Adapting NCI's Clinical Trials System to a Changed Clinical Research Environment

James H. Doroshow, M.D.
NCI Deputy Director for Clinical and Translational Research

NIH NATIONAL CANCER INSTITUTE

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Overview

- Initial & continuing effects of the pandemic environment on cancer clinical trials
- NCI's 2030 strategic vision for clinical trials
- Activities to ameliorate current clinical research workforce issues

COVID-19-related & Ongoing Roadblocks to Clinical Trial Accrual

From the start of the pandemic:

- In-person study activities
  - informed consent
  - visits to receive investigational study drug
  - assessments of patient safety and study adherence
- Required use of imaging and laboratory facilities specified by trial documents and for the collection of abundant test data of limited importance
- Need to collect low grade adverse events despite potential lack of clinical relevance to study endpoints
- Limited access to cancer care personnel/facilities; reprogramming clinical research resources for care

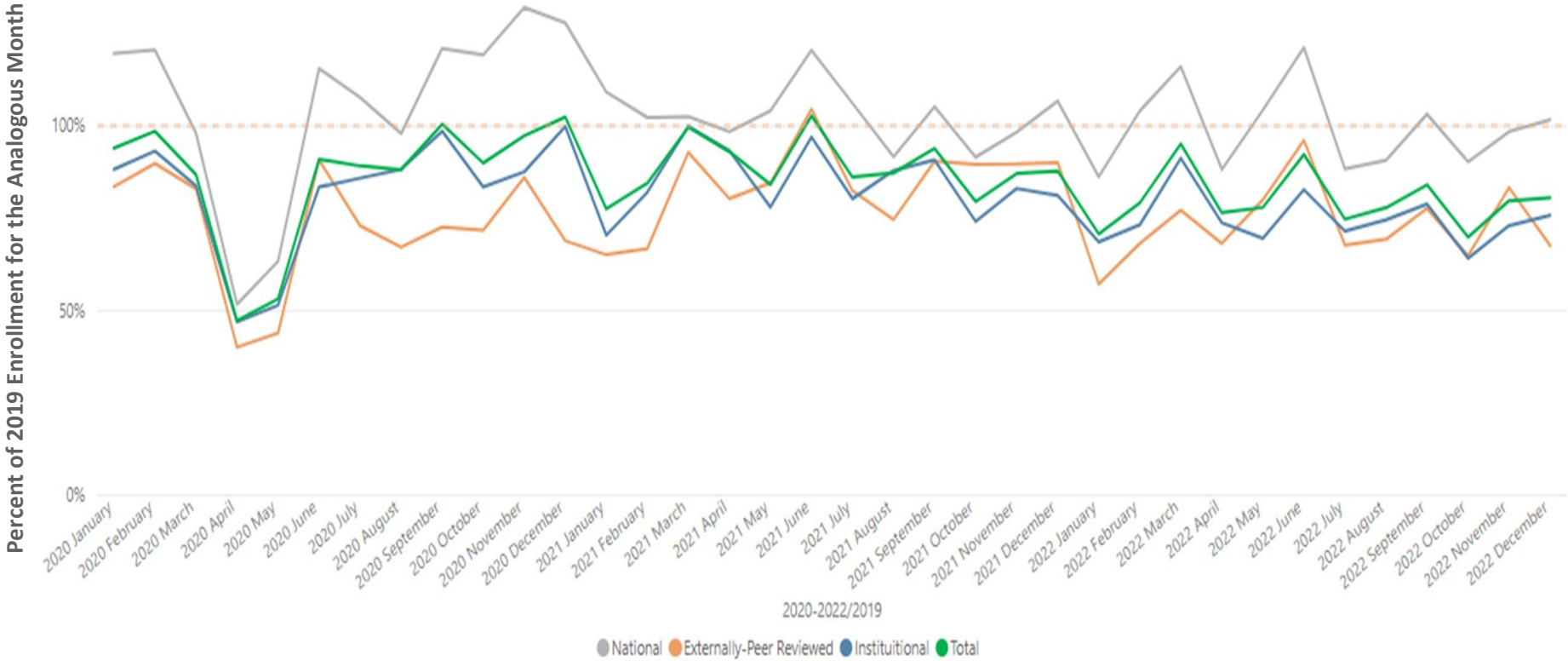
Major ongoing issues:

- Critical shortages of research nurses, CRAs, & research office regulatory staff, as well as essential health care workers (Nursing, Radiology & Pathology) and institutional central research services (IRB, legal/contracting) has diminished trial availability and accrual including for underserved populations, and led to substantive delays in results reporting

NCI's Clinical Trials Programs: Response to Pandemic

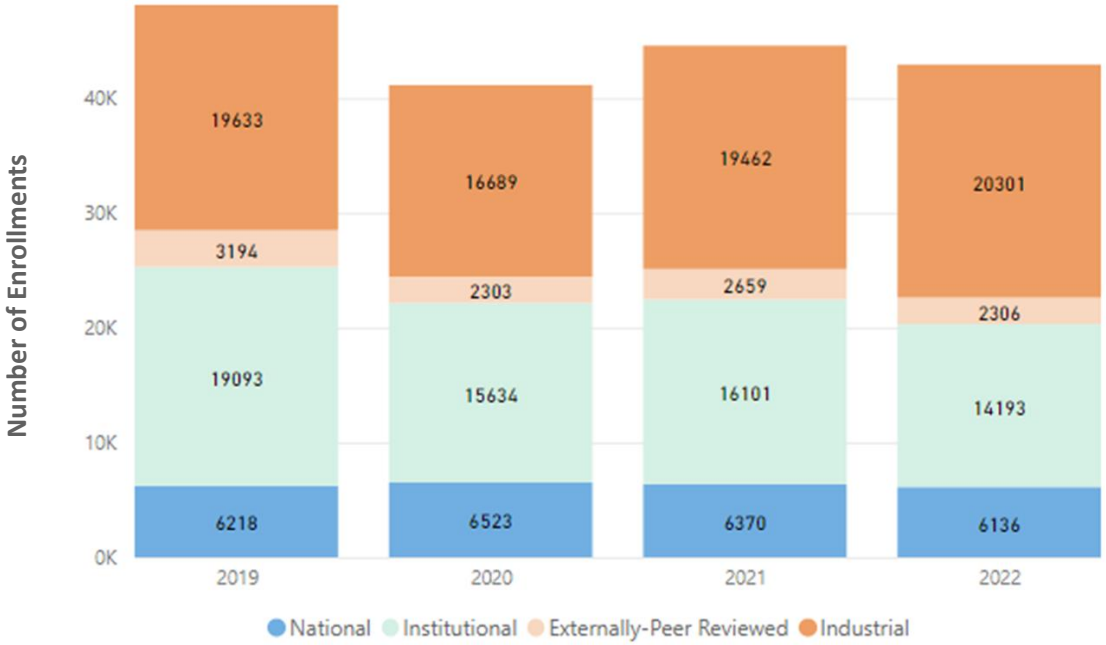
- Changed to use of electronic consenting
- Provided oral investigational agents directly to patients
- Initiated electronic, rather than in person, study audits
- Facilitated use of telemedicine for study visits
- Limited impact of minor study deviations on trial conduct/evaluation
- Implemented decentralized testing for required lab and imaging studies
- Developed new strategic plan for NCI's clinical trials programs which is now being implemented

Monthly Enrollment of Treatment Trials: NCI-Designated Cancer Centers
% Increase or Decrease in Comparison to 2019 by Study Source
(excludes Industrial Trials)



Data source: NCI's Clinical Trials Reporting Program (CTRP)

Annual Enrollment to Treatment Trials by Study Source* NCI-Designated Cancers: 1/1/19-12/31/22



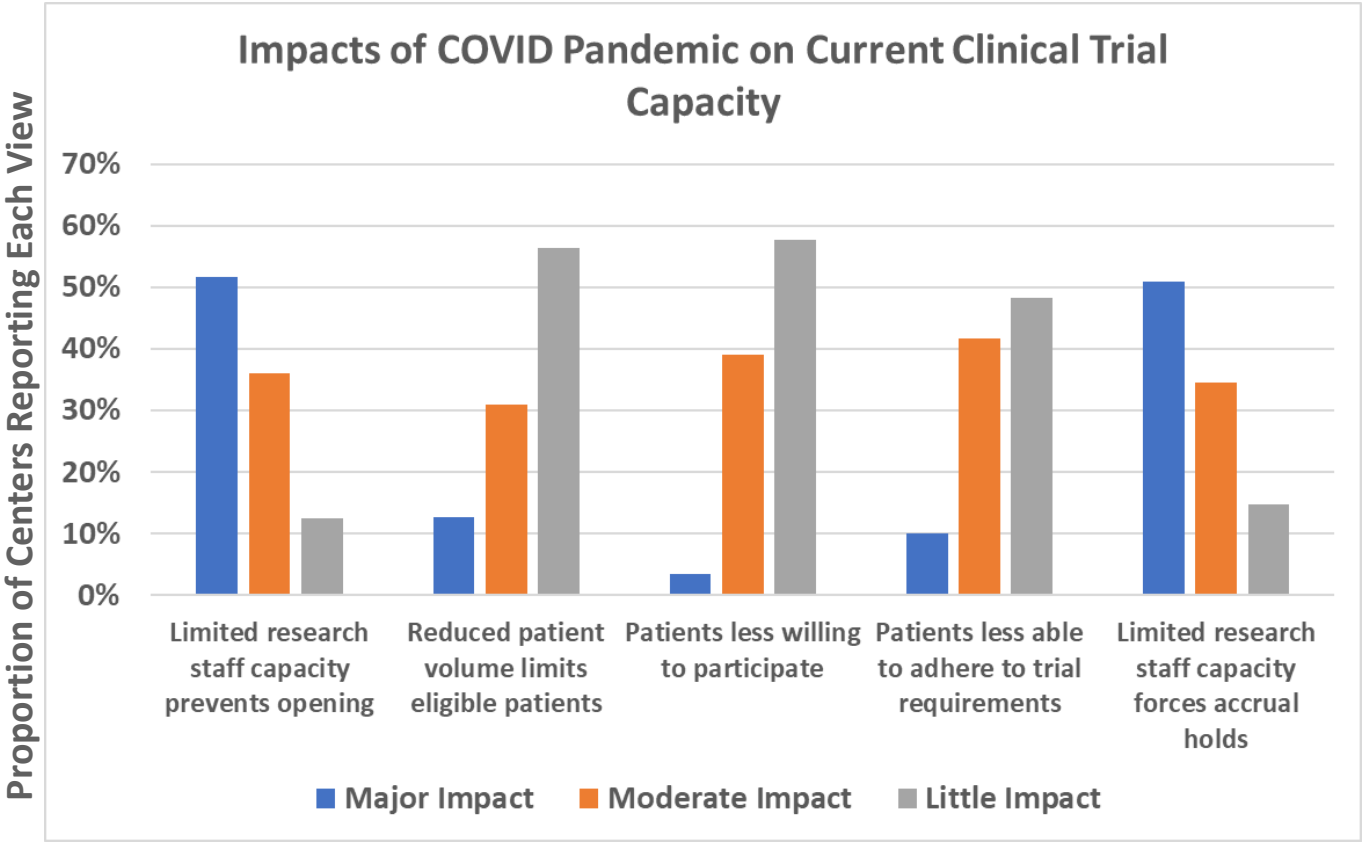
Data source: NCI's Clinical Trials Reporting Program (CTRP)

***NCI P30 Cancer Center Support Grant Data Table Guide v3.1.1**

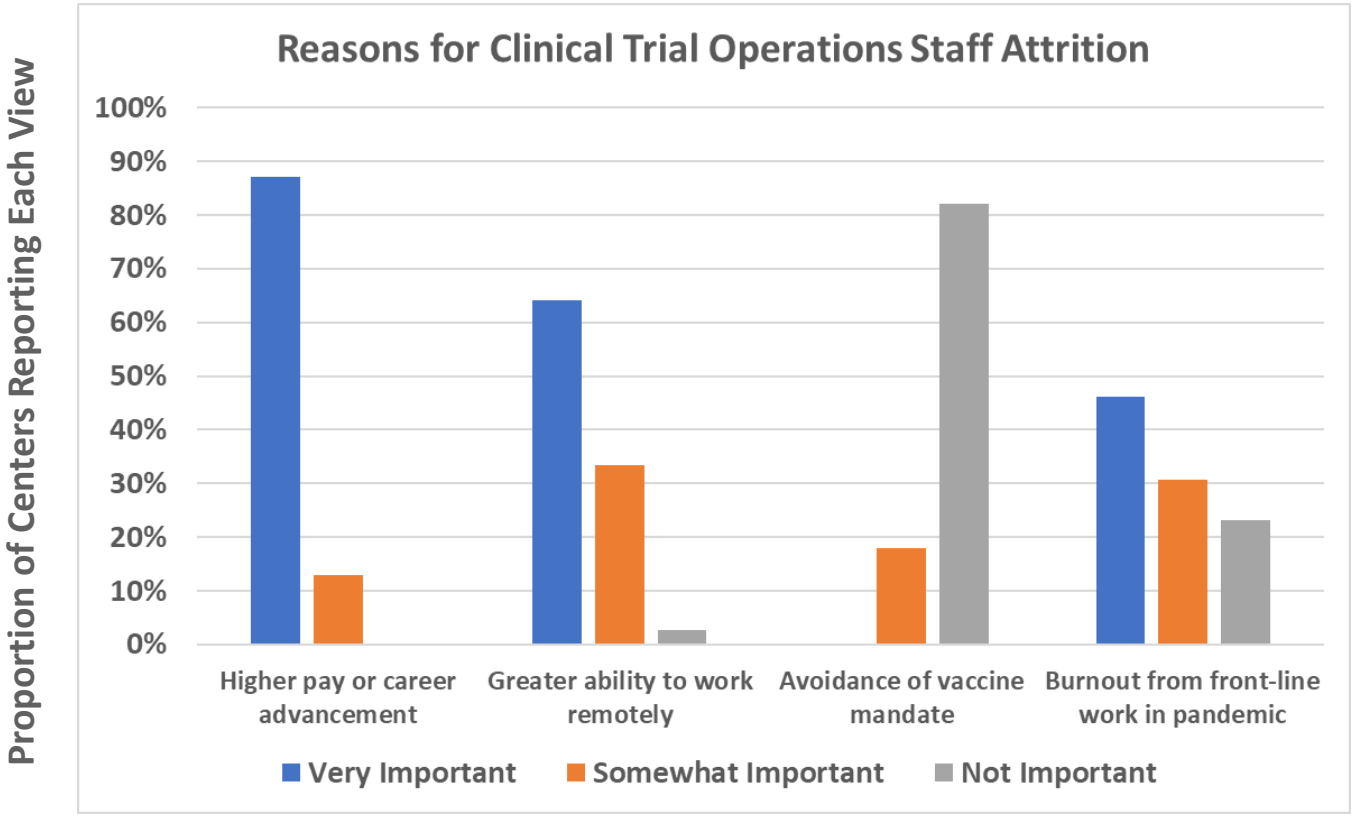
https://cancercenters.cancer.gov/GrantsFunding/DataGuide

NCI Cancer Center Clinical Trials Workforce Survey

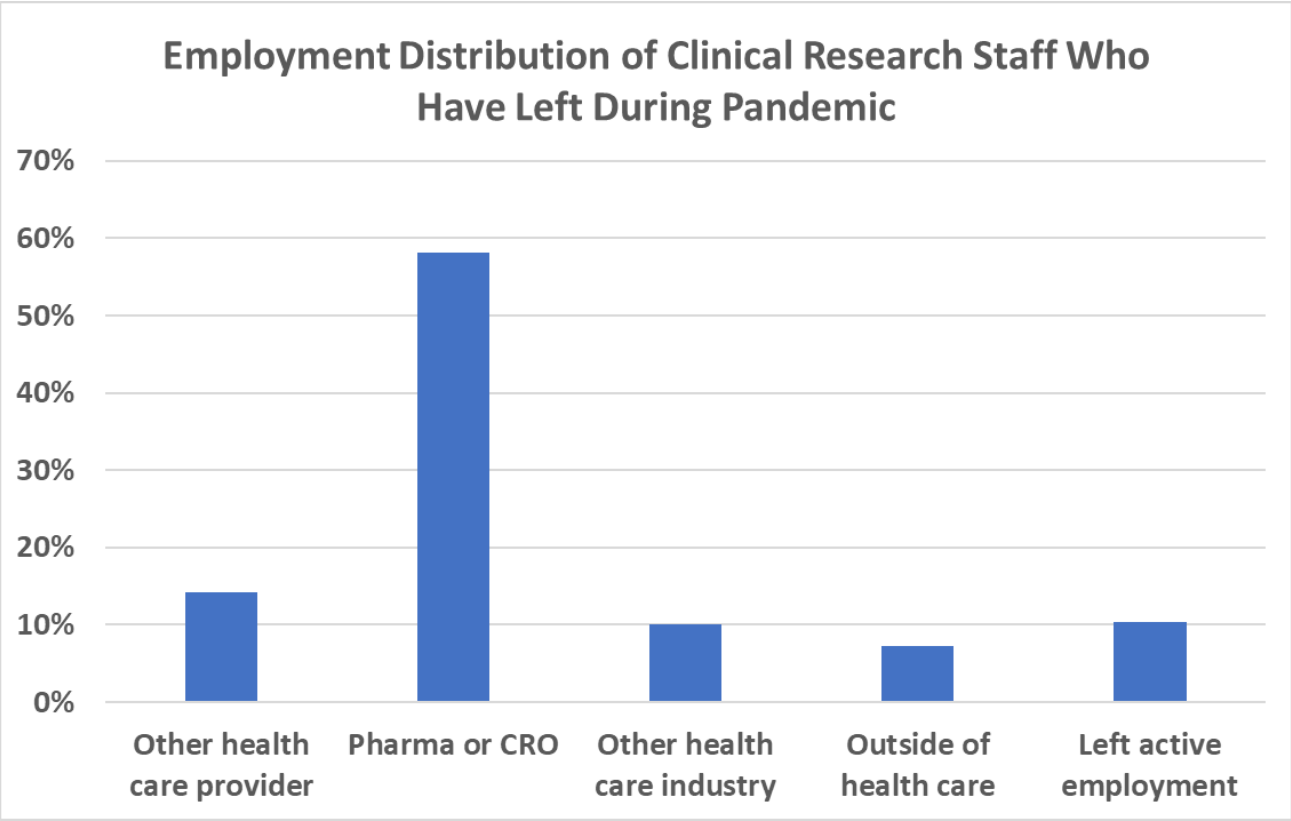
- Purpose: Assess the ongoing impact of the COVID-19 pandemic on the capacity of Cancer Centers to conduct ***treatment*** trials
- Administered by the Science Technology Policy Institute (STPI)
- Response rate: 100% (64/64 clinical Cancer Centers)



Respondent group for this question: all 64 clinical Cancer Centers



Respondent group for this question: the 38 clinical Cancer Centers that reported <90% pre-pandemic clinical research operations staff FTE



Respondent group for this question: the 38 clinical Cancer Centers that reported <90% pre-pandemic clinical research operations staff FTE

Additional Observations on Clinical Research Staff Turnover

- Effects of pharma/CRO “poaching”
  - ✓ Loss of staff, both senior and recently-trained
  - ✓ Smaller pool of qualified candidates for replacement hires
  - ✓ Higher compensation spurred by competition from pharma/CRO makes Centers less cost-effective for pharma/CRO work, threatens important research opportunities as well as income stream to support clinical trial office functions

NCI's 2030 Vision for Clinical Trials

Strategic Planning Working Group Report

Clinical Trials and Translational Research Advisory Committee (CTAC)

NCI Clinical Trials and Translational Research Advisory Committee Strategic Planning Working Group Overview

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

NCI Strategic Vision for Clinical Trials: 2030 and Beyond

Develop **flexible**, **faster**, **simpler**, **less expensive**, **high-impact** clinical trials that seamlessly integrate with clinical practice

- Streamline processes for trial design and execution
- Focus on essential endpoints
- Decrease regulatory hurdles and broaden trial access
- Increase efficiency of data collection

Streamlining Clinical Trials

	Recommendation	Recent Activity
Limiting Data Elements Collected	**Limit clinical trial data collection in late phase trials to essential data elements**	• **Analyzed recent phase 3 treatment protocols and characterized data collected** • **Convene expert group to review findings and advise on ways to optimize data collection**
Using EHRs to support clinical trials	**1) Engage vendors to create mechanisms for automatically integrating study-specific documents into local implementations of their products** **2) Resolve the logistical and data quality challenges of extracting clinical trial data from electronic health records**	• **Funded administrative supplements to P30 CCSG grants to develop approaches to facilitate integration of study-specific documents into local CTMS and EHR systems [MD Anderson Consortium & Big 10 Consortium]**

Candidate Low-Value Data Elements

Scope of Recommendation

- The recommendation and proposed standard practices are intended to apply initially 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)

Proposed Standards: Categories

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

Candidate Low-Value Data Categories* (1)

- Adverse events
  - √ Low-grade
  - √ Attribution and start/stop times
  - √ If agent toxicity profile is well-characterized for population
- Laboratory data
  - √ Beyond standard of care
  - √ Unrelated to study endpoints or safety monitoring
  - √ Unused components of panels, including unnecessary repetition of full panels
- Imaging
  - √ Beyond standard of care

*NCI CTAC SPWG Report

Candidate Low-Value Data Categories (2)

- History and Physical
  - √ Concomitant medications not relevant to the protocol
  - √ Start dates for concomitant medications not linked to protocol eligibility or safety
  - √ Start dates for histories not linked to protocol eligibility or safety
  - √ Patient position and resting status for vital signs

Goals

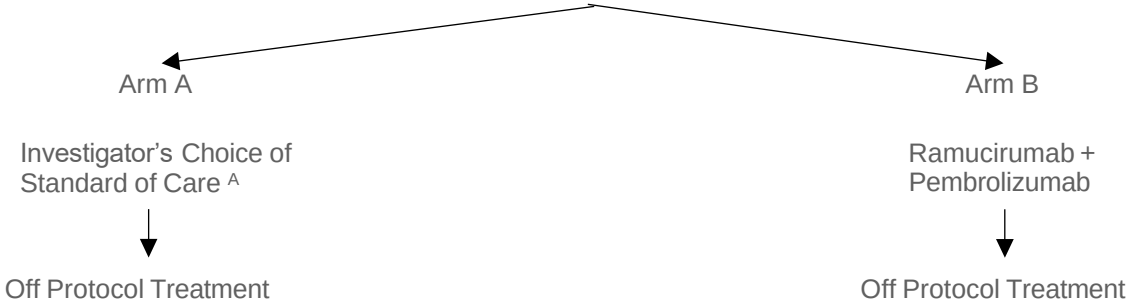
- Timely implementation of a set of standard practices for data collected in NCI phase III and phase II/III adult, IND-exempt, treatment trials is expected to:
  - √ Reduce operational burden
  - √ Provide important insights that will inform development of data collection standards for other types of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

Project Pragmatica: Follow-Up to SWOG 1800a

PRIVILEGED COMMUNICATION FOR INVESTIGATIONAL USE ONLY

SWOG CANCER RESEARCH NETWORK

S2302, **PROJECT PRAGMATICA**: A PROSPECTIVE RANDOMIZED STUDY OF RAMUCIRUMAB (NSC 749128) PLUS PEMBROLIZUMAB (MK-3475; NSC 776864) VERSUS STANDARD OF CARE FOR PARTICIPANTS PREVIOUSLY TREATED WITH IMMUNOTHERAPY FOR STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER IN STANDARD PRACTICE



A The Investigator's Choice of Standard of Care agents include docetaxel, gemcitabine, pemetrexed, or ramucirumab plus docetaxel.

EHR Study Builds

The Study Build Challenge

- Each study protocol requires a unique implementation of study documents and forms in the local EHR
- Clinical trial sites vary in their drug formularies, clinical practice guidelines, clinical practice SOPs, and local EHR customization
- Variation across study protocols in clarity and completeness with which clinical trial operational requirements are specified adds further complexity
- These local implementations are highly burdensome – recent NCTN CRP survey estimated a **minimum of 26.5 hours of effort to build the treatment plan for a single study arm in Epic**
- Local resources expended without knowing if a patient will be accrued

NCI Initiatives: Standardized Electronic Study Builds

- Goal of facilitating development of standardized electronic treatment plan builds for NCI-supported clinical trials
- Two consortia supported via CCSG supplemental awards
  - √ Clinical Trials Rapid Activation Consortium (CTRAC) – MD Anderson lead
  - √ Big Ten Electronic Health Record Consortium (Big Ten-EHRC) – Indiana University lead
- Work continuing through a single integrated consortium with participating institutions and project management provided by Leidos Biomedical Research

General Approach

- Develop standard representations of protocol-specified pharmacotherapy and other required therapeutic and assessment procedures
- Develop an approach to “packaging” the standardized requirements in a form that can either be imported directly into a site’s EHR or at least will facilitate local customization
- To economize on future effort, build a library of modules that are considered likely to be reusable across trials

Addressing Critical Clinical Trial Workforce Issues

- Streamline/standardize trial activation processes
- Reduce the volume of trials staff are responsible for (particularly complex trials)
- Increase flexibility for remote work
- Improve alignment of institution and Cancer Center hiring processes related to staff recruitment and retention including compensation
- Consider new NCI training grant program (post-Bac focus) supporting development of careers in clinical trials at NCI-designated Cancer Centers; formal curriculum; ? masters degree; prioritized for underserved communities: grow the pipeline
- ‘Virtual Clinical Trials Office’ pilot study

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