A continuum approach to evidence generation in post-approval phase linked to healthcare budget spending

D. Ardigò, MD PhD

R&D Rare Disease Unit Head
Corporate Research & Development
Chiesi Farmaceutici S.p.A.
Disclaimer

The opinions expressed in this presentation are the results of my own personal perspective and should NOT be considered as representative of the opinions and views of Chiesi Farmaceutici SpA or IRDiRC.
GOAL 2: More than 1000 new drugs in the next 10 years to treat rare diseases
Development of a drug (small molecule, large indications)

**Pre-clinical package to support FIH**
- Proof-of-Concept
- PK/ADME
- Genotoxicity
- Safety pharmacology
- Acute/short-term toxicology

Two species tox

**Information package**
- Animal ADME
- Safety and short-term tox
- NOAEL (MABEL)

**Phase I**
- Safety & PK in healthy volunteers
- Food effect
- DDI and special populations safety/PK
- Cardiac safety
- Bioequivalence (new formulation)

**Phase II**
- Safety & PK in patients
- PoC
- Dose selection
- Long-term toxicology

**Phase III**
- Two pivotal trials
- DDI and special populations safety/PK
- Cardiac safety
- Bioequivalence (new formulation)

**Post-approval**
- PASS/(PAES)
- Registries
- Additional PV
- Phase IV studies
- Pediatric studies

**Information package**
- Pivotal efficacy
- HTA data
- "Large"safety database
- Data in special populations and sub-groups

**Information package**
- Proof-of-efficacy
- Dose-response
- Phase III dose
- Phase III sample size

- Consolidated
- Based on risk management and gate reviews
- Almost linear progressive increase in costs
- Long-term predictability

MA
Consequences of rarity in drug development

- Less understanding of disease mechanisms and progression
- Less confidence in PoC and dose
- Lower statistical power in pivotal studies
- Lower confidence in traditional end-points
- “One shot only”

RISK CARRY OVER

- Risk Management
- Post-approval data
- Value uncertainty
Where to act…

- A better use of the tools that we already have
  - EJP-RD
  - IRDiRC Drug Development guide
  - Repurposing

- Integrate care, research, and development
  - Disease registries
  - Clinical and research networks

- New models to fund access to innovative treatments
  - Reimbursement models and payment schemes
  - Centralized HTA
Registries and data creation
A registry is...

“A patient registry is an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes.”

Expectations…

- **Physicians**: Improve disease understanding and management for themselves and future patients.
- **Regulators**: Statistically-inferable, GCP-compliant data to inform benefit-risk decisions, especially in sub-populations.
- **Industry**: Generate R&D data for label confirmation/expansion in parallel with commercial returns.
- **Patients**: Generate valuable population data for clinical decision making and scientific advancement.
- **Payers**: Establish value-for-money in individual reimbursed cases.
## Types of registries

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Post-approval Registry / PASS / PAES

- **It is NOT** a traditional study
  - Living organism
  - Multiple stakeholders

- **It IS** a full clinical trial
  - Detailed protocol
  - Real study (CRF, monitoring, etc.)

- **It is an heavy study**
  - Interim analysis (every year)
  - Reconciliation between database and pharmaco-vigilance system
  - Costly study (number of countries and centers “disproportionate” to the number of patients)
A vision for the future: a multi-sided reality…

- **PATIENT**
  - Electronic health record
  - PROs and other patient-data collection

- **PHYSICIAN**
  - Electronic health record
  - “Consumer’s” analytics

- **RESEARCHER**
  - Data collection
  - Observational or interventional research

- **INDUSTRY**
  - Understand natural history
  - Generate RWE for benefit/risk

- **REGULATOR**
  - Assess benefit-risk
  - Perform GCP audits

- **PAYER**
  - Confirm value in the population
  - Assess response in the single

- **PLATFORM PROVIDER**
  - Independent provider
  - Different data quality levels
  - Business model similar to Google, LinkedIn, etc.