

NCI Experimental Therapeutics
Clinical Trials Network
(ETCTN)
NCAB 9 September 2014

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Cancer Therapy Evaluation Program

Program Director, Experimental
Therapeutics Clinical Trials Network

Goals and Objectives of The ETCTN

Research and Development for New Treatments

- Dose and schedule in early treatment trials
- Novel combination therapies

Tumor Characterization in Biomarker-driven studies

- Molecular characterization: expression, sequence and epigenetics
- Validated biomarker assays in qualified labs
- Functional imaging

Enhanced understanding of cancer biology

- Bedside to bench and back

Education and Training for young investigators

Challenges for the Experimental Therapeutics Clinical Trials Network

Accrual

- Smaller patient populations due to molecularly-defined diseases
- A scalable/flexible program that can rapidly adapt to accrual needs

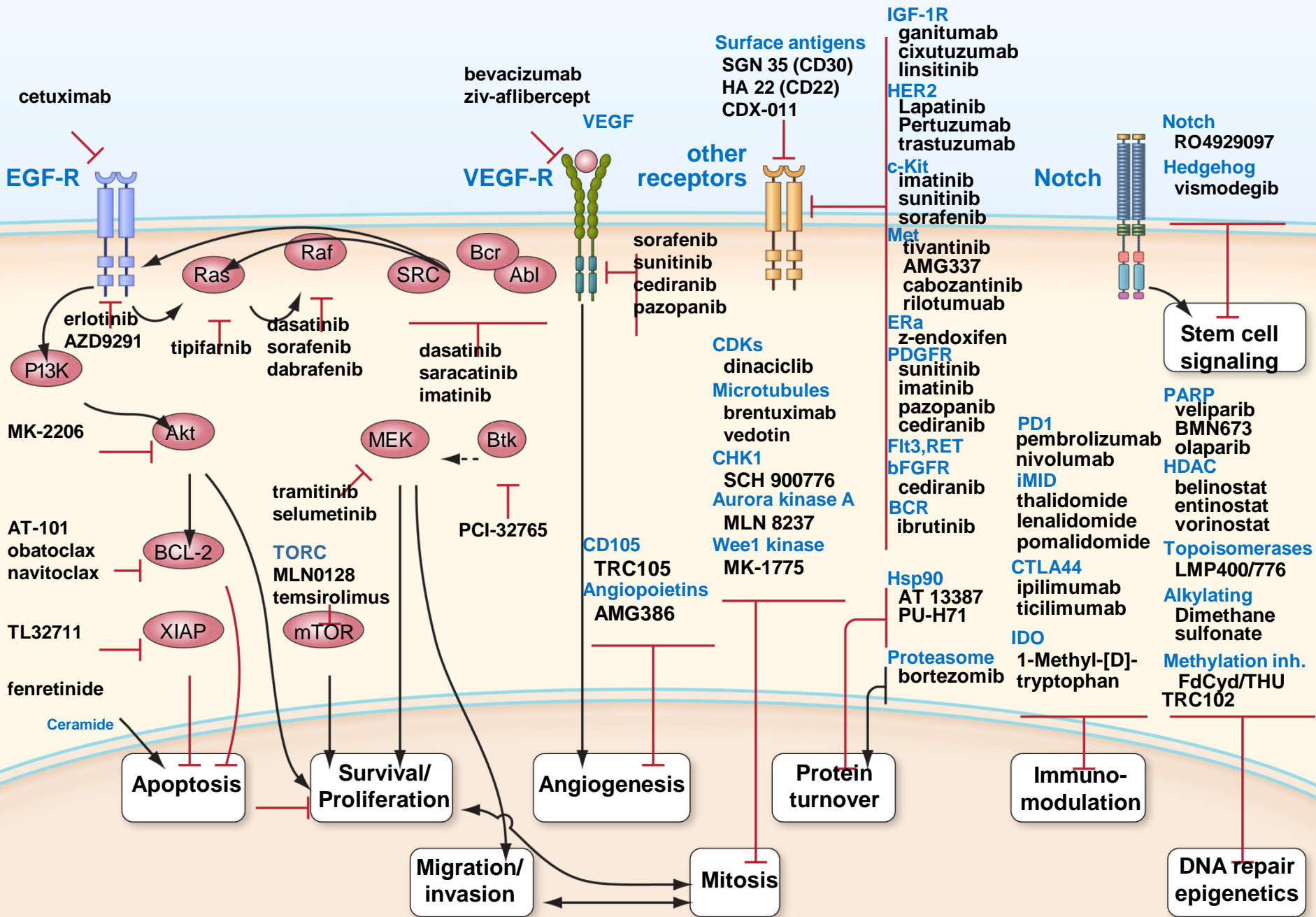
Biomarkers

- Often requires biopsies
- Fit for purpose, validated assays
- Functional imaging

More Facile Mechanisms for Translation

- To and From Bench to Bedside Collaborations
- More predictive animal models to evaluate tumor heterogeneity

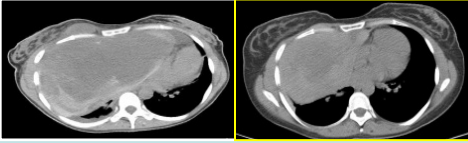
High Priority Targets and DCTD/CTEP Agents



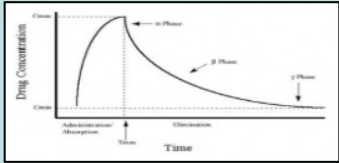
Clinical Translational Research and Cancer Biology: Bedside to Bench and Back

*Clinical observations:

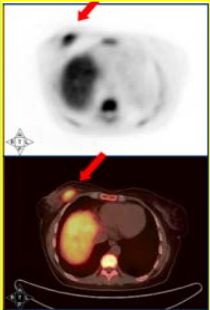
- Clinical response



- PK

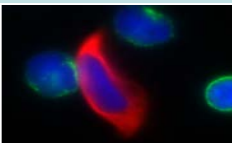


- Functional imaging



- Tumor and normal tissue PD markers

- CTCs, CECs



- Tumor-initiating cells

Patients eligible for early phase clinical trials

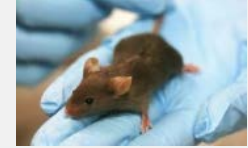
Analysis of tumor and Other tissues for pathway activation or biomarker *

Patient assigned to trial Based on molecular characterization of tumor

Patient monitoring *

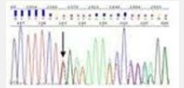
Patient monitoring: Post-treatment molecular re-analysis for response/resistance *

Non-clinical models for targets

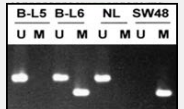


Translational research with clinical models

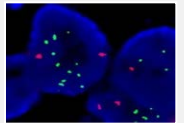
- Sequencing



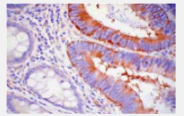
- Methylation



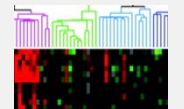
- FISH



- IHC



- Expression array



NCI ETCTN: Scientific Changes

Scientific Elements	Legacy Program	ETCTN
Molecular Characterization	Occasional	Expected
Team Science	Infrequent	Required
Drug Development Plan	Trials not on industry's development plan	Tackle critical unanswered questions: <ul style="list-style-type: none">• Disease-based• Biomarker-based• Drug combinations

NCI Team Science- Drug Development Project Teams

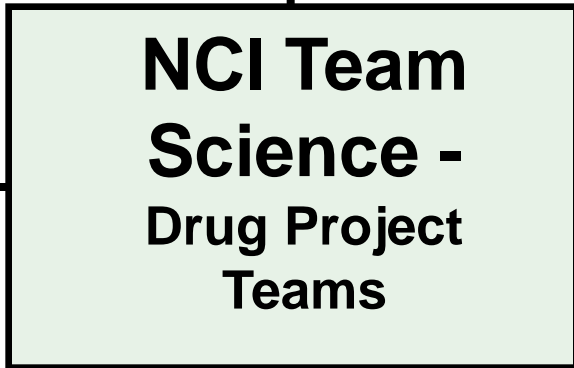
Clinical
(Experimental
Therapeutics Clinical
Trial Network)

Translational

**NCI Team
Science -
Drug Project
Teams**

**Centralized
Support**

**Cancer
Biology**



Extramural Project Team

Team members

- Clinical scientists
- Translational scientists with biomarker and imaging expertise
- Cancer biologists

Tasks

- Initial NCI agent drug development plan
- Description of clinical projects/protocols
- Biomarkers appropriate for agent development
- Outline of preclinical studies- preliminary or concurrent

Presentation

- Initial NCI agent drug development plan
- Input from the Investigational Drug Steering Committee

Project Team Announcement and the Project Team Member Application

- Project Team Announcement (PTA)
 - Replaced the Mass Solicitation
- Project Team Member Application (PTMA):
 - Investigator applies as a clinical or translational project team member
 - NIH biosketch with statement indicating pertinent expertise
 - Specify affiliation (UM1, U01, NCTN, Consortium)
 - PRC review to select PT members
- Clinician Project Team (PT) members
 - Principal Investigators on the trials
 - Identified by the PT for the agent development plan

ETCTN Program Portfolio Management Portal

Provides the ability to manage and track experimental therapies from application submission through protocol accrual

AD-389234

Libraries

- Site Pages
- Shared Documents
- SAC Meeting Materials
- Drug Development Plan
- SAC Meeting Summary
- Project Team Applications (PTA)

Lists

- Calendar
- Application
- Project Detail
- SAC Reviews
- Publications
- Drug "X" Project Contact List
- Protocols
- Project Tracking
- Project Schedule
- Phases and Measures
- Metrics By Phase

Drug "X" Project Overview

Project Detail

Title	Project Name	Drug Team Lead	EMMES Project Manger	Status	Reason Behind Schedule
Pilot Project	Hsp90	Dr. Alice Chen	Amy Gravel	Open	

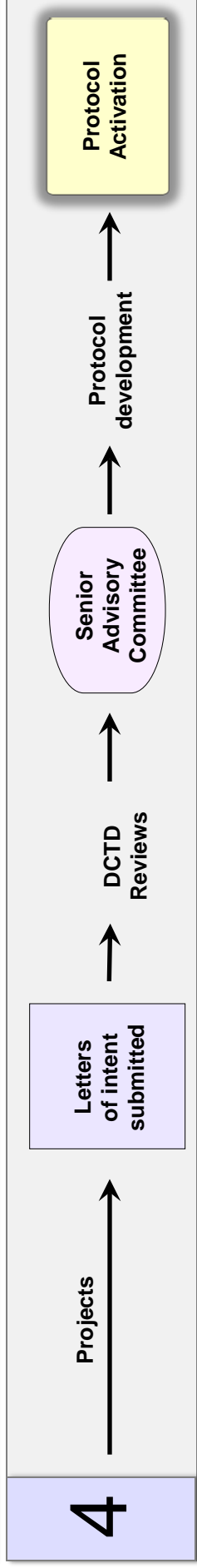
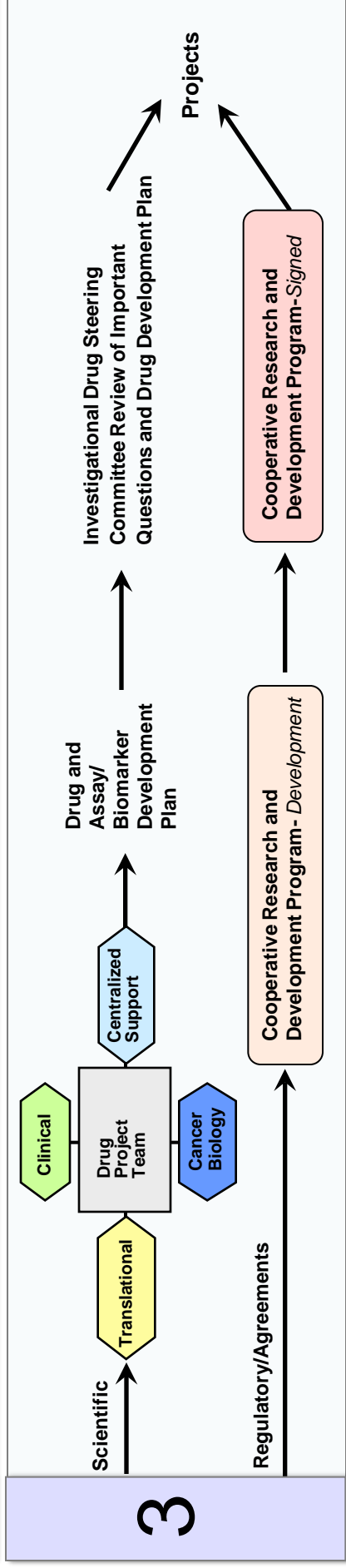
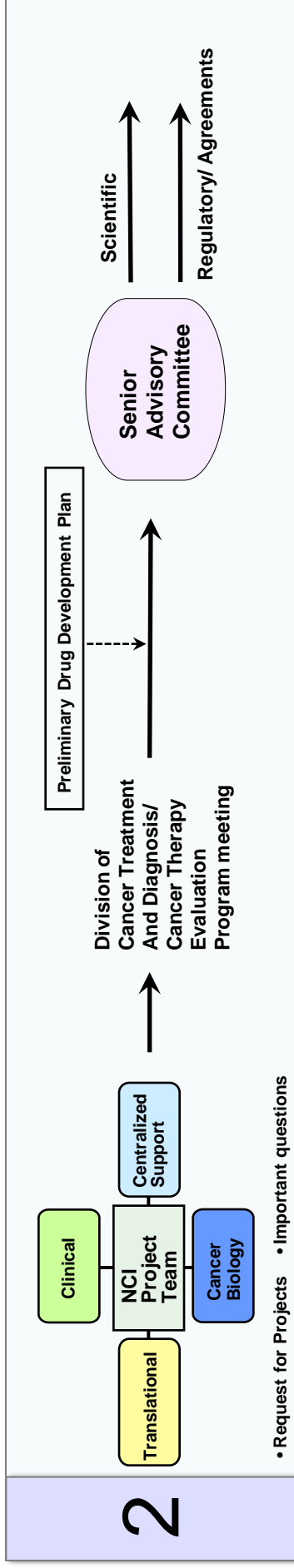
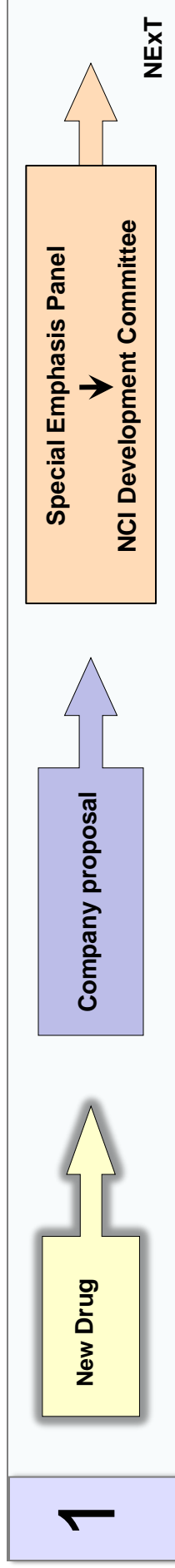
Project Schedule

	Task	Task Name	Start Date
	0	Drug X Project Schedule	8/18/2013
	1	NExT Application; Drug Development Plan (DDP) (1)	8/18/2013
	1.1	NExT PMO provides SEP Summary to IDB Leadership	8/18/2013
	1.2	IDB Leadership assign a Drug "X" Team Lead (DTL)	8/19/2013
	1.3	Drug "X" Team Lead selected	8/19/2013
	1.4	IDB Leadership requests an EMMES Project Manager	8/20/2013
	1.5	EMMES PM assigned	8/20/2013
	1.6	Drug "X" Team Lead prepares presentations for NCI	8/21/2013
	1.7	NDeC selects application for development	8/28/2013
	1.8	EMMES PM creates project site	8/29/2013

8/18/2013 8/2 [▲]

S M T W T F S S

New Development Cycle for NCI Experimental Therapeutics



New Development Cycle for NCI Experimental Therapeutics

NExT Special Emphasis Panel and Development Committee Reviews



NCI Project Team and CTEP Program Meeting: Preliminary Development Plan



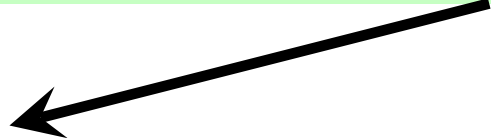
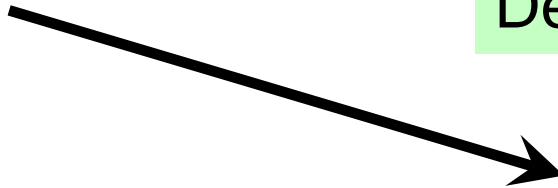
SAC I Review



CRADA negotiation



Extramural Project Team: Finalized Development Plan & IDSC Review



Sac II Review



LOI/Protocol submission

NCI ETCTN: Operational Changes

Operational Elements	Legacy Program	ETCTN
Organization	In Silos (14 sites)	Integrated Network (10 sites)
Centralized Support	<u>Limited:</u> <ul style="list-style-type: none"> • Safety • Auditing 	<u>Comprehensive:</u> <ul style="list-style-type: none"> • Safety • Auditing • Data capture/monitoring • Central Institutional Review Board • Registration/Roster/Regulatory • Project management • Pharmacokinetics
Timeline-LOI approval	~21 months	~15 months
Resources for Molecular Characterization and Sample Acquisition	Limited	<ul style="list-style-type: none"> • Fewer sites, fewer trials, more extensive characterization

NCI-Sponsored Infrastructure for ETCN Trials



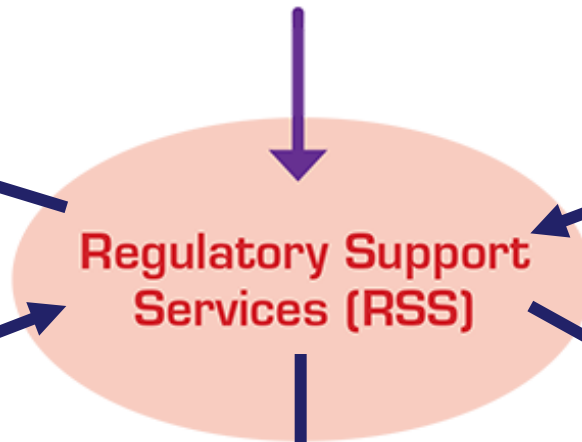
1. Investigators and Associates register with CTEP. CTEP IAM accounts required for access to applications.

CTEP Enterprise

6. *Other Tasks:*
CTEP-AERS,
Agent Ordering,
Monitoring/Audits,
OEWG Reporting



2. Access Protocol Documents and Check Regulatory Status



3. Obtain CIRB Approval

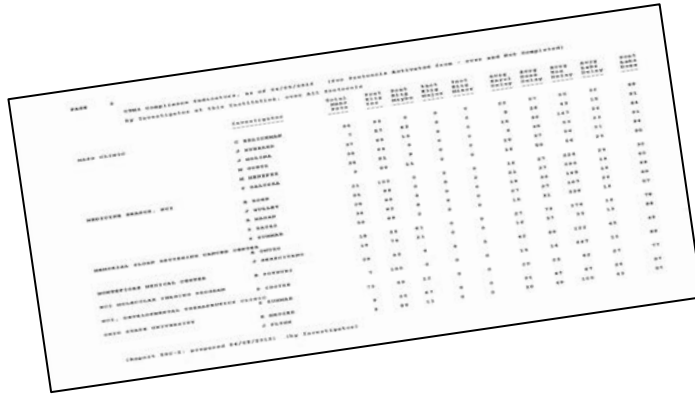


5. Enter and Manage Patient Data



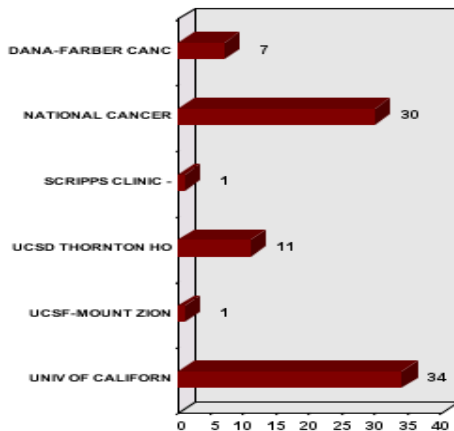
4. Enroll Patients

Theradex Instance of Medidata Rave: Web-based Reporting

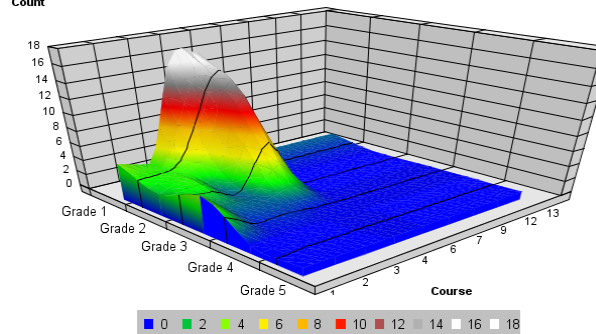


August 1, 2014 NCI/CTEP
 Moved from paper to web-based reporting
 for early clinical trials

Enrollment by Site



Event Count by Course and Grade

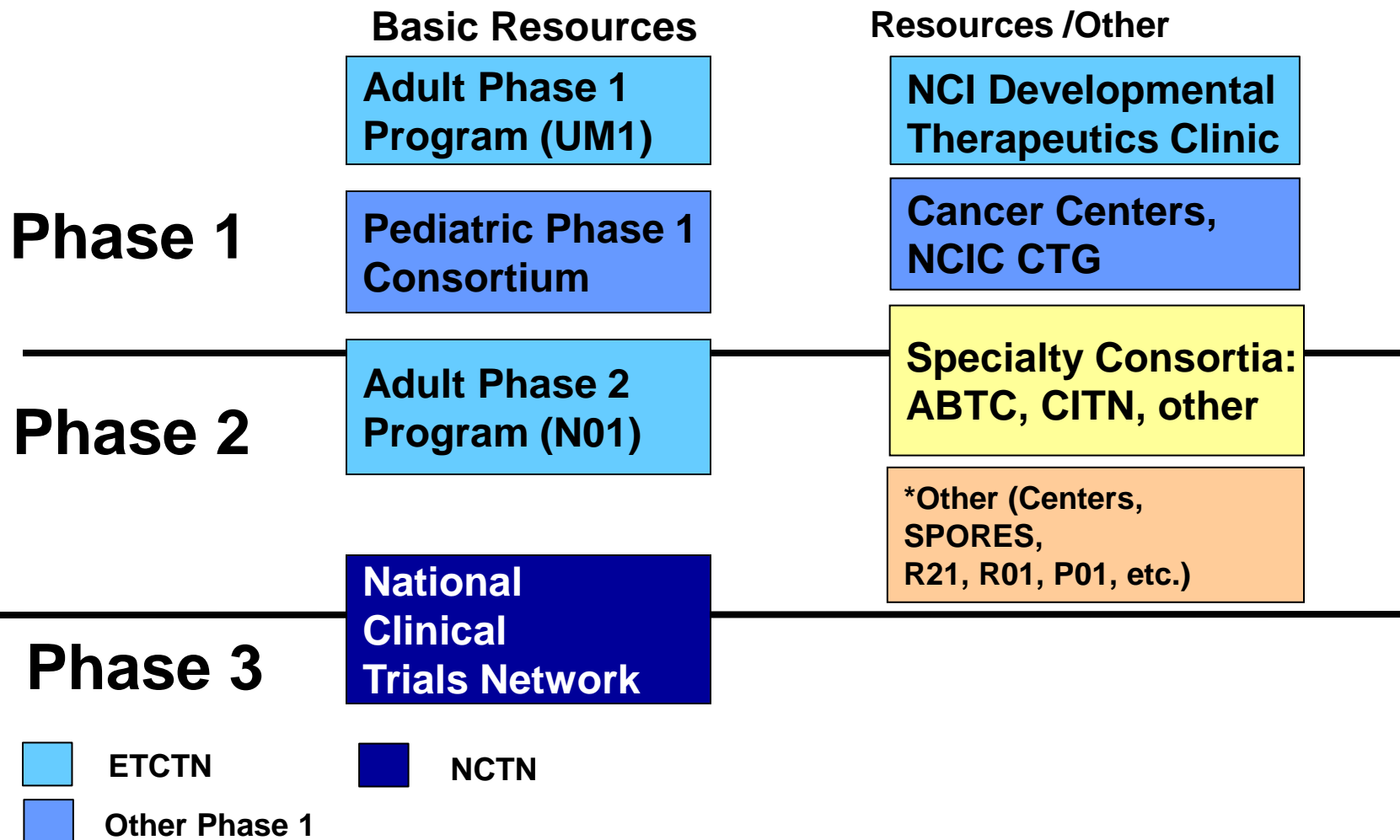


Compliance Overall for a Protocol
 Protocol: 5582

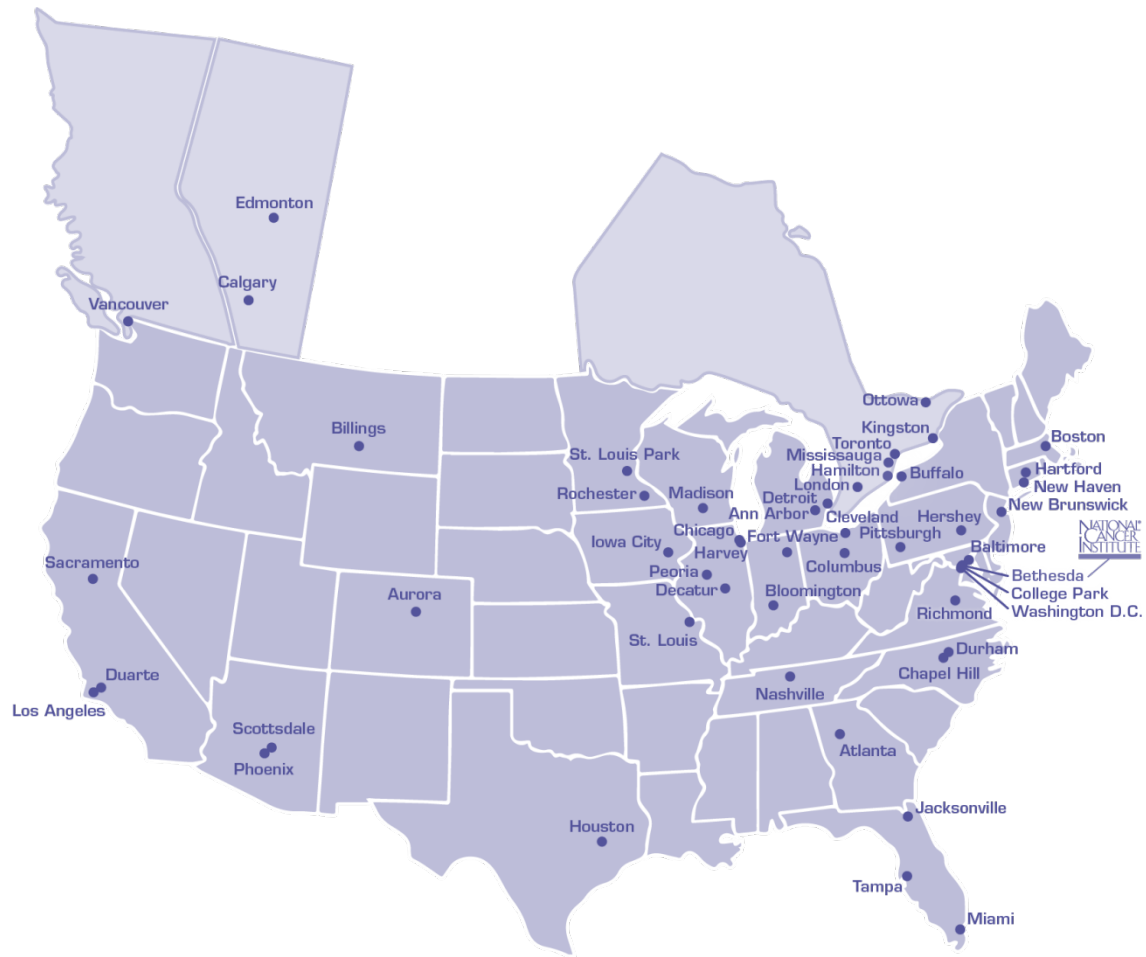
	Value	Percent
Number of Patients	51	
Number of Courses	101	
Investigator Eligible Patients	50	98.0%
Investigator Ineligible Patients	1	2.0%
Monitor Eligible Patients	49	96.1%
Monitor Ineligible Patients	2	3.9%
Monitor Missing Info	0	0.0%
Courses Evaluable	96	95.0%
Courses Complete	85	84.2%
Courses with Dose Modifications	47	46.5%
Courses with Significant Toxicities	70	69.3%
Average Lab Delay (Days)	69	
Labs Completed per Protocol	9644	81.3%

* Real time, interactive, web-based, data summaries for monitoring and data mining/analysis

Transformed NCI Experimental Therapeutics Clinical Trials Program



NCI Drug Development Programs: ETCTN



ETCTN Education and Training

Since program launch, we have held a number of educational webinars for ETCTN members:

- For Leadership:
 - Kick-off and Overview
 - Rosters and Roles
 - Patient Enrollment
 - NCI CIRB
 - PIO Updates
 - Data Management
 - Biomarkers
 - Implementing Drug Project Teams
 - Web Reporting
- For Site Staff:
 - Introduction to the ETCTN, Centralized Services, and the CTSU Website
 - Patient Enrollment
 - Regulatory Processes
 - Data Management

Educational Materials

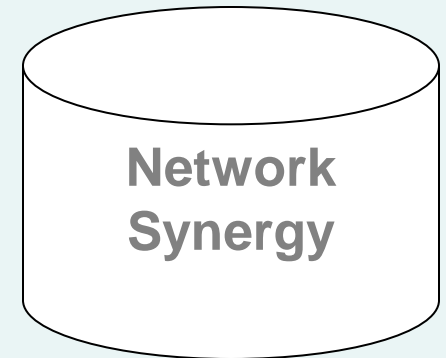
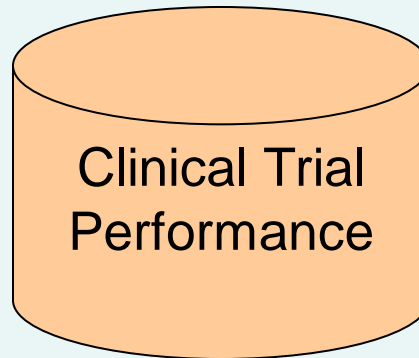
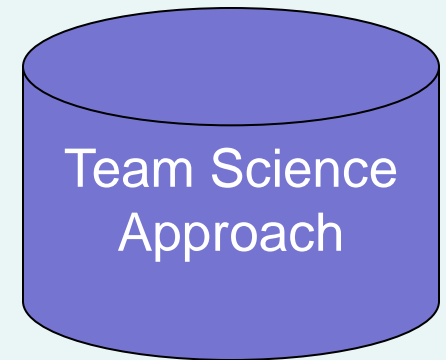
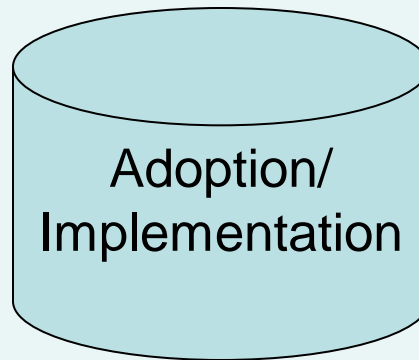
- Educational Materials on the ETCTN-CTSU website includes: links to the webinar recordings, checklists, and information sheets on 14 different topics :
 - Protocol Development
 - Protocol Amendments
 - Person Registration & CTEP-IAM
 - Rosters & Roles
 - The CTSU
 - Protocol Access & Communications
 - Regulatory Processing
 - The NCI CIRB
 - Patient Enrollment
 - Agent Ordering
 - Data Management
 - SAE Reporting
 - CDUS Reporting
 - Auditing and Monitoring
- All documents will be posted to the ETCTN pages on the CTEP website once development is complete

Evaluation of the ETCTN

Goals:

- Document ETCTN's implementation
- Identify course corrections if needed
- Provide data to guide decision making for program's subsequent funding cycle

Assess Four Key ETCTN Domains





NATIONAL[®]
CANCER
INSTITUTE



Backup Slides

ETCTN Principal Investigators

Institutions	PIs
City of Hope/Beckman Res. Inst.	Newman, Edward Lenz, Heinz-Joseph
Dana-Farber/Harvard Cancer Center	Kufe, Donald Flaherty, Keith Shapiro, Geoffrey
Duke U. North Carolina Wash. U.	Hurwitz, Herbert Dees, Elizabeth Lockhart, Albert
Johns Hopkins	Carducci, Michael Gocke, Christopher Gojo, Ivana Rudek, Michelle
Mayo - Rochester	Erlichman, Charles Huluska, Paul Sausville, Ed
NCI-DTC	Kummar, Shivaani

Institutions	PIs
Ohio State U.	Grever, Michael
Rutgers-Cancer Inst. NJ U. Wisconsin	DiPaola, Robert Liu, Glenn
U. Chicago	Ratain, Mark Maitland, Michael
U. Health Network	Siu, Lillian Sullivan, Dan
U. Pittsburgh	Chu, Edward Beumer, Jan
U. Texas – MDACC U. Colorado – Denver	Yao, James Eckhardt, Gail Meric-Bernstam, Funda
Yale University	Lorusso, Patricia Eder, Paul Berlin, Jordan

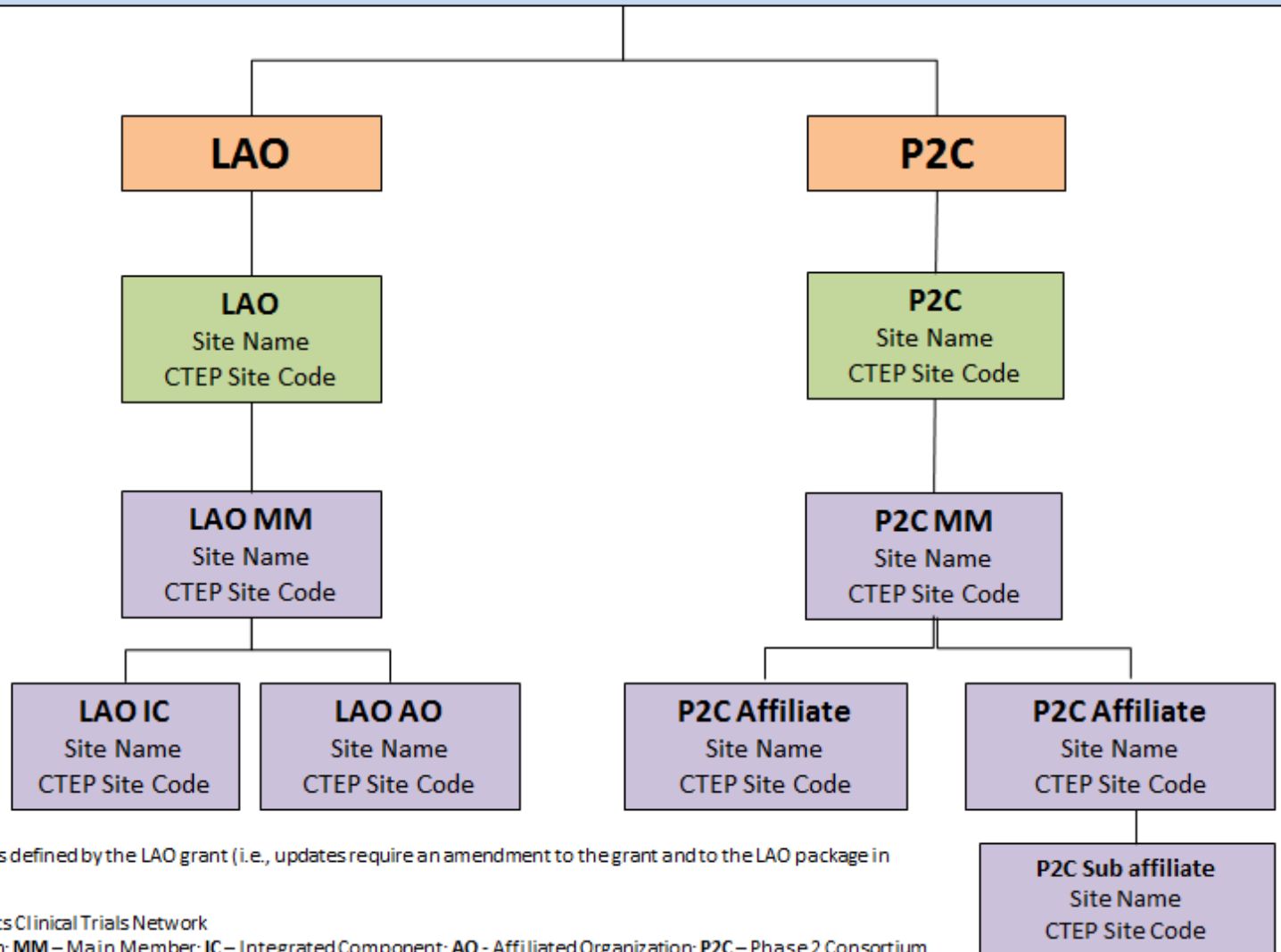
ETCTN Organization Structure

Roster Level

Org Type

Roster Owners
Grantees

Treating Sites*



*For LAO, the treating site roster is defined by the LAO grant (i.e., updates require an amendment to the grant and to the LAO package in CTEPSYS).

ETCTN – Experimental Therapeutics Clinical Trials Network

LAO – Lead Academic Organization; MM – Main Member; IC – Integrated Component; AO – Affiliated Organization; P2C – Phase 2 Consortium

Agents currently tracked for PTA/PTMA

Agent	NSC/IND	MOA	CRADA/CDA *	PTA/PTMA
AT13387	749712/109876	Hsp90i	11/02/2009	To IDSC
BMN 673	771561/119558	Oral PARPi	06/21/2013	Mass Solicitation
AZD9291	781254/-----	EGFRi, 3 rd Gen	04/03/2014	In prep
VX-970	780162/-----	ATRi	05/29/2014	In prep
SGI-110	780463/-----	DNMTi	11/20/2011*	In prep
AMG-337	779337/-----	cMeti	08/09/2013	In prep

Glossary

- **IAM** – Identity and Access Management
- **Regulatory Support System (RSS)** - An application created within the CTSU Enterprise system to create and manage institution, person, and regulatory data for CTEP-supported Cooperative Groups, contractors, and grantees. It is also used to manage CTSU-specific enrollment and delinquency tracking data.
- **Oncology Patient Enrollment Network (OPEN)** - The web-based registration system for patient enrollments onto NCI-sponsored clinical trials. The system is integrated with the CTSU Enterprise System for regulatory and roster data, and with each of the Cooperative Groups' registration/randomization systems for patient registration/ randomization. OPEN provides the ability to enroll patients on a 24/7 basis.