Dostępność nowoczesnych terapii, – dokąd zmierzamy i co nas czeka w przyszłości?

Availability of modern therapies – where we are heading and what’s the future?

Nick Sykes
Senior Director, Pfizer
(on behalf of EFPIA)
The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the pharmaceutical industry operating in Europe. Through its direct membership of 33 national associations and 40 leading pharmaceutical companies, EFPIA is the voice on the EU scene of 1,900 companies committed to researching, developing and bringing to patients new medicines that will improve health and the quality of life around the world.

EFPIA sees the implementation of the Clinical Trials Regulation as an opportunity to demonstrate Europe’s commitment to clinical innovation, scientific collaboration and transparency of clinical trials information. Successful implementation of EU CTR is one of EFPIA’s priorities.
Aim of today’s presentation

• Outlining challenges in clinical development of new drugs
• Providing an overview of some of the ways we are changing how we manage and run clinical trials
• Addressing some of the challenges and highlighting the opportunities
Challenging global medicine development environment

- Challenging Intl’ environment
- Evolving science
- R&D costs escalation
- Heterogeneous CTA timelines
Rising to the Challenge

- Making crisp, objective decisions
- Allocating resources appropriately
- Looking for ‘early signs of clinical activity’ & “Killer” experiments
- Increasing Phase 2 success Rates
- Improving cycle time
- Seeking expedited pathways

Results being seen: Recent big ‘game-changers’:
- Cures for Hepatitis C
- Immuno-oncology
Current Challenges in Clinical Development: Solutions being Adopted

• Greater efficiencies in running trials using innovative trial design approaches and technology

• Move towards a patient-centered approach to drug development
  • Personalized treatments
  • Drug-diagnostic co-development

• Research and care need to be better integrated, anticipating real life implementations
Adaptive Clinical Trial Design

Many designs possible

- Sample Size Re-estimation
- Seamless Phase
- Dose Selection
- Group Sequential
- Bayesian Borrowing
- Dose Allocation
- Model-Based Dose Escalation
- Population Enrichment
Paving the Way for Innovation

Will the EU Clinical Trial regulation meet its stated objective of quicker access to new and innovative medicines?
### Regulatory Guidance

<table>
<thead>
<tr>
<th>Activity</th>
<th>Changes brought by CTR</th>
<th>Risk/Opportunity for Adaptive design</th>
<th>Mitigation/Action</th>
</tr>
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</table>
| Assessment        | • Centralised Assessment  
                   • Loose criteria for a country to opt-out | • Issues with one MS might impact the others  
                   • Countries opting out  
                   • Easier operationally | • Choice of the RMS will be key  
                   • Implementation: No substantial amendment should be required to submit interim analysis |
| Interim Analysis  | • Potential for alignment on submission of interim analysis | • If substantial amendment requested, it might cause delays  
                   • Consistency | |

- Sharing experiences between Member States
- EU guidance could be updated to get alignment between MSs and between EMA and MSs
- In addition, possible ICH guidance
Strategic Planning

**Activity**

- **Substantial amendment**
  - Comments to be provided on time

- **Protocol writing**
  - Protocol needs to be strategically written to allow for operational flexibility to match adaptability of design

**Changes brought by CTR**

- Failure by the sponsor to provide comments in time will result in automatic withdrawal from the process.

**Risk/Opportunity for Adaptive design**

- RMS to assess protocol in the round

**Mitigation/Action**

- Sponsors must therefore set up efficient systems to engage with the new approach
- Protocol needs to explain:
  - Sponsor’s decision making process
  - Set boundaries
  - When sponsor will go back to regulators
Timing for Changes

Activity: Adding a country & Substantial Amendments: new sites etc.

Changes brought by CTR:
- Adding a country cannot be in parallel of initial approval & no substantial amendment possible in parallel
- Potentially longer assessment timelines

Risk/Opportunity for Adaptive design: Risk of delay

Mitigation/Action:
As those are key enablers of the adaptability of the design, Sponsors could:
- Strategically plan within protocol
- Take advantage of the sequential submission of part I and part II
Transparency

- **Activity**
- **Changes brought by CTR**
- **Risk/Opportunity for Adaptive design**
- **Mitigation/Action**

**Interim analysis**
- Summary of 'intermediate' analysis to be published within a year of analysis date

**Commercially Confidential Information?**
- Integrity of the trial?
- Bias issues?

- Importance of the implementation guidelines
Adaptive Trials: To Sum Up

Many designs possible

- Sample Size Re-estimation
- Seamless Phase
- Dose Selection
- Group Sequential

Bayesian Borrowing
Dose Allocation
Model-Based Dose Escalation
Population Enrichment

All requiring flexibility

- Centralized assessment
- Strategic protocol writing
- Adding countries/sites
- Substantial amendments
- Interim analysis
- Transparency

Implementation of the CT Regulation must allow enough flexibility to enable the adaptability required for a timely access by patients to innovative treatments.
The Changing Clinical Research Pathway: Towards a Life-Cycle Approach to Evidence Generation

From trials “designed to learn” to real life situation

Early clinical trials (R&D)
- Biology / imaging driven
- Integrated TR
- Screening platforms
- Collection of high quality data from various sources

Pivotal trials
- Highly targeted
- Large differences

Population-based studies
- Real world data
- Quality of life
- Health economics
- HTA
- Pragmatic trials

Sustainable Model of Drug Development – Efficiencies through Patient Selection

Diagram:
- Diagnostic Test
  - Prognosis: **Responder** for drug A
    - Patient gets drug A
  - Prognosis: **Non-Responder** for drug A
    - Patient gets drug B
  - Prognosis: **Severe side-effects**
    - Patient gets drug C
Example of 21st century personalized medicine trial

Such projects are at the edge of several regulations: Clinical trials, data protection and IVD
Fragmentation of the regulatory framework in Europe: a major bottleneck
Streamline - Simplify - Harmonize

Europe must build an integrated and harmonized legal and ethical framework to foster relevant international clinical research.
The Potential for Real World Data

Takeda Enlists Real World Evidence To Boost Marketed Entyvio

Executive Summary
Japan’s Takeda says it has confirmed the benefits of its best-selling inflammatory bowel disease therapy Entyvio in US medical practice through the collection of real world evidence.

by John Davis
john.davis@informa.com

Relvar/Breo “Real World” Asthma Benefits Help GSK – But Can't Remove Generic Threat

Executive Summary
Top-line data from a second patient group, asthmatics, in the Salford Lung Study indicate that switching from usual therapy to GSK’s’s Relvar Ellipta improves symptoms, but the results may not be enough to encourage switching before generic Seretide/Advair takes hold.

by John Davis
john.davis@informa.com
Real-World Data/Evidence is relevant throughout the drug development lifecycle

**Discovery**
- Epidemiology of the Condition
- Biomarkers
- Treatment algorithm
- Compliance to clinical Guidelines

**Early Development**
- Set scope for Regulatory and HTA early scientific advice

**Full Development**
- Study designs optimised for registration, but anticipate HTA
- Feasibility of potential studies to address regulatory and HTA commitments

**Registration/Market Access**
- Post launch studies to address regulatory and HTA commitments
  - Support initial regulatory B/R decision-making

**Life Cycle Management**
- Deliver post-approval safety and efficacy data to confirm initial B/R determination
  - Drive B/R decision-making for product enhancements

**Orphan, Paediatrics, Feasibility**
- Optimised (adaptive) evidence generation plan

**Support MAA, HTA, B/R profile through lifecycle**
Technology can help.

Advances such as electronic data capture, and prevalence of wi-fi connectivity are driving changes in how clinical trials are conducted and analysed.
Trends in Technology Helping in Clinical Trials

• Using patients own health data from other systems
  • Electronic health records
  • Data captured on their own smartphone

• Making research participation more accessible
  • Self-reporting and tracking using technology in their pocket
  • Wearable sensors capturing data and transmitting the data to a remote location
Challenges remain...

Reaching the potential:

- Sustainability
- Access
- Quality Standards
- Governance

Partnership across all stakeholders needed to realise value
In Summary – Many opportunities to maximise efficiency

• Novel approaches to running/managing clinical trials are being adopted
  • Innovative trials designs
  • Patient-focussed approaches
  • Use of real-world data
  • Advances in technology

• Hurdles still to overcome
  • Legislative
  • Ensuring quality
  • Subjective
Questions