How to speed up clinical trials and what can patients do?

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Outline – 10 minutes

• General overview of the products from the 3 FP7 consortia
  • Asterix
  • Ideal
  • Inspire

• The patient perspective
  • Registries
  • The POWER-tool
  • Goal Attainment Scaling
The 3 FP7 consortia

FP7 Call – HEALTH.2013.4.2-3
New methodologies for clinical trials for small population groups

Three projects were funded:

- **ASTERIX** (PI Kit Roes)
  Advances in Small Trials dEsign for Regulatory Innovation and eXcellence

- **IDeAl** (PI Ralf-Dieter Hilgers)
  Integrated Design and AnaLysis of small population group trials

- **InSPiRe** (PI Nigel Stallard)
  Innovative methodology for small population research
• statistical design innovations in **individual and series of trials**
• **framework for rare diseases** wrt rational trial design choices
• include **patient level info & perspectives** in design and decision making throughout the clinical trial process
• re-consider the scientific basis for **levels of evidence** to support decision making at the regulatory level
• **validation of new methods** against real life data and regulatory decisions
• assessment of **randomization**
• extrapolation of **dose-response information**
• **adaptive** trial designs
• optimal experimental designs in **mixed models**
• **pharmacokinetic** and **individualized designs**
• **simulation** of clinical studies
• involvement and identification of **genetic factors**
• **decision-theoretic** considerations
• evaluation of **biomarkers and surrogate endpoints**
• early dose-finding trials
• decision-theoretic designs
• confirmatory trials in small trials and personalized medicines
• evidence synthesis in planning and interpretation of clinical trials in small populations
The POWER-tool

Patient participation in Outcome Measure WEighing for Rare diseases

A tool for investigators to involve patients in determination of outcome measures and choice of measurement instruments

3 steps approach

Developed together with Asterix Patient Think Tank and end users

Road-tested in ongoing SMA trial

Goal Attainment Scaling

1. What are your goals?
2. Definition of 5 levels of attainment per goal
3. Which goals are most important to you (weights)?
4. Intervention
5. Independent assessment:
   At what level is each goal attained?

When is GAS useful?

Useful:
• Chronic disease
• Effect of intervention expected on behavioral ability, that can be assessed independently
• Concurrent blinded controls

Not useful:
• Acute, episodic or unpredictable diseases

Patient Involvement in Rare Disease Clinical Research

What is the issue?
Imagine three boys with a rare, severe, life-threatening disease, who are in different stages of the disease. For the three boys, the disease is different, but they all have the same disease. Regular measurement instills hope that with care and support, the disease may be better. How can we measure when the disease becomes a success?

Why should patients be involved?
Patients and parents of a child with a rare or ultra-rare disease can make an important contribution to the diagnosis, treatment, and care of the disease. They know their children's needs and are in a unique position to provide information about their experiences and perspectives. This information can be crucial for research and development.

What is the process?
1. First, a doctor or therapist decides what the goals of the disease are, and they can be defined in five years. The goals can be ordered in terms of importance.
2. The patient receives the intervention, which may be a new drug or something else. Preferably, the patient and doctor do not know what the intervention is called true intervention and what is to be studied is called blinding.
3. The patient and doctor are examined later to check if the goals have been attained.

Roles of Patients in Clinical Research
This diagram represents the different roles that patient representatives play in the clinical trial process: a research subject, an information provider, an advisor, a reviewer, a co-researcher and a driving force. This diagram was developed in the EU project Patient Partnership based on the Participation ladder of American, a vertical ladder. All roles are necessary and important, and there is no hierarchy of one above the other, thus the ladder was turned. Patients can be involved in clinical trials in various ways: setting the research agenda, design of clinical trials, recruitment and dissemination of the results. The Asterix project studies the design of better clinical trials.

Example: Cystic Fibrosis registry
Disease: progressive, genetic disease affecting the lungs and intestines. Buildup of mucus in the lungs limits breathing and causes lung infections. Life expectancy is between 42 and 50 years.
Goal of registry: to measure aspects of CF and its treatments, to provide data for epidemiological research and drug development, and identification of specific groups for clinical trials (feasibility).
Examples of variables included: gender, age (demographic), first/second mutation (diagnosis), antibiotics, pancreatic enzymes (treatment), 1 minute forced expiratory volume (FEV1), survival (outcomes).

What to do need to take
European collaborations on patient involvement

http://www.asterix-fp7.eu
Let’s work together!

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Decision makers need evidence

The European legislation on orphan medicinal products [Regulation (EC) No 141/2000] emphasises that patients suffering from rare conditions should be

• “... entitled to the same quality of treatment as other patients.”

• Current rationale is to present evidence at the same confidence levels

• Small populations guidance does stimulate alternatives for design and analyses

• Careful case-by-case decisions are made, that essentially may “relax” level of evidence