NCI Update

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NIH NATIONAL CANCER INSTITUTE

CTAC Meeting
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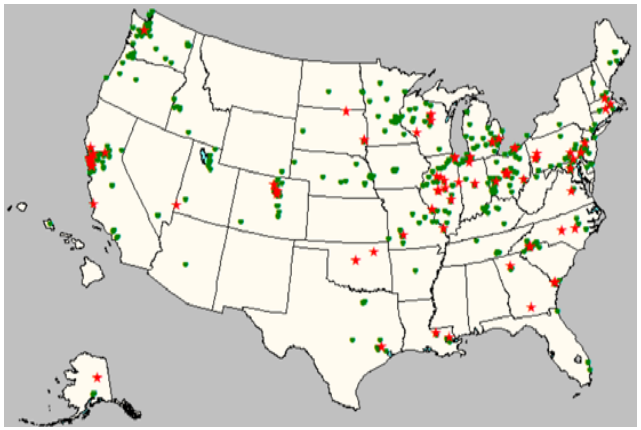
Status and History of NCI-MATCH Trial

- Trial opened August 12, 2015, with 10 treatment arms.
- Trial temporarily closed to new accrual November 11, 2015 for built-in interim analysis.
- 795 patients screened between August 2015 opening and November 2015 temporary closure (3 month period).
- Original estimate of 50 screens per month greatly surpassed (100/week during latter period).
- Approx. 900 approved sites
- 192 active sites (at least 1 patient)
  - **Active : 2/3 community, 1/3 academic**
- Trial re-opened May 31, 2016, with 24 treatment arms.



NCI-MATCH Interim Analysis Conclusions

1. A trial of therapy based on genetic characteristics of the tumor is feasible in the institutions of the NCTN and NCORP
2. The 87% completion rate for tumor testing that was achieved in the first cohort can be maintained for the remainder of the trial
3. A high proportion of less common malignancies in this early analysis opens options for advances in these cancers
4. Analysis early in the trial permits enhancements to the study structure
5. Early analysis also permits realistic planning for additional drugs/targets

Full analysis: ecog-acrin.org/nci-match-eay131/interim-analysis

NCI-MATCH Changes

Main changes:

- Increase in screening goal to 5,000 patients
- Increase in number of arms (24 currently and 8-10 in development)
  - Match rate expected to be 23% overall (more with additional arms)
- Greater focus on communication to influence patient selection
- Expansion of analytical capacity to accelerate return of results for patients

Other changes:

- Mandating needle aspiration in all cases
- Allowance of tumor samples obtained up to six months prior to registration, with qualifications
- Allowance of data from specific other genetic platforms for arms that have rare variants as inclusion criteria

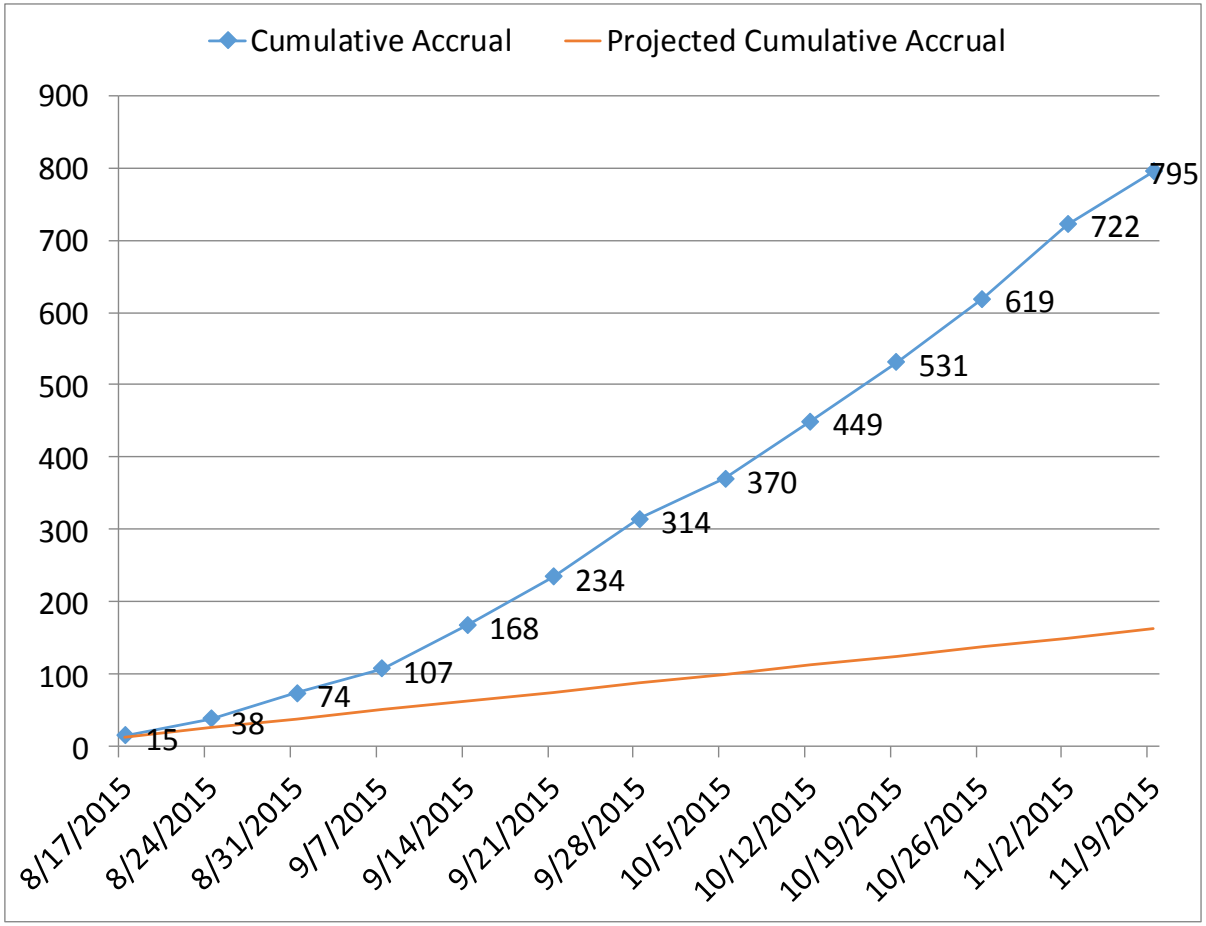
NCI-MATCH Expanded to 24 Arms May 31, 2016

(8-10 additional arms in review/in development)

Arm / Target	Drugs(s)
A EGFR mut	Afatinib
B HER2 mut	Afatinib
C1 MET amp	Crizotinib
C2 MET ex 14 sk	Crizotinib
E EGFR T790M	AZD9291
F ALK transloc	Crizotinib
G ROS1 transloc	Crizotinib
H BRAF V600	Dabrafenib+trametinib
I PIK3CA mut	Taselisib
N PTEN mut	GSK2636771
P PTEN loss	GSK2636771
Q HER 2 amp	Ado-trastuzumab emtansine

Arm / Target	Drug(s)
R BRAF nonV600	Trametinib
S1 NF1 mut	Trametinib
S2 GNAQ/GNA11	Trametinib
T SMO/PTCH1	Vismodegib
U NF2 loss	Defactinib
V cKIT mut	Sunitinib
W FGFR1/2/3	AZD 4547
X DDR2 mut	Dasatinib
Y AKT1 mut	AZD 5363
Z1A NRAS mut	Binimetinib
Z1B CCND1,2,3 amp	Palbociclib
Z1D dMMR	Nivolumab

NCI-MATCH Weekly Accruals Far Exceeded Projections



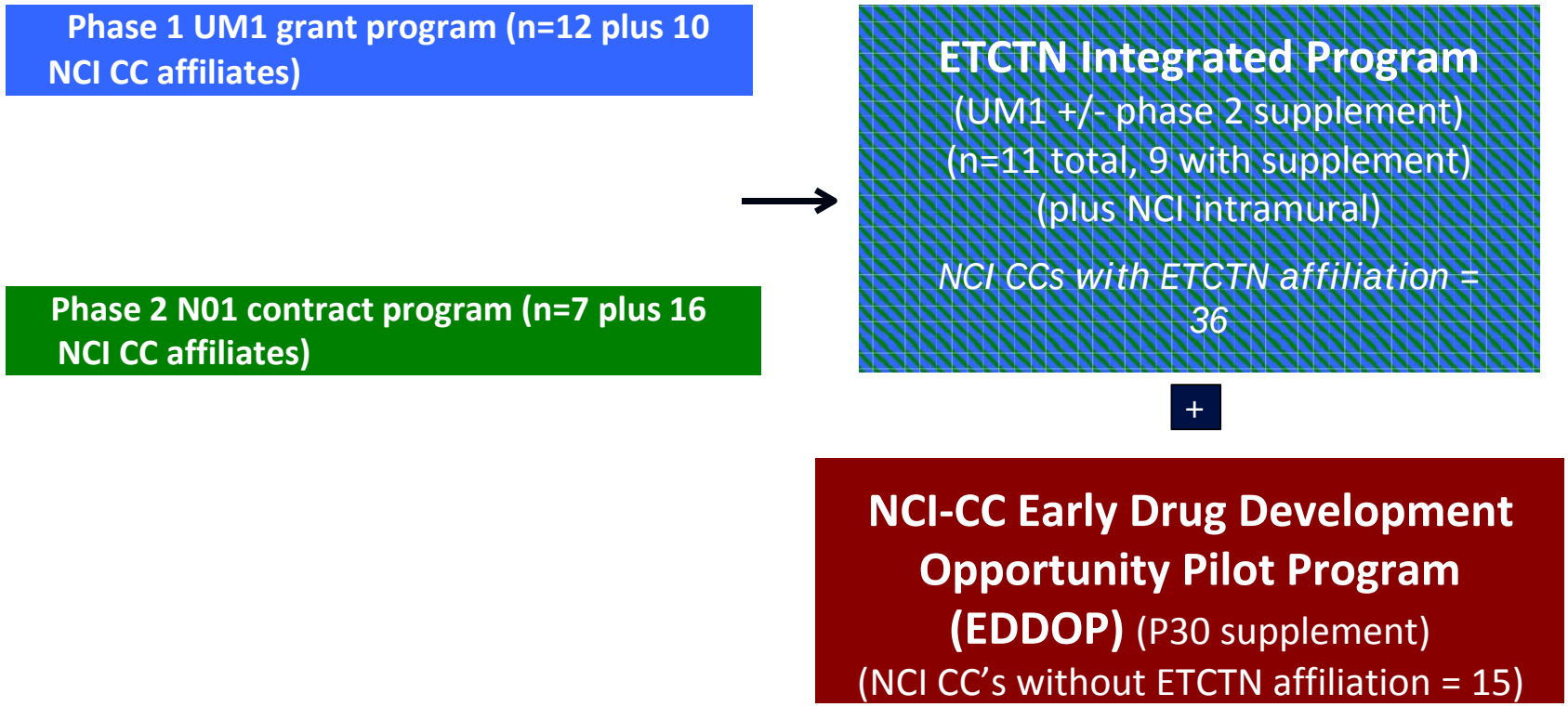
Projected 50 Cases/Month at Start and

Gradual Ramp-up in Year 1

Current Status: as of July 3, 2016

- 1025 Patients registered (230 since 31 May)
- 690 Patients screened (45 since 31 May)
- 31% of screened patients assigned to a treatment arm since 31 May.
- Estimated median assay turnaround time is 12 days

ETCTN Revision Initiative



ETCTN Combined Phase 1 and Phase 2 Program

36 NCI-Designated Cancer Centers Participate

MD Anderson CC
U. Colorado CC

City of Hope CC
UC Davis CC
USC Norris CC
Stanford CI

Ohio State U.
Case/Cleveland Clinic
U. Kentucky Markey CC

U. Pittsburgh Cancer Center
U. Penn Abramson CC

Johns Hopkins Kimmel CC
U. Virginia CC
Thomas Jefferson Kimmel CC
Emory Winship CC
Memorial Sloan Kettering CC

Yale U. Cancer Center
Vanderbilt-Ingram CC
UCSD Moores CC
UCSF H Diller Family CC
BA Karmanos CC

Rutgers CINJ
U. Wisconsin CC

Dana Farber Cancer Institute

Mayo Clinic
U. Iowa Holden CC
U. Maryland Greenbaum CC
Columbia U. Irving CC

Duke Cancer Institute
UNC Lineberger CC
Wash. U. Siteman CC

Princess Margaret UHN
Moffitt Cancer Center
British Columbia Cancer Agency
Virginia Commonwealth U. CC

ETCTN Combined Phase 1 & 2 Sites

ETCTN Revision Initiative

Phase 1 UM1 grant program (n=12 plus 10 NCI CC affiliates)

Phase 2 N01 contract program (n=7 plus 16 NCI CC affiliates)

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ETCTN Integrated Program
(UM1 +/- phase 2 supplement)
(n=11 total, 9 with supplement)
(plus NCI intramural)

NCI CCs with ETCTN affiliation = 36

+

NCI-CC Early Drug Development Opportunity Pilot Program (EDDOP) (P30 supplement)
(NCI CC's without ETCTN affiliation = 15)

Past

Present

Early Drug Development Opportunities Pilot Program (EDDOP) Accrual Supplement Program

- NCI intends to make **awards to 15 NCI Cancer Centers** for the Early Drug Development Opportunities Pilot Program (EDDOP) to support accrual to select ETCTN studies.
- EDDOP institution rosters are currently being built to allow access and permissions for all ETCTN centralized clinical trial management systems, including OPEN and Medidata Rave
- One training session with clinical research personnel from EDDOP sites was held on June 27

EDDOP Accrual Supplement Awardees

NCI-CC	Project leader
Baylor College of Medicine - Dan L. Duncan Cancer Center	Martha P. Mims, MD, PhD
University of Alabama Comprehensive Cancer Center	Mansoor N Saleh, MD
Norris Cotton Cancer Center – Dartmouth	Konstantin H. Dragnev, MD
UT Southwestern - Harold Simmons CCC	Muhammad Shaalan Beg, MD
University of Michigan	Ajjai Alva, MD
Albert Einstein CC	Joseph Sparano, MD
University of Arizona CC	Daruka Mahadevan, MD, PhD
Huntsman Cancer Institute – Utah	Sunil Sharma, MD
Langone Medical Center – NYU	Jeffrey Weber, MD, PhD
Roswell Park Cancer Institute	Marc Ernstoff, MD
University of Kansas Cancer Center	Stephen Williamson, MD
Robert Lurie CCC – Northwestern	Francis Giles, MD
Fox Chase Cancer Center	Margaret Von Mehren, MD
Fred & Pamela Buffett CC – Nebraska	Apar Ganti, MD
University of Chicago	Walter Stadler, M.D.

ETCTN Combined Phase 1 & 2 Sites + EDDOP Sites

www.cancer.gov **www.cancer.gov/espanol**