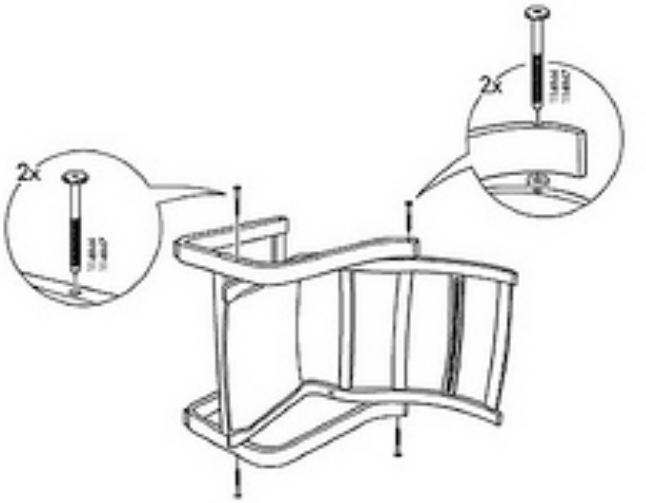
Brief Study Chair Guidelines

Gini Fleming, MD

Alliance Young Investigator's Meeting, 3 November 2016

RÖN STUDY CHAIR



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Going from Idea to Concept

- Concept path depends on type and originating committee
  - Prospective clinical intervention
    - Cancer Therapy Evaluation Program (NCI CTEP)
    - Cancer Prevention or Symptom Intervention (NCI DCP)
    - Alliance Foundation Trial (AFT)
  - Biospecimen reqest: Use of specimens previously collected in Alliance studies
  - Data-only studies: Analysis of data from a previously published trial (or set of trials)

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Data-Only Studies

- Alliance Data Request Form
  - Brief background, goals, patient /trial identification, analysis plan, budget https://allianceforclinicaltrialsinoncology.org/main/public/standard.xhtml?path=%2FPublic%2FDatasharing
- Approval of sponsoring committee chair and statistician are required
- Committee statistician estimates effort
  - Concepts requiring < 25 hours SDC effort are approved by SDC
  - Concepts requiring ≥ 25 hours SDC effort are approved by Alliance Executive Committee

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Biospecimen Requests

- Process is currently migrating from Alliance-led to NCI-led
- Current Specimen Request Form
  - https://allianceforclinicaltrialsinoncology.org/main/public/standard.xhtml?path=%2FPublic%2FSpecimens

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Biospecimen Requests

- **Current process** is managed by the Alliance Translational Research Program (TRP)

Alliance triage form for TRP stake holders to review

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NCTN-CCSC proposal development

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TRP executive committee full review

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NCI-NCTN CCSC review

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Paper work and specimen release

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What is NCI-NCTN CCSC?

-**C**ore **C**orrelative **S**cience **C**ommittee

- CCSC is charged with scientific review & prioritization of proposals requesting use of banked, non-reserved biospecimens collected from NCTN trials

- Includes NCTN Network Group Representatives, Bank representatives, advocates, & NCI representatives, with appropriate clinical, statistical, and scientific expertise to provide review & consideration of use of irreplaceable biospecimen resources.

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NCTN-CCSC Proposal Form

Includes the following

- Abstract, Objectives and Hypotheses, Background and Significance
- Trial(s) from which samples are being requested
- Preliminary data and study justification
- Research Design and Methods
- Tissue/Biospecimen type
- Data-sharing Plan
- Statistical Considerations
- References and Appendices
- Letters of collaboration from each co-investigator
- Confirmation sent by NCTN bank or SDC regarding sample or data availability

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Biospecimen Requests

- ***In the near future (TBD),*** this process will be managed by NCI/CTEP

Investigator submits LOI through NCI front door (TBD)

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NCTN-CCSC proposal development

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~~TRP executive committee full review~~

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NCI-NCTN CCSC review

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Paper work and specimen release

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In the near future (TBD),

- To identify available biospecimens from Alliance Trials, investigators can either contact Alliance TRP, *OR* use NCI Navigator system

- Navigator system is not launched yet, but a brief video is available https://navigatoruat.wustl.edu/nctn-navigator/public/home

- Alliance TRP will provide letter of support for the proposals reviewed/approved by TRP prior to CCSC review

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Letter of Support for NIH Grant Application

-The Alliance TRP can provide letters of support for NIH grants. Letters will be signed by the TRP PI Dr. Fraser Symmans and/or Group Chair Dr. Monica Bertagnolli

- For LOS or other questions regarding correlative studies and specimen requests, please contact

Yujia Wen, MD, PhD
Director, Translational Research Operations
E-mail: ywen@medicine.bsd.uchicago.edu
Phone: 773-834-7973

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Clinical Interventions-NCI

- NCI CTEP *Letter of Intent (LOI) Form* (Ph 1 and 2, <100 patients)
- NCI CTEP *Concept Submission Form* (Ph 2, 2/3, and 3 > 100 patients)
- *DCP-sponsored symptom intervention/prevention (list of required elements)*
- Check with committee protocol coordinator for appropriate form

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Get Buy In

- Speak with Alliance Committee Chair(s)
  - Work in conjunction with associated scientific/modality/discipline committees (eg Radiation Oncology, Health Outcomes, Transplant, etc.)
  - Co-sponsoring committee representatives (including statistician) should review final concept draft
  - All Alliance studies (except data sharing and TRP) require community oncology committee co chair and input ***at concept stage***
- NCI has established steering committees and associated task forces for most disease sites
  - Prior to submission to the Alliance, concepts may require submission of your idea to a disease-specific task force

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Study Concept Review Committee (SCRC) Submission

- Forward finalized concept to committee statistician(s) at least two weeks prior to SCRC submission
- Alliance Committee Chair/CCP Program Manager submits concept to Alliance Study Concept Review Committee
- SCRC review occurs on a rolling basis on Tuesday afternoons within 8-10 days of concept submission
- SCRC conducts operations/feasibility review

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Study Funding

- Alliance U24 biorepository grant supports biospecimen storage and initial processing at the Alliance biorepository.
  - Specimen distribution, complex specimen processing and study kit distribution are not included in the U24 support.
- NCI provides funding to reimburse sites for basic specimen submission.
  - Complex procedures (eg. research biopsy) will require investigators to raise funding for sites.

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Study Funding

- Additional funds may be required for
  - Biomarker screening
  - Translational research (biospecimen acquisition, processing, laboratory analysis)
  - Pathology review (especially real time)
  - Any non-standard-of care tests
  - Drug distribution
- Identify needs early!!!

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Potential Funding Resources

- Industry Partners
- Grants
  - Investigator (R01)
  - NCI supplemental grants to the Alliance U10 grant (eg. for drug resistance biomarkers).
  - NCI Biomarker, Imaging, & Quality of Life Studies Funding Program (BIQSFP)

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BIQSFP

- NCI funding for ***integral*** or ***integrated*** biomarkers, imaging and quality of life components (not for *exploratory* biomarkers)
- Phase III and randomized phase II concepts >100 patients are eligible
- BIQSFP applications with ***integral*** correlative science must accompany the initial concept to NCI
- BIQSFP applications with ***integrated*** correlative science must occur by first protocol submission.

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Study Funding

- Integral studies
  - Assays and tests that must be performed in order for trial to proceed
  - Inherent to the design of the trial (determine eligibility, stratification, treatment assignment)
  - Must be performed in real time for conduct of trial
  - Require CLIA certified laboratory
- Integrated studies
  - Identified as part of the trial from the beginning
  - Intended to validate or identify assays or markers and imaging tests planned for use in future trials
  - Include complete plans for specimen collection, laboratory measurements, cutpoints, and statistical analysis

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Study Funding

- You and your study team are responsible for BIQSFP application preparation

  https://www.cancer.gov/about-nci/organization/ccct/funding/biqsfp

- You with Alliance will develop budgets to present to Industry
  - DO NOT independently discuss budget with industry
  - Your Alliance Executive Officer, an oncologist part of your study team, along with Alliance contract and budget specialists will direct industry negotiations

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Alliance Protocol Development

- After NCI concept approval, you must help ensure the timely development and activation of your trial by
  - Adhering to study development timelines set by Alliance protocol coordinators
  - Attending all study team teleconferences (protocol + CRFs)
  - Working with your Alliance co-chairs and Executive Officer to help define and incorporate correlative components
- Protocol development process represents a coordinated activity involving investigators, statisticians, data coordinators, executive officers, and is driven by your committee protocol coordinator

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Alliance Protocol Development

- An Alliance Model Protocol Template will be provided, along with a schedule of protocol and forms development milestones
- NCI Operational Efficiency Working Group (OEWG) mandates strict protocol development timelines
  - Phase I, I/II and II study activation 450 days
  - Phase III study activation 540 days

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NCI Operational Efficiency Working Group (OEWG)

- NCI CTEP
  - Phase I, Phase I/II, and Phase II studies that will accrue < 100 patients: final draft submission 60 days from concept approval
  - Phase I/II, or II protocols >/= 100 patients: final draft submission 60 days from concept approval
  - Phase II/III or Phase III protocols: final draft submission 90 days from concept approval.
- NCI DCP
  - Final draft submission 90 days from concept approval

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A021502 Details of protocol development

	% Con		Task Name	Duration	Start	Finish	Baseline Duration	Baseline Start	Baseline Finish
0	**15%**		**A021502 Protocol development timeline**	**307 days**	**Mon 3/21/16**	**Wed 1/11/17**	**307 days**	**Mon 3/21/16**	**Wed 1/11/17**
1	**15%**		**Protocol activation**	**307 days**	**Mon 3/21/16**	**Wed 1/11/17**	**307 days**	**Mon 3/21/16**	**Wed 1/11/17**
2	**100%**	✓	**LOI/Concept**	**30 days**	**Mon 3/21/16**	**Mon 4/18/16**	**90 days**	**Mon 3/21/16**	**Wed 6/15/16**
3	100%	✓	Concept review	1 day	Mon 3/21/16	Mon 3/21/16	1 day	Mon 3/21/16	Mon 3/21/16
4	100%	✓	NCI teleconference held	21.75 days	Tue 3/22/16	Mon 4/11/16	14 days	Tue 3/22/16	Mon 4/4/16
5	0%		~~Revised LOI/concept and consensus review response compiled and submitted~~	~~14 days~~	~~Tue 3/22/16~~	~~Mon 4/4/16~~	~~14 days~~	~~Tue 3/22/16~~	~~Mon 4/4/16~~
6	100%	✓	NCI LOI/Concept approval	8.25 days	Mon 4/11/16	Mon 4/18/16	74.75 days	Mon 4/4/16	Wed 6/15/16
7	**100%**	✓	**Protocol development**	**125 days**	**Tue 4/19/16**	**Wed 8/17/16**	**93 days**	**Wed 6/15/16**	**Tue 9/13/16**
8	100%	✓	PC sends seeded Model Protocol/consent to author(s) and schedules Draft 1 call	2 days	Tue 4/19/16	Wed 4/20/16	2 days	Wed 6/15/16	Fri 6/17/16
9	100%	✓	Seeded model review and content provided	19 days	Thu 4/21/16	Mon 5/9/16	14 days	Fri 6/17/16	Fri 7/1/16
10	100%	✓	PC compiles content into Draft 1	2 days	Tue 5/10/16	Wed 5/11/16	7 days	Fri 7/1/16	Thu 7/7/16
11	100%	✓	PC and EO meet to review Draft 1	0 days	Wed 5/11/16	Wed 5/11/16	1 day	Fri 7/8/16	Fri 7/8/16
12	100%	✓	Study team reviews Draft 1 and provides revisions	13.5 days	Thu 5/12/16	Tue 5/24/16	7 days	Sat 7/9/16	Fri 7/15/16
13	100%	✓	Draft 1 call	0 days	Wed 5/11/16	Wed 5/11/16	7 days	Fri 7/8/16	Thu 7/14/16
14	100%	✓	PC compiles content into Draft 2	2 days	Wed 5/25/16	Thu 5/26/16	8 days	Fri 7/15/16	Sat 7/23/16

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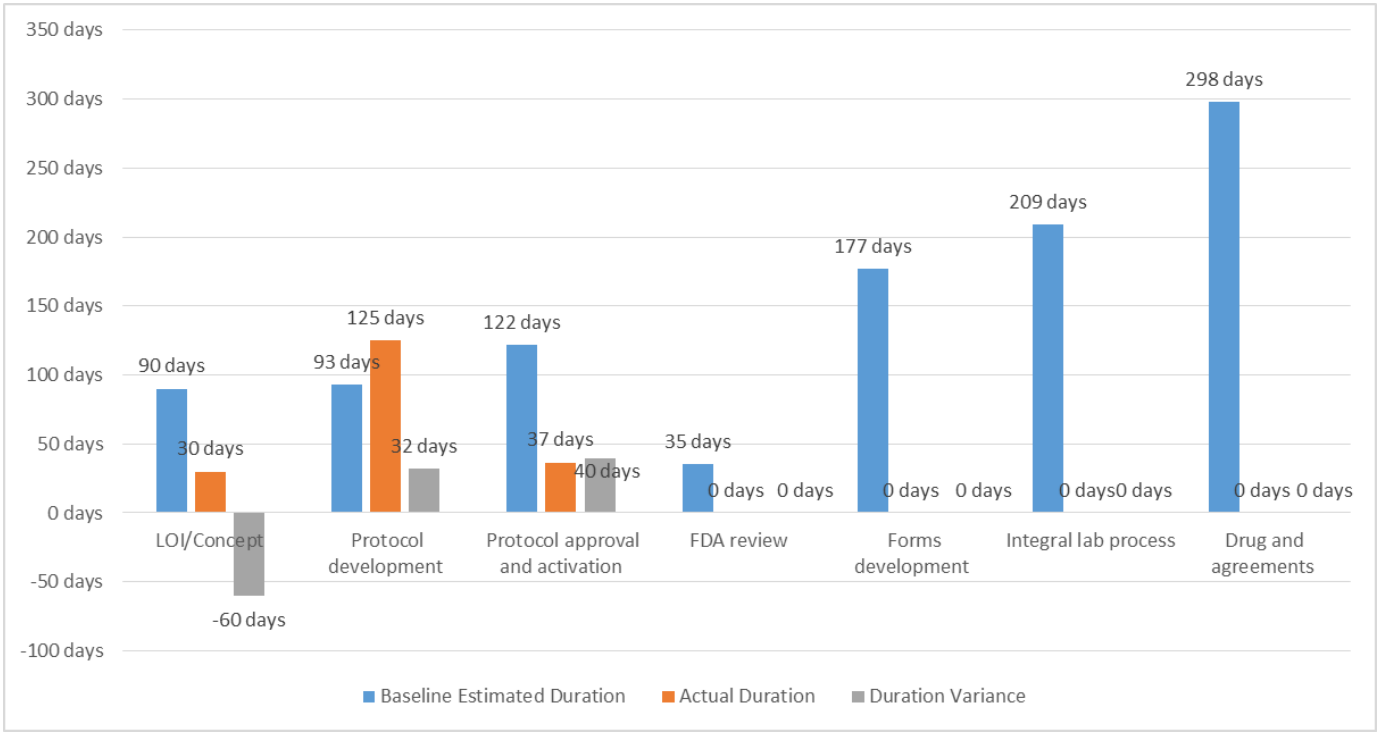
A021502 OEWG versus Actual Duration



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Alliance Protocol Development

- Carefully consider ***all*** study eligibility criteria and required testing/procedures
  - Criteria should be absolutely required for anticipated scientific inference or patient safety
  - Criteria should be unambiguously defined and capable of verification at time of audit
  - Criteria should NOT be regulatory, legal, or other requirements
- Consider all testing and frequency for insurance reimbursement, patient convenience, and site management burden
  - Fixing eligibility and testing procedures after the fact is time consuming and labor intensive

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Alliance: Improving Eligibility in Clinical Trials

C9710

PHASE III RANDOMIZED STUDY OF CONCURRENT TRETINOIN AND CHEMOTHERAPY WITH OR WITHOUT ARSENIC TRIOXIDE (As_2O_3) (NSC # 706363) AS INITIAL CONSOLIDATION THERAPY FOLLOWED BY MAINTENANCE THERAPY WITH INTERMITTENT TRETINOIN VERSUS INTERMITTENT TRETINOIN PLUS MERCAPTOPURINE AND METHOTREXATE FOR PATIENTS WITH UNTREATED ACUTE PROMYELOCYTIC LEUKEMIA

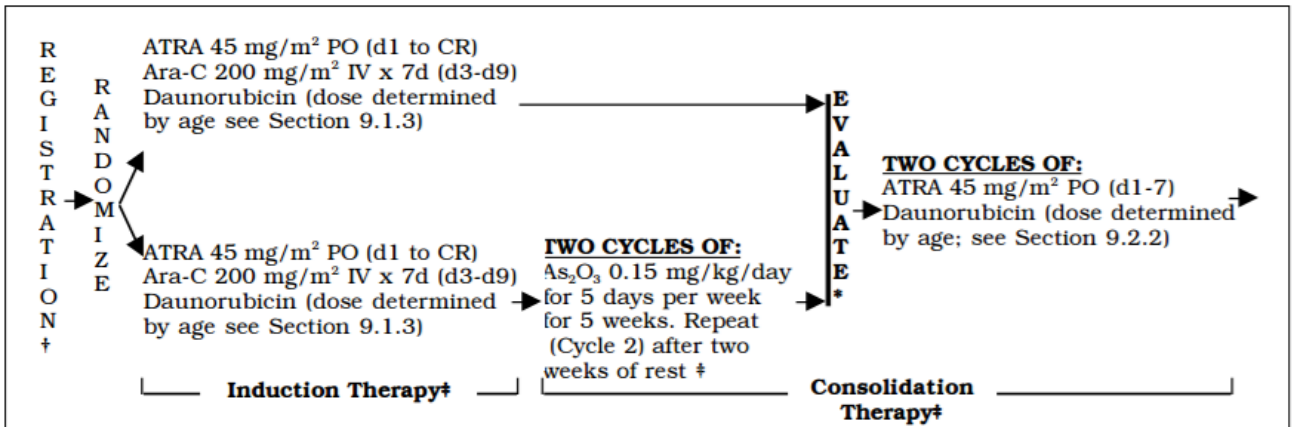
Eligibility Criteria (see Section 5.0):

The only explicit eligibility criteria on this study are defined below.

- Diagnosis of acute promyelocytic leukemia (APL) with proof of APL morphology (FAB-M3) confirmed by RT-PCR assay (see Section 5.1).
- Prior Treatment: No systemic definitive treatment for APL, including cytotoxic chemotherapy or retinoids. Prior therapy with corticosteroids, hydroxyurea or leukapheresis will not exclude the patient.
- Non-pregnant, non-nursing. Treatment under this protocol would expose an unborn child to significant risks. Patients should not be pregnant or plan to become pregnant while on treatment (see Section 5.3).

See also Section 4.0 for general guidelines on the type of patient appropriate for this study and Section 6.0 for other requirements.

TREATMENT SCHEMA



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Alliance Protocol Development

- Alliance studies incorporate “on-study guidelines”
  - Guidelines are not exclusion criteria
  - Allow physician judgment for any given patient
- “Physicians should carefully consider the risks and benefits of any therapy, and therefore enroll patients for whom this treatment is appropriate. Physicians should consider whether any of the following may render the patient inappropriate for this protocol…”
  - J Clin Oncol. 1996 Apr;14(4):1364-70. Reducing patient eligibility criteria in cancer clinical trials. George SL

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Study activation requirements

- The following are required prior to study activation
  - A NCI-final approved protocol
  - IRB approval
    - Randomized phase II and III trials along with select NCI DCP trials will use the NCI Central Institutional Review Board
    - In the absence of the CIRB, an initial institutional review board approval by one institution will suffice
  - Set-up by all systems required to support study enrollment (Medidata Rave [eCRFs], OPEN, etc.)
  - Drug availability
  - Signed contracts and agreements supporting primary study endpoint

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Once your study opens…

- Study chairs are responsible for answering study-specific questions that may arise once your trial has opened, generally regarding eligibility, treatment or dose modifications.
  - Ensure Awareness: include other study team members (Executive Officer, Data Manager, Statistician, Protocol Coordinator, Nurse Oncologist) on responses
  - Maintain Coverage: Assign backup Alliance member (eg, study co chair) if you are unavailable to answer study related questions
  - Maintain Contact Info: Provide study team members with the best way to communicate with you (eg, phone, email) as well as contact information for assistant or secretary

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Study Conduct

- You may not grant eligibility waivers, although you may interpret how a given patient meets criteria
  - This is/is not a complete resection, a stage x
  - This does/does not qualify as prior therapy
- Nobody else may grant eligibility waivers either

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Study Conduct

- Abide by Alliance Policies and Procedures
- Avoid providing information that would allow patient identity to be deduced
- Do not furnish data to directly to industry. Follow appropriate Alliance channels.
- Section 14.4 (Confidentiality of patient information)
- Section 12.2 (Confidential and proprietary information)

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Accrual monitoring

- NCI monitors accrual to all studies to ensure trials meet anticipated monthly accrual goals

Phase 3	Phase 2	Phase 1
When?	**When?**	**When?**
In quarters 5 &6	End of quarter 3	End of quarter2
What is expected accrual?	**What is expected accrual?**	**What is expected accrual?**
>20% of target quarterly accrual	>/=50% of target accrual for past 6 months	>/=50% of target accrual
Possible actions	**Possible actions**	**Possible actions**
Stop trial if </=20%	NCI will request corrective action	NCI will request corrective action
Allow 6 months to improve if > 20 but < 50%		

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Accrual Monitoring

- Study chair should monitor accrual
- Intervene if accrual is not adequate
  - Give talks, web-in-airs, prepare slide sets
  - Identify what accrual barriers are and seek to resolve them
- Prepare corrective action plans for NCI as needed

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Publications

- It is your responsibility to lead the publication of your trial results, whether in a poster, abstract or manuscript
- You must adhere to Alliance Policies and Procedures regarding release of study data and review of all publications using Alliance data

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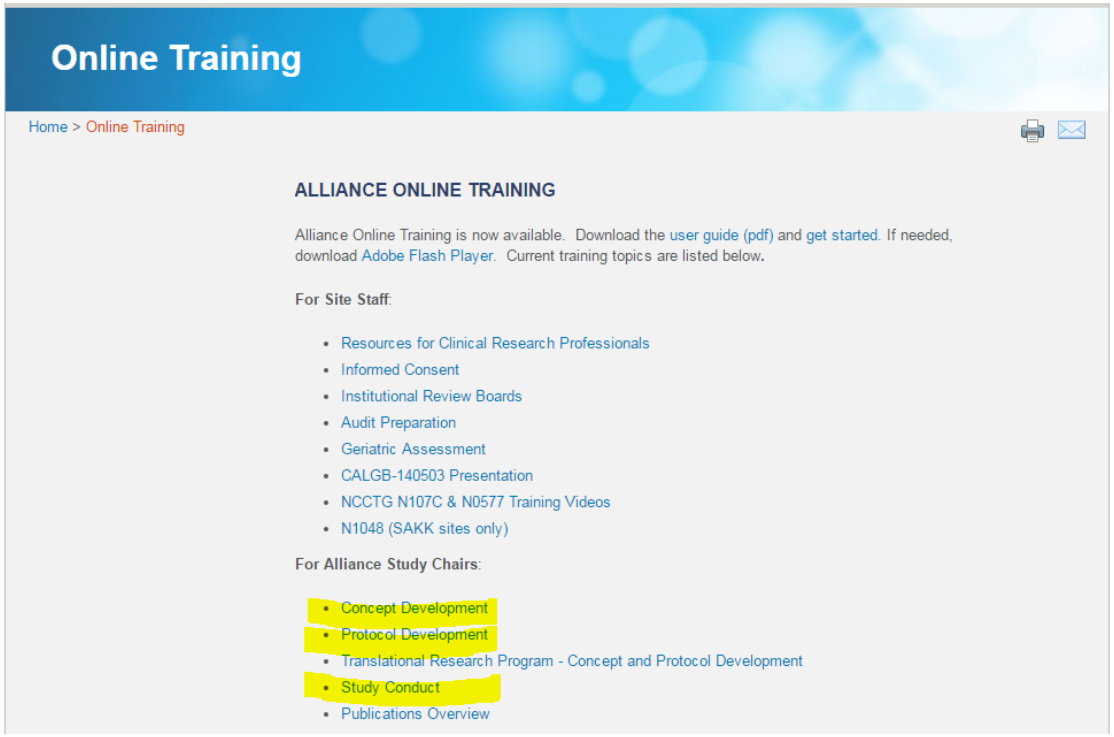
Study Chair Training Modules

- Available on Alliance web site
- Self-paced learning modules, approximately 15-20 minutes
- Cover NCI CTEP & DCP concept submission
- Protocol development process
- Study conduct policies
- Publication policies



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Getting help…

- At any time, if you need help, you may contact
  - Your committee chair
  - Your committee statisticians
  - Your committee protocol coordinator
  - Your committee executive officer
  - Cancer Control Program (CCP) Program Manager
  - Translational Research Program (TRP) Executive Officer

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