

Update: NCI Formulary & NCI-MATCH Trial

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NCI Virtual Drug Formulary

- Access to investigational drugs for investigator initiated studies is difficult and time consuming, often the cost-benefit of negotiating an agreement with a Pharmaceutical Collaborator is prohibitive or so difficult and time consuming that the study is never initiated.
- This process is especially burdensome for multi-agent combinatorial studies, and more burdensome still when one or both of those agents are investigational and proprietary to different collaborators.
- Major roadblock to precision medicine clinical trials

NCI Virtual Drug Formulary: Development

- Created a system within the NCI that leverages our existing mechanisms to provide PIs with Investigational agents for investigator held INDs
- The program:
 - ✓ Agent menu; 8 week turn-around time for Pharma review (approval or not) of proposals
 - ✓ Utilizes pre-existing agreements/infrastructure that current Pharmaceutical Collaborators are already familiar with
- Agents provided for both clinical and pre-clinical studies
- INDs held by investigators/institutions, not CTEP/NCI; no NCI funding for trials
- Agreement terms standardized or pre-approved so as to substantially decrease the transactional costs of study initiation; NCI funds drug distribution and tracking of trials
- Launched January 2017; Currently: 26 agents from 7 companies:
 - Agents: Alectinib; Atezolizumab; Bevacizumab; Cobimetinib; Durvalumab; Ensartinib; Ipilimumab; Larotrectinib; LY3039478; Mogamulizumab; Nivolumab; Obinutuzumab; Pertuzumab; Prexasertib; Savolitinib; Selumetinib; Trastuzumab; Tremelimumab; Vemurafenib; Vismodegib; Vistusertib; AZD1775; AZD5069; AZD5363; AZD8186; MEDI9447
 - Companies: Bristol-Myers Squibb; Eli Lilly; Genentech; Astra-Zeneca; Kyowa Hakko Kirin; Loxo; Xcovery

NCI FORMULARY



Additional Resources

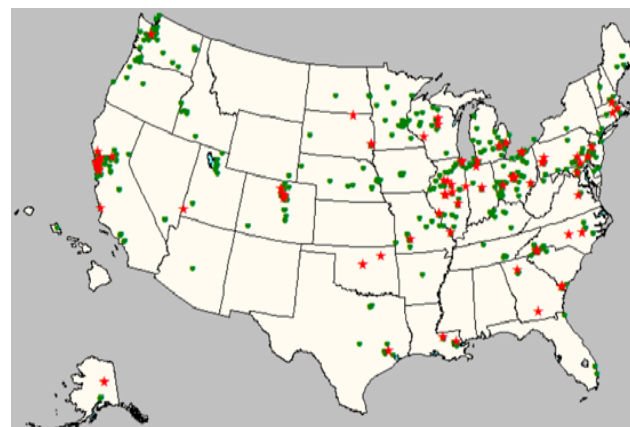
- [Available Agents Table](#)
- [Cancer Moonshot](#)
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NCI Formulary: A Public-Private Partnership

The National Cancer Institute (NCI) agent formulary (NCI Formulary) is a public-private partnership between the NCI and pharmaceutical and biotechnology companies with a purpose of providing academic investigators with rapid access to agents or combinations of agents for cancer clinical trial use; particularly, trials focused on agents targeting molecular pathways from multiple collaborating pharmaceutical companies. As genomic sequencing data become mainstream in cancer therapy, requests for and access to multiple targeted agents for the conduct of clinical research studies are becoming more common. The NCI Formulary will support an efficient mechanism to provide pharmaceutical company

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).
- **Over 1000 approved sites**
- Trial re-opened May 31, 2016, with 24 treatment arms.



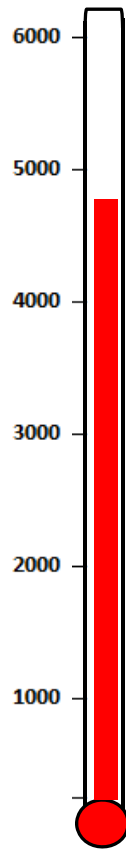
Participation Rates by Site Type:

NCORPS ~ 90%

NCI Cancer Centers ~ 80%

(28/30 LAPS)

NCI-MATCH Testing and Enrollment as of 3/12/17



4702 patients with tumor samples (N=6000)

3516 patients had received their test results

722 had a gene abnormality matching an available treatment

And proceeded to be further evaluated for the specific eligibility for the arm to which they matched

495 patients had enrolled for treatment

NOTE: These are strictly numbers reflecting a point in time and cannot be used to calculate overall rates; some are assigned and still in evaluation for eligibility for an arm; estimated 72% of those assigned will enroll

Current: as of March 12, 2017

- **100-120 registrants/week**
- **Weekly assignments (20% of screened): 20**
- **Weekly enrollments on an arm: 14-15**
- **Assay success rate 94%**
- **Median assay turnaround time 16 days**
- **Toxicity acceptable**

Primary Disease Sites of Patients Enrolled for Screening: Oct 2016

	All Screened	Assigned Treatment
Anal Cancer	15 (1%)	4 (1%)
Bladder/Urothelial	35 (2%)	9 (3%)
Breast	235 (14%)	52 (17%)
Cervical Cancer	23 (1%)	9 (3%)
CNS	17 (1%)	5 (2%)
Colorectal Cancer	244 (14%)	43 (14%)
Gastroesophageal Cancer	58 (3%)	16 (5%)
Head and Neck	73 (4%)	16 (5%)
Kidney	24 (1%)	3 (1%)
Liver and Hepatobiliary Cancer	82 (5%)	15 (5%)
Lymphoma	11 (1%)	0 (0%)
Melanoma	26 (2%)	2 (1%)
Mesothelioma	10 (1%)	3 (1%)
Neuroendocrine Cancer	53 (3%)	10 (3%)
NSCLC	129 (8%)	18 (6%)
Ovarian	192 (11%)	24 (8%)
Pancreas	104 (6%)	4 (1%)
Prostate Cancer	40 (2%)	8 (3%)
Sarcoma	78 (5%)	11 (4%)
Small Cell Lung Cancer	33 (2%)	2 (1%)
Uterine Cancer	111 (7%)	32 (10%)
Other	111 (7%)	21 (7%)
Total	1704	307

NCI-MATCH: Baseline Demographics: 10/2016

	Enrolled for Screening Pre Pause (Step 0, n = 795)	Enrolled for Screening Post Pause (Step 0, n = 1639)	Assigned to Treatment Post Pause (n = 253)
Male	305 (38%)	633 (39%)	88 (35%)
Female	490 (62%)	1005 (61%)	165 (65%)
Not Reported		1 (0.1%)	
Age (min, 25%, med 75%, max)	(24, 54, 63, 70, 93)	(18, 54, 61, 68, 100)	(19, 50, 60, 68, 86)
White	646 (81%)	1332 (81%)	212 (84%)
Black	88 (11%)	131 (8%)	20 (8%)
Asian	37 (3%)	59 (4%)	5 (2%)
Native Hawaiian	1 (0%)	8 (0%)	1 (0%)
Native American	4 (1%)	5 (0%)	1 (0%)
Race not reported	29 (4%)	104 (6%)	14 (6%)
Hispanic	36 (5%)	75 (5%)	17 (7%)
PS 0	--	635 (39%)	92 (36%)

NCI-MATCH: Accrual by State

States	Number Registered
California	177
Minnesota	144
Ohio	143
Pennsylvania	128
Michigan	115
Illinois	113
Wisconsin	101
Oklahoma	100
Georgia	97
Texas	73
Maryland	61
Colorado	58
Missouri	56
South Carolina	55
Indiana	52
New York	52
Washington	49
Louisiana	39
Florida	31
Alabama	26
Idaho	26
Delaware	24
North Carolina	24
Virginia	24
Iowa	23
Hawaii	22
Kentucky	19
South Dakota	19
New Jersey	18
Rhode Island	18
Utah	18
Massachusetts	17
Nebraska	16
New Hampshire	13
North Dakota	13
Oregon	13
Maine	12
Connecticut	10
Tennessee	10
Montana	9
West Virginia	9

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

Red = accrued 35 patients;

Green = nearing 35 patient

Arms added: March 13, 2017

- EAY131-J: Herceptin + Perjeta/HER2 Amp (**to follow Arm Q**).
- EAY131-L: MLN0128/mTOR Mutations (**New target**)
- EAY131-M: MLN0128/TSC1/TSC2 Mutations (**New target**)
- EAY131-Z1C: Palbociclib/CDK4/CDK6 Amplification (**New target**)
- EAY131-Z1E: Loxo 101/NTRK Fusions (**New target**)
- EAY131-Z1I: AZD1775/BRCA1, BRCA2 mutations (**New target**)

7 arms met accrual goal

- Arm I: Taselisib for PIK3CA mutations (nearing 70 in expansion)
- Arm W: AZD4547 for FGFR abnormalities (in expansion for mut/fus, nonbreast cancer)
- Arm P (GSK drug for loss of PTEN expression)
- Arm Q: trastuzumab emtansine for HER2 amplification (in expansion)
- Arm S1: trametinib for NF1 mutation (expansion pending)
- Arm Z1A: binimetinib for NRAS mutation (in expansion excludes colorectal cancer)
- Arm Z1D: nivolumab for MMR deficiency (in expansion)

Nearing Accrual goal: 4 arms

- B: afatinib for HER2 mut: (26 pts)- expansion planned
- R: trametinib for BRAF other mut and fusions: 20 patients discussions for followup ongoing
- Y: AKT1 mut: discussions for followup ongoing (19 patients)
- Z1B: palbo for CCND1 amplification (19 patients): expansion planned;

Rare variant initiative (expected May 2017)

- Several arms are not expected to fill even with sequencing 6000 patient tumors, due to the rarity of the variant in the population
- However, good evidence exists these variants are drivers and may respond to drugs in NCI MATCH
- Tumor sequencing is now more commonly done in clinical practice
- Enrichment: Four additional CLIA certified labs will participate in finding these patients and letting their doctors know they may be eligible for NCI MATCH
 - 2 commercial labs
 - Foundation Medicine Inc
 - Caris
 - 2 clinical labs (using their own, non-MATCH assay)
 - MD Anderson Cancer Center
 - Memorial Sloan Kettering Cancer Center
 - Results will be verified with the MATCH assays retrospectively

Questions?