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

asterix

- 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

Universitair Medisch Centrum Utrecht

VSOP

amc

Academisch Medisch Centrum
Universiteit van Amsterdam

MEDICAL UNIVERSITY OF VIENNA

PSI

MHH Medizinische Hochschule Hannover

UAB Universitat Autònoma de Barcelona

Integrated DEsign and AnaLysis
of small population group trials

- 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**

InSPiRe
Innovative methodology for small populations research

- 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 UNIVERSITY OF WARWICK

UNIVERSITÄTSMEDIZIN GÖTTINGEN UMG

MEDICAL UNIVERSITY OF VIENNA

Inserm
Institut national de la santé et de la recherche médicale

BfArM
Bundesinstitut für Arzneimittel und Medizinprodukte

Stockholms universitet

QUINTILES

CTCT Clinical Trials Consulting & Training Limited

The POWER-tool

Patient participation in **O**utcome **M**easure **WE**ighing for **R**are 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

Gaasterland et al. Health Policy 2018 Dec;122(12):1287-1294.

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?

Kiresuk and Sherman, Community Mental Health Journal 1968; 4 (6): 443.

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

Gaasterland et al. BMC Med Res Methodol. 2016;16:99.
Urach et al. Stat Methods Med Res. 2018:962280218777896.

Goal Att

Patient Involvement
in Rare Disease Clinical Research

es (RDRs)

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What is the issue

Imagine three boys with a
who are in different stages
three boys have different t
Regular measurement inst
specific enough to capture
How can we measure whet
successful?

What is the proce

1 First, a doctor or therapist
decide what the goals of t
they can be defined in five
can be ordered in terms of

2 The patient receives the in
may be a new drug or som
or a placebo. Preferably wh
patients and doctors do no
'true' intervention and wh
is called blinding.

3 The patient and doctor ass
have been attained. We ex
received the 'true' interver
goals and have a higher sc

Why should patients be involved?

Patients and parents of a child with a rare or ultra-rare disease can make an important contributi
becoming a success. As patients manage their disease on a day to day basis, they have
aspects of their disease should have priority for further investigation by research
unique perspective based on this experiential knowledge. Patients shou
measures in a trial and the composition of patient information
participation for them and their families, and can help
In this leaflet, we will show how patients can be

ted in a standardized
's' diagnosis, or type
le about the disease
ion about the variability and
tments are developed.

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 treatment, 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)

Co-researcher

Driving force

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 partner, based on the Participation ladder of Arnstein, 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

European collaborations on patient involvement

What to do we need to take

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