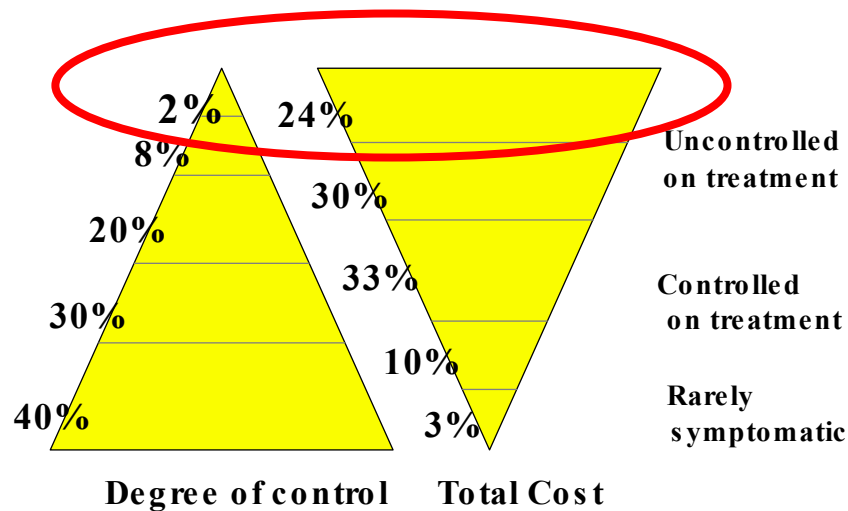
- To develop a measurement strategy to evaluate the benefits of COPD treatment from a patients' point of view
 - With contributions from the key customers and 'Subject Matter Experts'. For example...
 - University
 - Clinical centres
 - SME researchers
 - Patient groups
 - EMEA
 - Payers
 - Health Technology Assessment agencies
 - Agencies that make decisions about reimbursement
- ***It is important to link to and build on existing 'Initiatives for the measurement of PROs in COPD' to avoid redundancies***

Asthma an illness that afflicts all ages



1. Mild and moderate disease
 - Controlled for most patients
2. The most successful classes of drugs:
 - 35 years old

3



Understanding Severe Asthma Call: Background



- There is high unmet need for more effective, convenient and safe therapies, particularly for patients with moderately severe and severe disease.
- 10% of asthmatics with the most severe disease account for up to 50% of the total costs of asthma care.
- Disease understanding including epidemiology, diagnosis, assessment of severity, phenotyping, biochemical and genomic markers of severe asthma is key

Understanding Severe Asthma call: What are we trying to solve?



- **Issues, Needs, Background**

- A. Understanding natural history of severe asthma and disease mechanisms presents considerable challenges in the setting of disease heterogeneity, including its frequent co-morbidities
- B There is a need for further development of internationally agreed diagnostic criteria for mechanistic and therapeutic trials,
- C Need for research into disease mechanisms to provide for true-disease modifying therapeutic opportunities, biochemical and genomic biomarkers to identify patient characteristics associated with different phenotypes
- D There are groups working independently to address some of these questions. Need for standardised approach

- **Scope**

- **The asthma call for 2008 is to build an EU Severe Asthma network focused on disease understanding.**

Understanding Severe Asthma call: What are we expecting and going to do?



- **Deliverables**

- EU and globally agreed (ERS/ ATS as well as regulatory agencies) diagnostic criteria for severe asthma
- Identification as well as subsequent validation of novel targets for pharmacological intervention and biomarkers to assess pharmacological response or predict effects on clinical outcomes
- Understanding of aetiology and pathogenesis of asthma exacerbations as mechanism to identify new targets and therapeutic approaches
- Accurate targeting of an intervention to a particular, well-defined patient sub-population.
- Capability to develop translational models for appropriate prediction of clinical relevance through preclinical modelling.
- Access to defined patients which will facilitate enrolment and study of patients for clinical trials by academic and pharmaceutical research.

- **Project plan outline**

- 1 Consensus meeting
- 2 Form a scientific committee
- 3 Define common protocol for patient identification and assessment together with a common database or prospective registry
- 4 Undertake cross sectional and longitudinal study

Understanding Severe Asthma call: What is expected from a public Consortium?



A Consortium or 'Centre of Excellence'

- With contributions from the key customers and 'Subject Matter Experts'. For example...
 - University
 - Clinical centres
 - SME researchers
 - Patient groups
 - EMEA
 - CRO
- Other global initiatives to be followed/contacted to avoid redundancies and build on synergies

The utility of a properly constructed and maintained patient cohort

