Research Professionals Network Workshop Series

MANAGING A MULTI-CENTER TRIAL

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BU Clinical & Translational Science Institute

Boston Medical Center — Exceptional Care. Without Exception.

The University of Vermont Larner College of Medicine

The University of Vermont Medical Center

Introductions

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This presentation uses QR codes throughout for Q&A-style polls

Steps:

1. Open your camera app on your smartphone device
2. Hover over QR code image in the slide presentation
3. Click the pop-up/link to the online question
4. The question will load in your phones web browser
5. Respond to the question

Let’s give it a try:

Aims of this Presentation

1. Identify three lead site/sponsor responsibilities for multi-site trials
2. Identify at least two levels of safety event reporting in a multi-site trial
3. Discuss three key concepts to data management methods in a multi-site trial

Summary of Study

- Kids Face-to-face And Computer-Enhanced Formats Effectiveness study for Anxiety and Related Symptoms
- Large-scale Randomized Controlled Trial
- Enrolling children ages 3-18 with moderate anxiety
- Randomly assigned to receive either face-to-face or online-delivered CBT treatment
- Intervention will be administered within 16 weeks
- Participants will be monitored over the course of two years
- Outcomes will be assessed at five points: Baseline (Week 0), Week 8, Week 16, Week 52, and Week 104

The KFF Team

- 2 Study PIs – Dr. Lisa Fortuna and Dr. Donna Pincus
- 1 Qualitative Data Lead – Dr. Michelle Porche
- 1 Quantitative Data Lead – Dr. Jon Comer
- 10 Clinic Sites
- 4 Regional Principal Investigators and Enrollment Sites
  - Boston Medical Center – Dr. Andrea Spencer
  - Johns Hopkins – Dr. Rheanna Platt and Dr. Leslie Miller
  - University of Washington – Dr. Kathleen Myers
  - Florida International University – Dr. Jon Comer
- 15+ Research Assistants and Clinic Champions

BOSTON MEDICAL CENTER

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JOHNS HOPKINS BAYVIEW MEDICAL CENTER

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Summary of Adult Oncology Interventional Treatment Trials

130 Interventional Treatment Trials

- Industry Sponsored
- Cooperative Groups
- Investigator Initiated
  - Regional Multi-site Phase II and Phase III trials

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Summary of Adult Oncology Interventional Treatment Trials

130 Interventional Treatment Trials

A Phase 3, Multicenter, Open-label, Randomized Study of nab-Paclitaxel Plus Gemcitabine Versus Gemcitabine Alone as Adjuvant Therapy in Subjects With Surgically Resected Pancreatic Adenocarcinoma

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A Phase II, Open-label Evaluating the Safety and Activity of naI-IRI in Combination with 5-FU and Oxaliplatin in Preoperative Treatment of Pancreatic Adenocarcinoma (UF-STO-PANC-004)

- Regional Multi-site Phase II and Phase III trials

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Phase II Trial of the PARP1 Inhibitor, Niraparib, in BAP1 and other DNA Damage Response (DDR) Pathway Deficient Neoplasms (UF-STO-ETI-001)

- Regional Multi-site Phase II and Phase III trials

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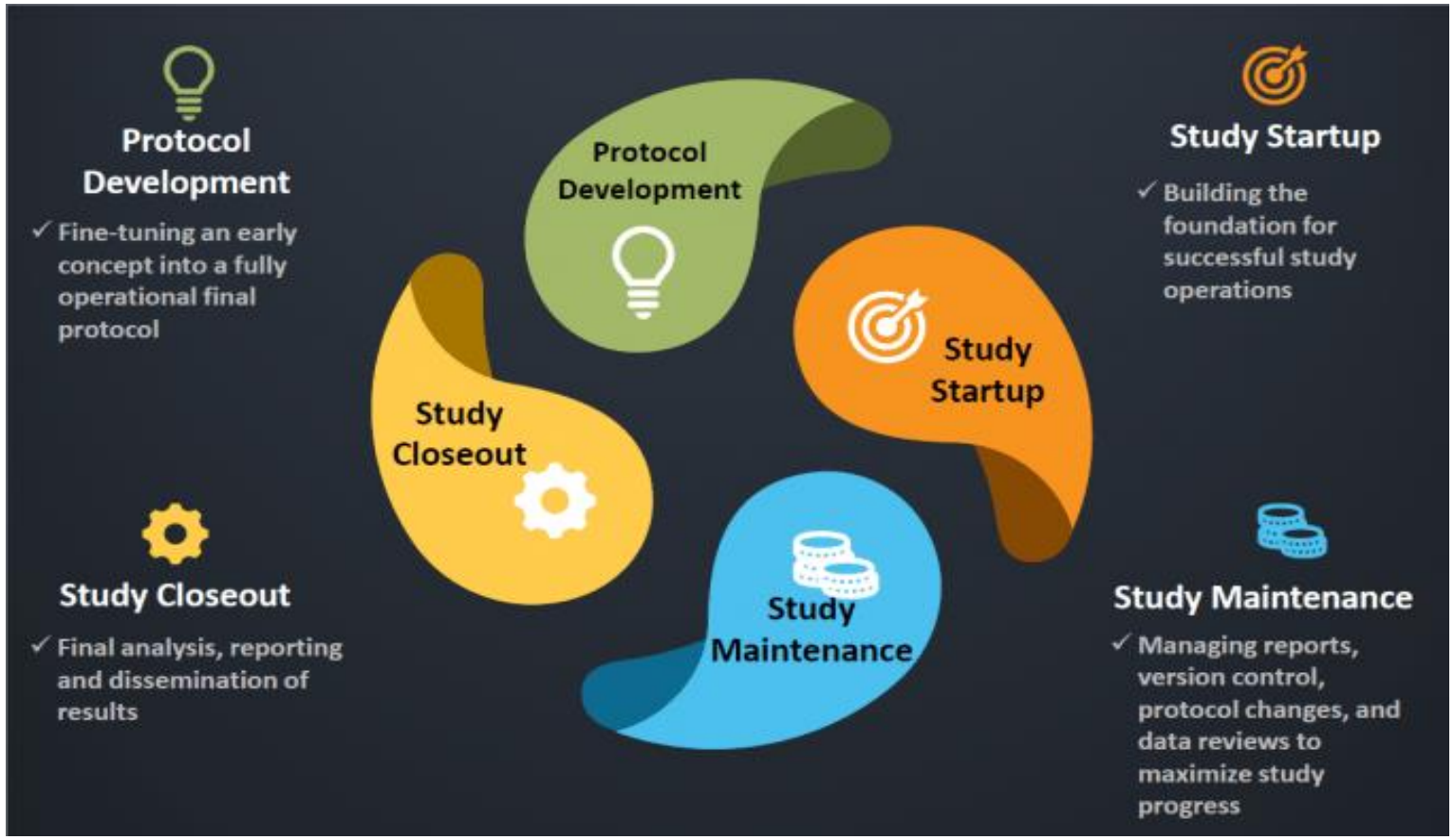
Protocol Management Office



Lead Site / Sponsor Responsibilities

1. Role of lead site vs sub sites
2. Communication plan meetings and monitoring
3. Sub site perspectives
4. Advisory Council/Board Meetings
5. Managing personnel

Lead Site/ Sponsor Responsibilities

- Providing protocol to sub-sites
- Providing Study Operating Procedures
- Monitoring participant recruitment
- Monitoring study progress and milestones
- Managing personnel
- Safety and Risk Evaluation
- Documentation
- Financial Management
- Regulatory Maintenance
- Data Management
- Reporting to Funder/ Sponsor
- Communication

Communication Plan

Establishing a communication plan for the entire study is key to monitoring

- Coordinator Meetings
- PI Meetings
- Exec Committee Meetings
- Advisory Council/ Board Meetings
- Data Team Meetings

Advisory Council/Board Meetings

- Patient and Family Advisory Boards
- Stakeholder Advisory Board
  - Providers
  - Policymakers
  - Community partners and organizations

Sub Site Perspectives

- Regulatory Concerns
- Accrual requirements and timelines
- Sub site study progress local requirements
- Feasibility
  - Personnel
  - Committee reviews
  - Ancillary Service support
  - Budgeting/Contracting
  - Lab – equipment, freezers
  - EMR
  - CTMS/EDC

Managing Personnel

- Tracking certifications
- Trainings
- Staff turnover
- Staff support

Quality Assurance

- Protocol
  - Living document
  - Flexible to suit specific needs of clinics
- Standard Operating Procedures
  - Data capturing
  - Recruitment steps
  - Any diagnostic testing or imaging
  - Collection of bio specimen

Question

You are working on a multi-site clinical trial and have a recruitment pathway that requires every study clinic use a specific screening tool as standard of care. A positive screen will lead a clinician referring the patient to your study. Your sub-site coordinator informs you (lead site PM) that the screening tool is not billable in their clinic and they cannot use it as part of standard of care. What is your next step?

1. Remove the sub-site from the study
2. Discuss issue with PIs and identify other screening tools that can be used by this site
3. Amend protocol to include screening tools that can be used by the site.
4. Both 2 and 3

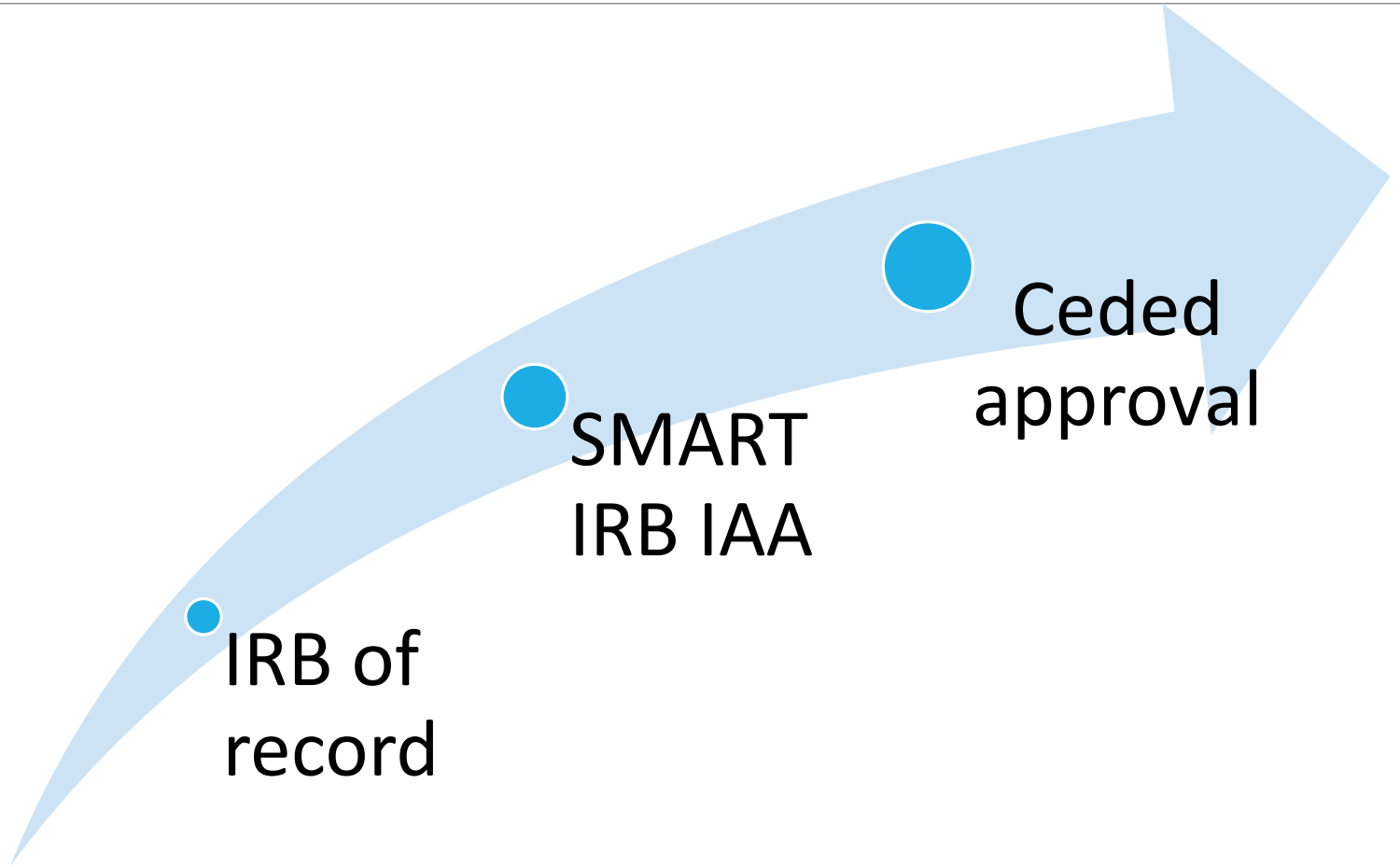
IRB

- Single IRBs (sIRB)
- Ceding of Studies
- NIH sIRB

Single IRBs (sIRB)

- Regulatory Review and Oversight
- Subsite local context matters
- IRB Authorization Agreement (IAA)

Ceding of Studies



NIH Single IRB Policy

- In effect 1/25/18
- Applies to domestic, non exempt studies
- Benefits and Challenges
- NOT-OD-16-094: Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

Question

You are the Project Manager of the lead site and your study has recruited a new sub-site that is not ceding to your institution's IRB. What are the essential resources to provide the sub-site in order to start-up?

1. Protocol
2. Standard Operating Procedures
3. Training certifications
4. IRB approval and considerations
5. Local laws (age of assent, guardian who is a minor etc.)
6. 1, 2, and 3

Safety

- Safety Plans
- SAE reporting
- Defining adverse events

Procedural Safety Plans

- Identifying safety concerns
- Training sites
- Reporting and notification
- Follow-up
- Example: Multiple safety protocols for KFF

SAE Reporting

- Reporting to lead site
- Reporting to other regulatory authorities
- Reporting timelines
- Follow-up information

Defining Adverse Events

- AEs, SAEs, unanticipated problems
- Study Definitions

Safety – Adverse Events

- Defining adverse events for your study
- Adverse events
  - Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.
- Study Definition: any abnormal or harmful behaviors, increasing severity of symptoms that are identified by the therapist, suicidal behaviors or attempts, breach in the protection of participant data or breach of confidentiality whether or not considered related to the participants' participation in the research.

Safety – Serious Adverse Event

- Serious adverse events
  - results in death;
  - is life-threatening (places the subject at immediate risk of death from the event as it occurred);
  - results in inpatient hospitalization or prolongation of existing hospitalization;
  - results in a persistent or significant disability/incapacity;
  - results in a congenital anomaly/birth defect;
  - or based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention
- Study Definition:
  - results in death;
  - is life-threatening (means that the event places the participant at immediate risk of death from the event as it occurred);
  - results in inpatient hospitalization or prolongation of existing hospitalization;
  - results in a persistent or significant disability/incapacity;
  - based upon appropriate medical judgment, may jeopardize the participant’s health and well-being and requires hospitalization, other mental health or medical stabilization, child protection services or other higher level of care.

Safety – Unanticipated Problem

- Unanticipated problems
  - experience or outcome that meets all three of the following criteria:
  - is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents (such as the IRB-approved research protocol and informed consent document); and (b) the characteristics of the subject population being studied; AND
  - is related or possibly related to participation in the research (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); AND
  - suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized
- Study Definition: defined as an event, experience or outcome that meets all three of the following criteria:
  - is unexpected; AND
  - is related or possibly related to participation in the research; AND
  - suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Data Management

- Data systems
- Developing a manual
- Data teams
- Monitoring/Auditing
- DSMBs

Question

What data systems are your teams using?

Regulatory Maintenance

- Trial Master Files
- Documentation
- Monitoring Plan

Trial Master File

- Collection of essential documents necessary for trial conduct and management
  - Purpose – to have documentation to evaluate the study's ethical and scientific integrity, and reconstruct
- Essential documents for the conduct of clinical trial (before, during, and after termination of study) - Section 8 on Page 52
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e6r2-good-clinical-practice-integrated-addendum-ich-e6r1
  - Choose documents that are essential for YOUR study
- Should be regularly updated – set time for site coordinators to update their documents

Documentation

- CVs
- Training logs and certifications
- Monitoring reports/ audits
- Regulatory Approvals
- Meeting Notes
- IRB approvals and amendments
- Consent Forms

Monitoring Plan

- Yearly Site Visit
- Delegate qualified personnel to be responsible for monitoring
  - Sub Site PIs/ Regional PI
  - Sub Investigators/ Clinical Champions

Activity: Case Study #1

You are a lead research coordinator at your academic medical institution and are approached by a PI about an investigator initiated, interventional treatment trial to be opened at your site plus 2 other regional affiliate, community clinic sites. Assume your facility has appropriate institutional agreements with the affiliates already in place.

Answer the following:

Questions

1. Identify the members of your study team and their roles

2. Discuss how you will ensure compliance with GCP throughout the conduct of the study, including study team training and adherence to ethical and quality concepts.

3. Describe a few elements of the SOP you will implement to guide Adverse Event reporting by affiliate sites

Activity: Case Study #2

Your institution is the sponsor of a multi-site clinical trial and your role is project manager. The sites participating in the trial, other than your own, are remote and have underserved, minority patient populations.

Answer the following:

Questions

1. Identify 2 strategies your lead site can employ to account for cultural/regional considerations at your affiliate sites.
2. Identify a communication plan that will facilitate trial activities and oversite.
3. What technological hurdles will you anticipate when considering data collection, auditing and monitoring, and adverse event reporting?

Activity: Challenge

You are the Project Manager of a multi-site clinical trial. The study team has made changes to the protocol and needs to implement the amendment quickly and efficiently across all sites. You have 3 minutes to identify the procedural processes that must be undertaken and how you will communicate the changes.

Gold Star Awarded!!

Questions?