Clinical Trials Accrual and Updated PAR-13-386 Perspective from Recent Site Visits

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Current Landscape at the Site Visits

- Clinical Research Programs, CPDM, PRMS, EPCRS, Data Tables 3 and 4
- Analyzed Summary Statements and PDs notes from the last four cycles (submission date September 25, 2014 – 2015) – **16 total centers**
- 33 Clinical Research Programs
  - Scored in range between Exceptional and Very Good
    - average between Outstanding to Excellent
- CPDM
  - Scored in range between Outstanding-to-Exceptional and Excellent
    - average between Excellent to Outstanding
- PRMS – all approved

Clinical Programs: What Drives Better Scores?

- Clear path to facilitate translational research (highlight INDs!)
- High accrual to clinical trials, especially to investigator-initiated trials
- Strong portfolio of developing new diagnostics and therapies for cancers of high incidence in the catchment area
- Inter-disciplinary and inter-institutional collaborative research measured by multi-PIs grants, participation in national trials, and other metrics stated in the FOA

Clinical Programs: What Makes Scores Worse?

- Common:
  - Limited translation of otherwise strong science
  - Few investigator-initiated trials, especially in programs that should be centerpiece of translation/clinical activity in a Center
    - It also affects the Senior Leadership review
  - Unbalanced portfolio of institutional and industry trials
    - What is the importance of industrial trials to CCSG review?
  - Low or flat accrual particularly to IITs and under-developed plans for rectifying deficiencies
- Occasionally:
  - No evidence of CCSG value-added measured by limited usage of Shared Resources, intra- and/or inter-programmatic activities and limited interactions of scientists and clinicians
  - Weak portfolio of clinical studies addressing problems specific to the catchment area

Centers Often Cited Reasons for Low Accrual

- Loss of critically important clinical investigators
- Shifts in patient referral
- Shifting RVUs make clinicians participation more difficult
- Development of molecularly targeted clinical studies
- Closure of high-accruing trials, particularly as a result of NCTN reorganization
- Trials of rare diseases and participation in NTCN

CPDM: What Drives Better Scores?

- Centralized infrastructure to support the development, execution of trials coordination and quality control functions at a center and its network
  - Experienced staff that works towards a beneficial transition from initial submission of a protocol, to approval and implementation
- Increasing accrual, especially to IITs
  - Efforts to facilitate minority accrual
- Effective training services, especially to junior faculty
- Significant improvement in trials activation time

CPDM: What Drives Worse Scores?

- Accrual:
  - low or flat; disparities across Research Programs and/or disease types
  - under-developed plan for rectifying deficiencies
- Lack of rigorous assessment of trial timing metrics (between PRMS approval and activation)
- Lack or not-fully-deployed trials management software
- Lack of consistency in common tasks (standardization, SOPs, quality control) across all research/ disease groups
- Lack of clear indication how the CTO staff will assist the investigators in enhancing accruals, if a trial is closed for under-accrual
- If a new partnership, weak evidence of clinical integration (centralized protocol prioritization, staff training, deployment of electronic software across all community sites, centralized data management and study coordination, clinical investigator operations committee)

PRMS: What Is Praised?

- Clear criteria for scientific review focusing on study rationale, design, adequacy of biostatistical input, and feasibility of proposed timeline
- Well described process for scientific review, protocol initiation, monitoring and termination
- Strong evidence of study closure authority
- Clear demarcation of authorities from DSMC and IRB
- Appropriate expertise and experience of committee
- Well-documented procedures

PRMS: What Is Criticized?

- Lack of stringent definition of quorum requirement
- Lack of transparency in management of COI for committee members in the review process
- Deficiencies in content and documentation of meetings' minutes
- Lack of evidence of meaningful involvement of a biostatistician in protocol development and/ or PRMS review
- A high proportion of junior faculty without appropriate expertise
- Unclear process for correcting poorly-accruing studies
- Unclear roles and communication of disease-oriented groups with PRMC

Data Table 3

- Is there a benchmark relationship between the number of "newly **registered** patients" and number of "newly **enrolled** patients"?
  - No, there is no benchmark relationship between these two categories. In fact, since patients newly **enrolled** in trials are usually first seen and undergo standard of care before being enrolled in trials (and hence newly registered before the reporting period), one would not expect an exact correlation between these two sets of data.
  - Should OCC consider eliminating **"newly enrolled patients"** to ensure that reviewers do not compare it to "newly registered patients"?
- Should patients seen by private-practice doctors that are located in Center space (either the primary clinical component or affiliated clinics) but are not part of the Center's health plan and cannot participate in trials be reported?
  - These patients should not be counted as "newly registered patients"

Data Table 4

- What should OCC allow in DT4 reporting? What "gray areas" about accrual do you need resolved? For example, if your CTO and PRMS oversees a trial but the PI is not a center member, should the center be able to claim credit for accruals to that trial?
- How do we handle screen failures in the era of precision medicine? How can we draw the line between PM trials and others types?
- Therapeutic accruals vs other types accruals – is the former really more important in the overall clinical enterprise?

Clinical Research Program Review Criteria

For Programs with clinical trials:

- **How successful is the Program in activating interventional trials that make a difference, e.g., advance the field or change medical practice?**
  - *What is the impact of the clinical trials in the program?*
- **How successful is the Program in moving research through the translational continuum, via coordination across clinical funding mechanisms of the NCI or collaborations with industry or other partners?**
  - *How successful is the program in translating research?*
- **How successfully do feasibility and other early phase trials capitalize on the scientific strengths of the Program?**
  - *Has the center translated its own basic research into clinical studies?*

Review Criteria cont.

- **Is the Program participating in accrual to, and leadership of, National Clinical Trial Network (NCTN) trials appropriate to its scientific agenda?**
  - *Is the Program a leader of the National Clinical Trial Network (NCTN), the Early Therapeutics Clinical Trial Network (ETCTN), and other NIH-funded clinical networks?*
  - *Does the Program participate in accrural to NCTN and other NIH-supported clinical trials?*
- **How appropriate is overall accrual to trials (taking into consideration those with unique accrual targets, *e.g.,* rare cancers, targeted therapies)?**
  - *What needs to change?*
- **How appropriate and effective are the Program Leaders in relation to expertise, program management, and time commitment?**

Clinical Research Programs – Specific Review Criteria

- How successful is the Program in activating interventional trials that make a difference, *e.g.*, advance the field or change medical practice?
- How successful is the Program in moving research through the translational continuum, via coordination across clinical funding mechanisms of the NCI or collaborations with industry or other partners?
- How successfully do feasibility and other early phase trials capitalize on the scientific strengths of the Program?
- Is the Program participating in accrual to, and leadership of, National Clinical Trial Network (NCTN) trials appropriate to its scientific agenda?
- How appropriate is overall accrual to trials (taking into consideration those with unique accrual targets, *e.g.,* rare cancers, targeted therapies)?

Clinical Protocol and Data Management

- How effective is CPDM in centralizing, managing, and reporting on the cancer clinical trials of the Center?
- To what extent does CPDM help to assure timely initiation and completion of clinical trial activities?
- How effective are the quality control functions and training services offered by the CPDM?
- How reasonable is overall accrual, based on the nature/type of the individual trials supported?

Protocol Review and Monitoring System

- How appropriate are the composition of the committee and the qualifications of its members for ensuring the breadth of expertise necessary to conduct a critical and fair scientific review of all institutional clinical cancer protocols?
- How appropriate are PRMS authorities and processes for initiating, monitoring and terminating all cancer clinical research protocols in the institution(s) comprising the Center?
- How appropriate are the criteria and processes for scientific review, taking into account the rationale and study design, potential duplication of studies elsewhere, adequacy of biostatistical input, and feasibility for completion within a reasonable time?
- How appropriate are processes for ensuring prioritization of competing protocols from all sources and optimal use of the Center's scientific resources?
- How adequate are the criteria for monitoring trials to ensure they are making sufficient scientific progress?
- Are the criteria and process for terminating trials that do not meet scientific goals (trials involving rare diseases are excluded) adequate and used appropriately?
- How adequate are metrics for moving trials forward through the PRMS system in a timely fashion?
- If a consortium Center, is there a single PRMS governing all cancer clinical trial protocols across the partner institutions?