Making the Clinical Trial Enterprise More Efficient

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Session Goals

- Understand the trial enterprise from a 30,000 foot view
- Major players describe clinical trial process from their unique perspective
- Dynamic discussion to develop more efficient processes
- Break down the communication barriers
Research Clinician Perspective

- Clinical research is a labor of love
- Patient benefit: provide most up to date care
- Intellectual curiosity
- Responsibility to advance field
- Juggle and balance expectations from many masters

Challenges: Raising the bar for study inclusion (moving the goalposts)

- Patient accrual and study completion is progressively more difficult
- Trial inclusion criteria are increasingly narrow due in part to progressive segregation based on specific mutations.
- Embedded/mandatory pharmacological measurements limit site availability due to processing requirements.
  - Does every subject in a 1,000 patient study need every drug PK draw?
- While patient safety is job #1, have we gone too far?
  - “A patient needs to be a triathlete to enroll in a clinical trial” - Ed Kim, Hem-Onco Today 8/2018
  - Due to a history of HIV, if Magic Johnson got cancer he would be ineligible for a trial
  - Inclusion/Exclusion criteria are often based on historical precedent/cut and paste rather than rationale evidence
  - Clinical trials, particularly phase III, should reflect “real world” populations

Do you ever feel like this?

Clinical investigator as portrayed by Sisyphus
Challenges for research sites as they relate to CROs

- Hard to develop relationships
- Both CRO and local staff can have a high turnover
- Mixed expectations—everyone has their own perspective and responsibilities
- Communication can be fragmented
- High bar to improve the overall process

Who is responsible to complete a research study?

Despite differing perspectives, we have more similarities than differences
- We all share the same goals
- Better understanding of the process will improve trial effort for all stakeholders
- Questions for the speakers to consider:
  - What is your unique role?
  - From your perspective, what are the inefficiencies that can be addressed?
  - How do the other stakeholders view your role?
  - What can be done to improved the process

The revolving door of CRO staffing as perceived by the investigational sites

Coming together

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Improving the Clinical Trial Enterprise

Define Ideal Trial Execution—What Is Perfection?

- Great Experience
  - Clinical Trial Participants
  - Investigators
  - Site Personnel
- Seamless Execution
  - Timely & Robust Enrollment
  - Timely & Quality Data Entry
  - Robust Sample & Tissue Collection
- Strong Communication
  - Investigators & Site Personnel
  - CRO Monitoring Vendor
  - Sponsor Clinical Research Physician
  - Sponsor Personnel

Areas of Problems, Delays & Frustrations

- Execution Issues
  - Delay in IRB Approval
  - Start Up Activities
  - Training
  - Documentation
  - Safety Reporting
  - Standard of Care Changes during Enrollment Period
- Enrollment Issues
  - Inadvertent Enrollment
  - Not Meeting Enrollment Expectations
- Quality Issues
  - Poor Data Entry
  - Inaccurate & Insufficient Documentation
  - Not following trial specific procedures
How Can Industry/Lilly Improve Trial Conduct?

- Simplify Study Materials
  - Protocol
  - Informed Consent Form (ICF)
  - Study Tools
- Enable One Portal for Study Communication
  - One time entry of information
  - Enable real time communication of changes
- Site/Patient Input to Trial Design & Feasibility
  - Better trial from the start with key stakeholder input

What Can The Clinical Research Site Do To Be More Efficient?

- Robust Communication
  - Accurate Enrollment Projection
  - Staffing/Resources
  - Monitoring Space Accessibility
  - Questions & Concerns
- Meet Protocol Requirements
  - Tissue Viability
  - Lab Samples
  - Data Quality
- Ensure Personnel Are Trained in Research

Are There In-House Projects/Initiatives Being Enacted?

Industry & Lilly
- Shared Investigator Platform (SIP)
  - Reduces redundant requests for information and training through automation and re-use of data
- Tissue Quality
  - Tissue quality review in real time for biomarker analyses
- Basket & Umbrella trials (Novel Trial Designs)
  - Many companies are using novel trial designs in an effort to conduct research more efficiently

ASCO Research Community Forum Annual Meeting: Improving the Clinical Trial Enterprise

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Disclosures

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No references to non-FDA approved uses of drugs/products in this presentation

Mission Statements

FDA: protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation’s food supply, cosmetics, and products that emit radiation.

Oncology Center of Excellence (OCE): achieve patient-centered regulatory decision-making through innovation and collaboration. We seek to create a unified and collaborative scientific environment to advance the development and regulation of oncology products for patients with cancer.

Drug Development Process

- Company develops drug and submits IND (Investigational New Drug) application to FDA
  - Primary focus: safety
  - Multidisciplinary approach: non-clinical, clinical pharmacology, statistics, clinical, etc.
- Company may request meetings with FDA to discuss drug development process
- Company eventually submits NDA (New Drug Application) package that includes all preclinical, manufacturing, clinical, etc. data

FDA Perspective: Current Challenges

- For patients:
  - Clinical trial language not patient-friendly
  - Eligibility criteria and diversity in trials
  - Logistical difficulties of participating in a trial
- For trialists/companies:
  - Clinical trial design
  - Biomarker development
  - Novel drug development
- For regulators:
  - Extent of adverse event reporting
  - Balancing access to drugs with sufficient data for approval
Opportunities for Improvement and FDA Initiatives

- For patients:
  - Patient-friendly endpoints
  - Joint effort with ASCO/FOCR on broadening eligibility criteria
  - Decentralizing clinical trial
- For trialists/companies:
  - Remote clinical trial site monitoring
  - Recent FDA Draft Guidances:
    - In Vitro Diagnostics Streamlined Submission Process
    - Blinding and Placebos
    - Expansion Cohorts
  - Biosimilars Action Plan

For FDA:
- Real Time Oncology Review:
  https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OCE/ucm612927.htm
- Assessment Aid:
  https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OCE/ucm612923.htm

Perception of FDA

Almost 100 m

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Improving the Clinical Trial Enterprise

Jill Johnston, BSc, CCRA, CPM
President, WCG Clinical, Site Activation Solutions

Ideal Trial Execution: CRO Perspective

- Adequate Resourcing
- Planning
- Organization
- Consistency
- Communication
- Decision Making
- Respect for one another
- Collective experience

Important Roles in Clinical Trials: CRO Perspective

- ‘Extension’ of sponsor study team
- Purpose:
  - Augment staff
  - Provide expertise
  - Provide specialty service
  - Allow for scale
- Models:
  - Consultancy
  - Specific functional service
  - Full-service

Challenges of Executing a Trial: CRO Perspective

- Inconsistency of approach & procedures
- Lack of standardization and decision making
- Info not shared in a timely manner
- Poor resourcing and forecasting
- CRO vs Sponsor tools and processes
- Multiple vendors working independently
- Info, documents & data in disparate systems
- Do:Say Ratio

Challenges of Executing a Trial: How Others See CROs

The Good:
- Staff augmentation or extension
- Highly process-oriented
- Focused on innovation
- Areas of expertise/consulting

The Bad:
- As a necessary evil
- Focused mainly on revenue and margins
- Arms & legs resourcing
- Goals not aligned to pharma/biotech
- Variation in quality of team/deliverables

Opportunities to Improve: CRO Perspective

- Understand the overall process
- See it, Own it, Solve it, Do it
- Be part of the solution
- Proactively plan
- Back to basics

Projects/Initiatives: CRO Perspective

Discussion
What can be done from YOUR perspective?

Perspective is an interesting phenomenon. The “truth” as we see it is often viewed differently by others. What can we do to improve the trial process?

Are there areas of misunderstanding that have been clarified?

Solutions-Challenging vs. Simple

What would you recommend?

\[ \nabla^2 \Phi = 4\pi G \rho + \frac{K_0}{2} \nabla^2 \rho + \alpha_6 \epsilon^{ij} \nabla_i \Phi \nabla_j \rho \\
+ \eta \rho^2 + \gamma \nabla \rho \cdot \nabla \rho + \epsilon_1 \nabla \Phi \cdot \nabla \rho \\
+ \epsilon_2 \Phi \nabla^2 \rho + \epsilon_3 \rho \nabla^2 \Phi + \ldots \]

OR

1+1=2

Thank you!