# 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; no NCI funding for trials
- Agreement terms standardized or pre-approved so as to substantially decrease the transactional costs of study initiation
- Launched January 2017 with 16 agents from 6 companies:

  Agents: Alectinib; Atezolizumab; Bevacizumab; Cobimetinib; Ensartinib; Ipilimumab; Larotrectinib; LY3039478; Mogamulizumab; Nivolumab; Obinutuzumab; Pertuzumab; Prexasertib; Trastuzumab; Vemurafenib; Vismodegib

  Companies: Bristol-Myers Squibb; Eli Lilly; Genentech; Kyowa Hakko Kirin; Loxo; Xcovery

https://nciformulary.cancer.gov/

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# NCI FORMULARY

Home | Participating Companies | Available Agents | PI/Institution Eligibility | Information for Investigators | Information for Companies | CTEP

## NCI Formulary: A Public-Private Partnership

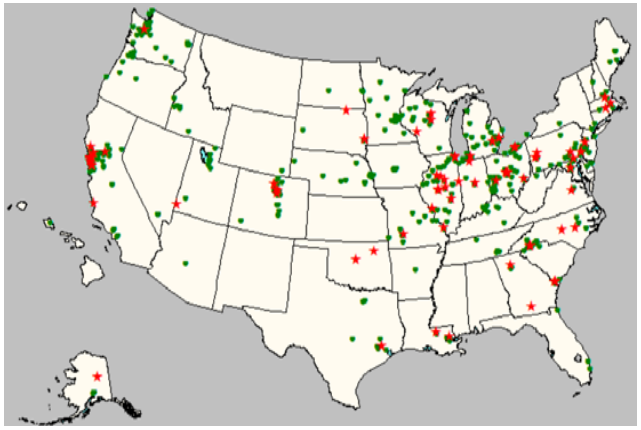
The National Cancer Institute (NCI) agent formulary (NCI Formulary) is a public-private partnership between the NCI and pharmaceutical and biotechnology companies with a purpose of providing academic investigators with rapid access to agents or combinations of agents for cancer clinical trial use; particularly, 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

**Additional Resources**

- Available Agents Table
- Cancer Moonshot
  - The White House
  - NCI
- CTEP
- Information For
  - Company Collaborators
  - Investigators
- Contact NCI Formulary

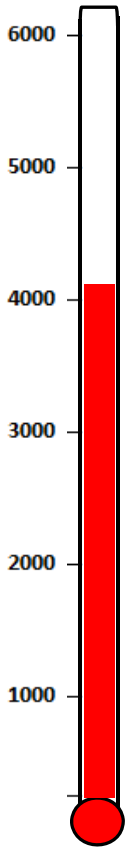
# Status and History of NCI-MATCH Trial

- **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 1/29/17




**4094 patients with tumor samples (N=6000)**

**3516 patients had received their test results**

**642 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

**429 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 January 29, 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**

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# 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

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## Arms to be added: Feb 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)***

# 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?