Clinical Research in Neurosciences: challenges and new frontiers

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Today’s Agenda

The Context

Key challenges and complexity

New frontiers

Conclusion
Once upon a time …
Roche Neuroscience focuses on three disease areas

**Psychiatric disorders**, including schizophrenia and treatment-resistant depression. Focus on treating negative symptoms and cognition.

**Neurodegenerative disorders**, including Parkinson’s disease, Alzheimer’s disease and Multiple Sclerosis. Focus on an early intervention and selection of patients eligible for a specific treatment based on biomarkers.

**Neurodevelopmental disorders**, including autism spectrum disorders, Down syndrome and Fragile X. Focus on the treatment of core symptoms, like social interaction, communication deficits and restricted repetitive behaviors.
Clinical Research: Current Trend Impacting Factors

Unsustainable R&D Costs

Estimated cost of bringing a new chemical or biological entity to market in USD million

199 226 451 625 1,031 1,506


Long start up and conduction timelines

Drug Life Cycle « Current Trend »

- Long start up and conduction timelines
- Increasing complexity
- Low development success rate
- Unsustainable R&D costs
- New regulatory/reimbursement requirements
Clinical Research in Neuroscience

- High cost of research and development of new molecules in neurology
- Delayed development of new drugs
- Low development success rate (number of inconclusive and/or negative studies)

CNS is perceived as high level risk area
Low development success rate

2002-2012: from 244 new drug in clinical development for Alzheimer's disease to 1 approval drug by FDA

Source: www.phrma.org
The most of current failure in phase II

Failure and delays resulting from suboptimal choices in four key areas:

1. Initial test subjects
2. Dosing and administration
3. Sensitive and early detection of therapeutic effect
4. Recognition of differences between animal models and human disease

Hurko et al. 2005
The Context

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- Recruitment hurdles
- Clinical endpoints and biomarkers
- Placebo effect

PATIENT POPULATION
- Patient Flow
- Rarity of Patients
- Physical Immobility
- Co-morbidities
- Concomitant treatments
- Ability to provide consent
- Compliance to study drug

SOCIAL CONTEXT
- Involve Caregiver
- Few disease awareness
- Social Stigmatization

STUDY
- Complexity of Study Design
- Screening Procedures
Key challenges and complexity

- Target population and management
- Clinical endpoints and biomarkers
- Placebo effect

It is expected to demonstrate efficacy on both a cognitive and a functional or global assessment scale.

Diagnose the disease in its early stages through the use of biomarkers to allow an early therapeutic intervention.
Key challenges and complexity

- Target population and management
- Clinical endpoints and biomarkers
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Innovative approach in clinical research

**Personalized Healthcare**
- To better understand disease diversity
- To identify the differences between patients
- To identify the best drug targets

**Patient Centric Model**
Easily and quickly reach targeted patients for clinical trials

**New Technologies**
- Biosensors/devices to objectively measure data traditionally self reported
- Provide an early intervention/coaching to enhance patient compliance and safety oversight

**Decentralized Trials**
- Increase trial participation/retention/compliance
- Ex. Mobile nurse, remote monitoring

Group of patients with the same syndrome
Adaptive design and Adaptive licensing

- Adaptive design trials offer flexibility and the potential to identify failures earlier and increase efficiencies by focusing resources on therapies that have a greater chance of success.
- Adaptive-licensing approach is based on a prospectively-planned process.

**ADAPTIVE DESIGN**

**Benefits to patients**
- Reduce the number of patients exposed to non-efficacious doses of the experimental drug.
- Early stopping so treatment practice can be changed rapidly.

**Benefits to the scientific quality of the study**
- Learn during the conduct of the study by improving the quality of decisions e.g. doses or schedules.
- Increased statistical power and precision of effect estimation.

**Benefits to Project overall**
- Improve project management and efficiency.
- Enhance efficiency and potentially decrease the duration of drug development.

**ADAPTIVE LICENSING**

Maximise the positive impact of new medicines on public health by balancing the need for timely patient access with the importance of providing adequate, evolving information on a medicine’s benefits and risks.

Particularly relevant for medicines with the potential to treat serious conditions where there is an unmet medical need.

European Medicines Agency launches adaptive licensing pilot project

Press release

19/03/2014

European Medicines Agency launches adaptive licensing pilot project

Improving timely access for patients to new medicines: pilot explores adaptive licensing approach with real medicines in development.
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Challenges and Opportunities

- High complexity
- Low development success rate

- Innovation
- Adaptive design and licensing
Why the investment in neurosciences?

Diseases of the nervous system may affect people in any stage of their lives and can substantially interfere with individual’s ability to live an independent and fulfilling life. This may cause a significant strain not just on the patient but also on families, caregivers and society.

We can build a better future with medicines that make a real difference to patients.
Doing now what patients need next

«Don’t be satisfied with the horizon, keep looking for infinity » Jim Morrison