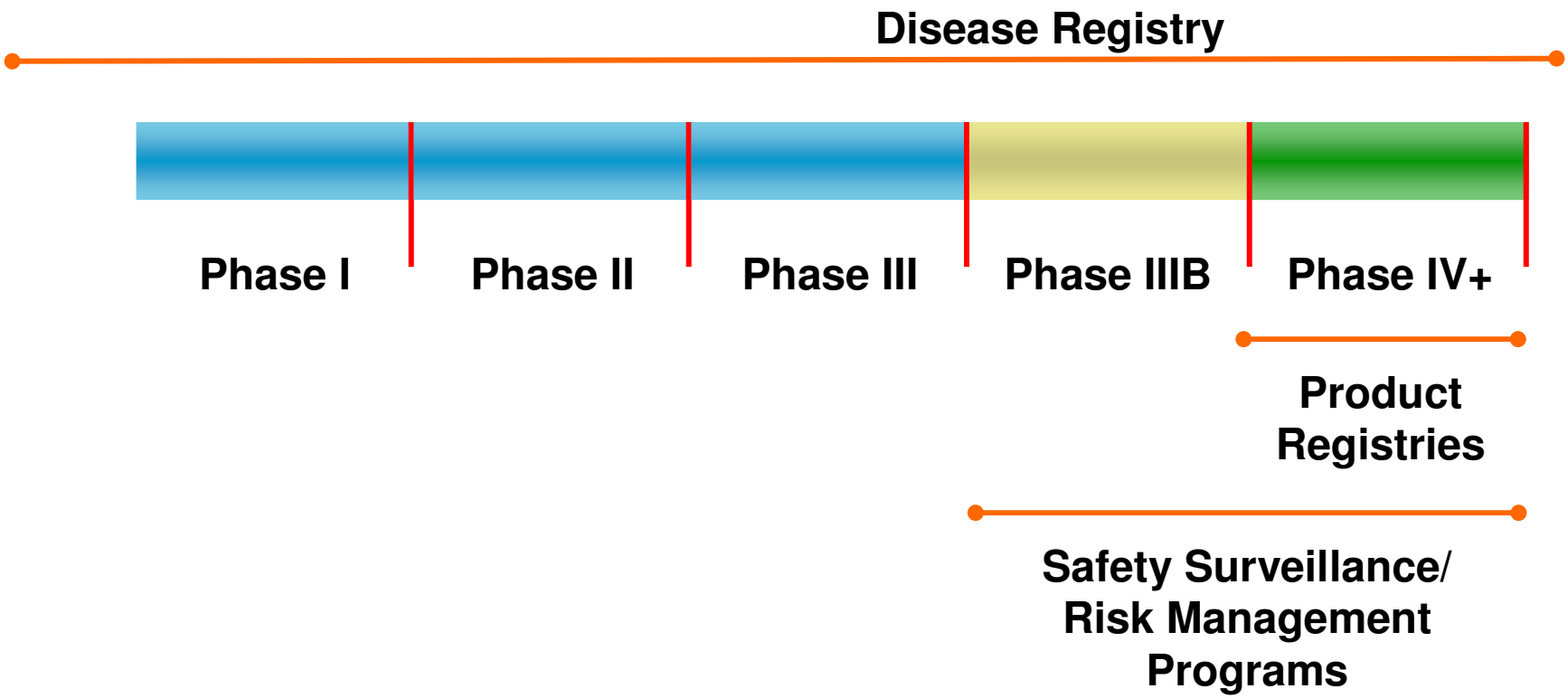
# Making the most of patient registries

*Elizabeth Hernberg-Ståhl M.Sc.*
*Late Phase Solutions Europe AB*

*Rare Disease Research Forum- Challenges and Solutions*
*Stockholm KI, February 21, 2011*

# The value of starting Patient Registries in early phases for Rare Diseases




Late Phase Solutions Europe

# Patient Registry Definition

” an organized system that uses observational study methods to collect uniform data (clinical or other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves a predetermined scientific, clinical, or policy purpose(s)”[1]

[1]Registries for evaluating patient outcomes: a users guide, AHRQ No 10-EHC049-1, September 2010

Late Phase Solutions Europe

# Randomized Clinical Trials (RCTs) vs Patient Registries

| Randomized Controlled Trials (RCTs) | Patient Registries |
| --- | --- |
| Small group of patients | Large, varied group of patients |
| Small number of treatment centres | Many treatment centres (multinational) |
| Rigid visit and dosing schedule | Visit and dosing schedule as per normal clinical practice |
| Restricted concurrent treatments and co morbidities | No restrictions on concurrent treatments and co morbidities |
| Treatments used as intended | Treatments used as per normal clinical practice |
| Comparatively short time-frame | Extended time-frame |
| Provide evidence of the *efficacy* of treatments in a highly controlled environment to reduce bias | Provide evidence of the *effectiveness* of treatments in the real-world |

**The use of treatments in the real-world is different to the use of treatments in the controlled environment of an RCT**

Late Phase Solutions Europe

# Hierarchies of Evidence are shifting; observational studies are no longer viewed as ”second class”

Vandenbroucke J. Observational Research, Randomised Trials and two views of Medical Science *PLOS Medicine 2008*

While RCTs are best for **evaluation** of interventions, they are poor in discovering assocations or explaining diseases.

Observational research is best at **discovery** and **explanation**.

Therefore, two hierarchies exist and both are needed.

- *”Without new discoveries leading to potentially better diagnosis, prevention, or therapy, what would we do clinical trials on?”*

Late Phase Solutions Europe

# NICE's Rawlins questions dependence on RCTs

**Press release Royal College of Physicians 16 October 2008**

"Randomised controlled trials…have been put on an undeserved pedestal. Their appearance at the top of "hierarchies" of evidence is inappropriate; and hierarchies, themselves, are illusory tools for assessing evidence. They should be replaced by a diversity of approaches that involve analysing the totality of the evidence-base…"

Sir Michael outlines limitations of RCT in several key areas:

Impossible-with treatments for very rare diseases where the number of patients is too limited

Late Phase Solutions Europe

# Orphan Drugs and Diseases

## Characteristics

- Restricted information from randomized clinical trials (RCT)
- Often conditional regulatory and reimbursement approvals
  - Need for real world data
- Low disease awareness, which affects referral and diagnosis
  - Need for communication
- Not optimal disease management
  - Need for improved treatment guidelines

Late Phase Solutions Europe

# Patient Registries for regulatory purposes

- Fulfils the increasing demands from FDA (FDAAA) and EMA on risk minimization plans.
- Meets the increased demands from reimbursement bodies and payers on data on long term effectiveness.

- Provides insight on current patterns of care which can be used to improve the evidence-based management of patients

Late Phase Solutions Europe

# Regulatory driven Patient Registries for Lysosomal Storage Disorders (LSD) and Drugs

- Evidence of real-world patient benefit;
  - Patient cohorts excluded from initial RCT (e.g. gender, age) benefit from treatment
  - Established cohort from which to address further information needs (hypothesis generating)

- Important tools in connecting network of expertise

  - Continuously increased knowledge about the diseases, earlier diagnosis and continually improved patient management to the benefit of all stakeholder, especially patients

Late Phase Solutions Europe

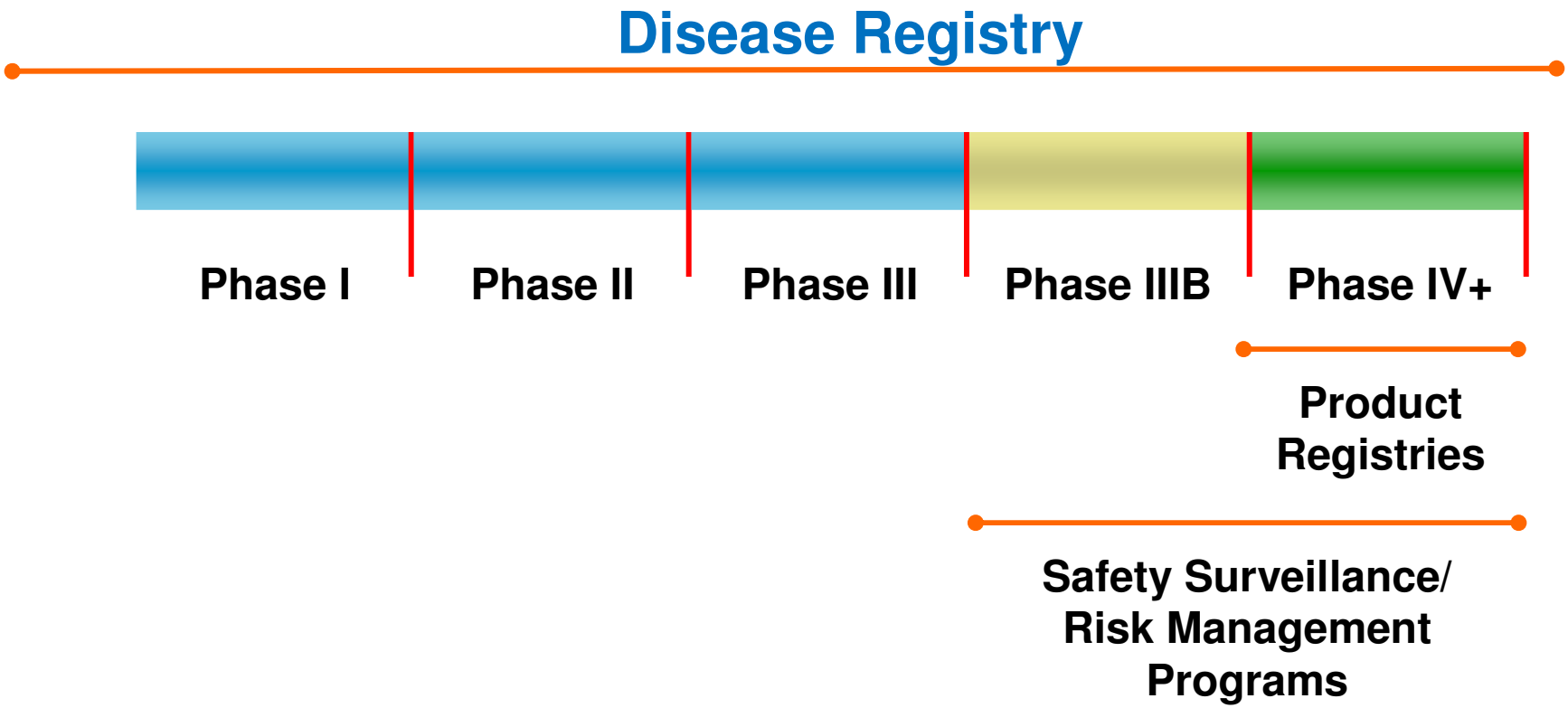
# Challenges/Short comings of many registries on Orphan Drugs

- What is an acceptable treatment outcome in a progressive disease?
  - Slower progression?
  - Stabilization?
  - Regression to normal?

- What to compare with?

- Often limited unbiased natural-history data available

# Value of “early” Natural History Data




Late Phase Solutions Europe

# Value of Rare Disease Patient Registries

- Better understanding of the natural history of the disease
- Develop sensitive Disease Severity Index
- Identify Genotype/phenotype correlations
- Collected natural history data can be used to develop and refine disease specific QoL questionnaires to collect patient perspective
- Collaboration research teams and patient organization and industry to help identify end points as well as effective patient recruitment for clinical trials
- To set the scene for collecting long-term real world data, as required by regulators and policymakers

Late Phase Solutions Europe

# Status Patient Registries for Rare Diseases

- Many research teams and patient organizations are setting up natural history databases or registries.
  - -244 rare disease registries registered on ORPHANET*.
  - -There is often duplication of efforts and researchers or patient associations are running uncoordinated initiatives

- A need of collaboration/coordination on a global level to not dilute knowledge on the few available patients

- Challenges when running patient registries:
  - -resources for analysis and programming, manuscript preparation
  - -resources to ensure continuous data entry, data quality and completeness.

Late Phase Solutions Europe

*Source: EPPOSI workshop on patient Registries, Brussels March 18-19, 2009

# A value to link data from different sources

*Generic Standards;*

- CDISC/CDASH
- HL7
- PhenX toolkit

*Several initiatives for harmonization and linking data from different sources:*

- National e g Swedish Association of Local Authorities and Regions (SALAR); proposition for 2011-2015
- European e g EHR4CR project (IMI)

Late Phase Solutions Europe

# The power of Patient Registries in general

- Increase the knowledge about diseases leads to improved care for the patients
- Contribute to improved awareness and understanding of disease and treatment practices – where the patient are the "winner"
- Being an important tool in connecting network of expertise

---

- *Fulfils the increasing demands from FDA (FDAAA) and EMA .*
- *Meets the increased demands from reimbursement bodies and payers on data on long term effectiveness.*

Late Phase Solutions Europe

# Patient Registries for Rare Diseases

- Few patients available avoid dilution of information
- Need for global collaboration to utilize all available knowledge and avoid double efforts
- Need of harmonized standards to be able to link data and knowledge
- There are several stakeholders involved, registries needs having multi purposes
- Collection of Natural History data is very important
- Output from registries are crucial to increase knowledge of rare diseases and best practices to

Late Phase Solutions Europe

*Improve Patient Management and Care*