CTAC Streamlining Clinical Trials Working Group

Interim Report

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CTAC Strategic Planning Working Group

November 2020 Report

Re-assess strategic vision for clinical trials system for 2030 and beyond

Review and address necessary clinical trials infrastructure

Developed 15 recommendations and 3 operational initiatives

Themes:
Trial Complexity and Cost
Decentralized Trial Activities
Promoting Accrual and Access
New Data Collection Approaches
PRO Data for Clinical Trials
Operational Burden
Statistical Issues
Workforce Outreach and Training

https://deainfo.nci.nih.gov/advisory/ctac/1120/SPWGreport.pdf

Streamlining Clinical Trials Working Group (SCTWG)

- Charged with addressing implementation of three Strategic Planning Working Group recommendations
  - Limit clinical trial data collection in NCI late phase trials to data elements essential for the primary and secondary objectives of the trial
  - Resolve the logistical and data quality challenges of extracting clinical trial data from electronic health records
  - Engage EHR and CTMS vendors to create mechanisms for automatically integrating study-specific documents into local implementations of their products

Streamlining Clinical Trials Working Group Membership

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Rationale for Interim Report to CTAC

- SCTWG rapidly came to consensus on one of its tasks
  - Addressing data collection in NCI late phase clinical trials
- Acceptance of an interim report allows NCI to consider its findings now rather than waiting for a final SCTWG report
- A final, comprehensive report will be submitted once deliberations for all tasks assigned to SCTWG are completed

Focus of Interim Report – Limiting Data Collection

- Strategic context
  - The growth in complexity and expense associated with cancer clinical trials threatens the entire enterprise
  - The COVID pandemic brought extensive operational and workforce challenges exacerbating existing problems
  - Mechanisms to streamline trial design and reduce the burdens of clinical trial operations without compromising scientific objectives or patient safety are urgently needed
- Limiting data collection to essential data elements is one strategy for addressing these issues

SCTWG Process for Addressing Data Collection

- July 13: First plenary meeting
  - Reviewed findings of protocol/case report form analysis
  - Discussed candidate low-value data categories
  - Clarified understanding of where reduction in data collection may be appropriate
- July - September: Draft of proposed standard practices prepared
- October 4/25: Second and third plenary meetings
  - Draft refined further and approved for broader discussion with CTAC
- November 9: Interim report to CTAC

Interim Report Recommendation

Recommendation

A set of standard practices for data collected in NCI phase III and phase II/III adult, IND-exempt, treatment trials should be established

Scope of Recommendation

- The recommendation and proposed standard practices are intended to apply initially only to trials that meet the following criteria:
  - NCI CTEP/CIB-managed
  - Phase III and Phase II/III
  - Interventional
  - Focused on treatment
  - Adult
  - IND-exempt (~ 40% of NCTN trials)

Scope of Recommendation (2)

- Future recommendations will address whether and how these practices can be extended to late-phase IND trials and pediatric trials

- Early-phase trials have distinctive scientific and clinical objectives that will require careful consideration of each of the topics covered in these recommendations

Application of the Proposed Standard Practices

- The proposed practices are intended to define a “new normal” for data collection that is less burdensome, more efficient, and more sustainable
- The practices are not intended to be applied rigidly at the cost of compromising key study objectives
- Investigators may depart from these standards, but for each proposed departure they must provide justification specific to the clinical details and scientific objectives of the trial

Proposed Standards: Categories

- Adverse Events (AE's)
- Medical History
- Concomitant Medications
- Physical Exam
- Laboratory Tests
- Imaging and Other Assessment Procedures
- Patient-Reported Data

1. Adverse Events (AEs)

a. Collect only AEs of grade 3 and higher, unless assessment of tolerability related to lower-grade AEs is a stated objective with a pre-specified analysis plan

b. For each AE, collect only CTCAE term and CTCAE grade

c. Do not collect AE attribution and AE start/stop times

d. Solicited AEs*, regardless of grade, should be limited to those that would result in dose modification, treatment discontinuation, or non-adherence

* *Solicited AEs* are defined as protocol-specified AEs that are required to be assessed and reported on a regular schedule (e.g., with each treatment cycle) as present or absent

2. Medical History*

a. Collect only those medical history items that are relevant to trial inclusion/exclusion criteria

* *Medical history* is defined as medical events or ongoing conditions identified at trial baseline either via patient report or via review of the patient's medical record

3. Concomitant Medications

a. At baseline, collect concomitant medications only if their use requires modification of the study treatment

b. During the trial, collect only changes in concomitant medications that cause modification or discontinuation of the study treatment

4. Physical Exam

a. Physical exams should be conducted according to standard of care, augmented by any trial-specific requirements

b. Only the following physical exam findings* are collected:

   i. Findings that are protocol-specified endpoints or are required to assess protocol-specified endpoints

   ii. Findings that represent AEs (per section 1 above)

   iii. Findings that result in dose modification or treatment discontinuation

* Performance status assessed during the trial is considered a physical exam finding and should be collected if it meets criteria specified in 4b

5. Laboratory Tests

a. Laboratory tests should be conducted according to standard of care, augmented by any trial-specific requirements

b. Only the following laboratory test results are collected:

   i. Test results that are protocol-specified endpoints or are required to assess protocol-specified endpoints

   ii. Test results that represent AEs

   iii. Test results that result in dose modification or treatment discontinuation

6. Imaging and Other Assessment Procedures

a. Limit imaging and other assessment procedures to those required to meet specified trial objectives (e.g., determining treatment assignment or modification, assessment of clinical outcomes)

b. The cost of any imaging or other assessment procedures not covered by insurance must be covered by the research study

7. Patient-Reported Data

a. Patient medication diaries should not be required unless the protocol defines how the data will be analyzed to address specified trial objectives

b. Data collection plans for patient-reported outcomes (PROs) must address how PRO instruments* will be chosen and data collection scheduled** so as to achieve specified scientific objectives while minimizing patient burden

* "PRO instruments" may include complete instruments, selected questions and/or rating scales, as appropriate to the trial's scientific objectives

** "Scheduling" includes timing, frequency, duration of follow-up and coordination with other data collection activities

Conclusion

- Timely implementation of a set of standard practices for data collected in NCI phase III and phase II/III adult, IND-exempt, treatment trials is expected to:
  - reduce operational burden
  - provide important insights that will inform development of data collection standards for other types of trials (e.g., late phase IND trials, pediatric)
- Broad stakeholder engagement will be necessary for successful implementation

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