Topics for Discussion

- NCI MATCH Trial
- NCI Patient-Derived Models Repository
- Virtual Formulary
- Cancer Clinical Investigator Team Leadership Awards
NCI-MATCH Testing and Enrollment as of 6/18/17

6398 patients with tumor samples (N=6000)
5482 patients had received their test results
983 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
660 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 June 18, 2017

- 25 treatment arms; ≈ 50% fully accrued; ≈ 25% well on the way; ≈ 25% will need additional accrual from ‘rare variant study’

- Assay success rate 94%

- Median assay turnaround time 16 days

- Toxicity acceptable

- Objective responses have been observed
NCI "MATCH" CANCER TREATMENT TRIAL: STATE BY STATE ENROLLMENT

ENROLLMENT PER 1 MILLION POPULATION

30 – 65

>8 – <30

FEWER than 8

MATCH = Molecular Analysis for Therapy CHOice
States with Enrollment of more than 30 patients per 1 Million Population

- Delaware
- Hawaii
- Idaho
- Maryland
- Minnesota
- Montana
- New Hampshire
- North Dakota
- Oklahoma
- South Dakota
- Wisconsin
## NCI-MATCH Expanded to 25 Arms May 31, 2016

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

<table>
<thead>
<tr>
<th>Arm / Target</th>
<th>Drug(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>BRAF nonV600 Trametinib</td>
</tr>
<tr>
<td>S1</td>
<td>NF1 mut Trametinib</td>
</tr>
<tr>
<td>S2</td>
<td>GNAQ/GNA11 Trametinib</td>
</tr>
<tr>
<td>T</td>
<td>SMO/PTCH1 Vismodegib</td>
</tr>
<tr>
<td>U</td>
<td>NF2 loss Defactinib</td>
</tr>
<tr>
<td>V</td>
<td>cKIT mut Sunitinib</td>
</tr>
<tr>
<td>W</td>
<td>FGFR1/2/3 AZD 4547</td>
</tr>
<tr>
<td>X</td>
<td>DDR2 mut Dasatinib</td>
</tr>
<tr>
<td>Y</td>
<td>AKT1 mut AZD 5363</td>
</tr>
<tr>
<td>Z1A</td>
<td>NRAS mut Binimetinib</td>
</tr>
<tr>
<td>Z1B</td>
<td>CCND1,2,3 amp Palbociclib</td>
</tr>
<tr>
<td>Z1D</td>
<td>dMMR Nivolumab</td>
</tr>
<tr>
<td>Z1I</td>
<td>BRCA 1/2 AZD1775</td>
</tr>
</tbody>
</table>

Red = accrued 35 patients; Green = nearing 35 patients.
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)
Rare variant initiative (Began 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: Initially, 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
- Soon, a process for qualifying other commercial and academic sequencing labs will be posted to encourage additional accrual to this phase of NCI-MATCH
NCI’s Patient-Derived Models Repository (PDMR): Open for 6 weeks

https://pdmr.nci.gov
NCI Patient-Derived Models Repository: Multiple Avenues for Discovery

Tumor/Patient Heterogeneity

Develop PDX Models and PDC (Tumor & Fibroblast) Lines
DNA, RNA, Protein, WES, RNASeq, Targeted Sequencing

Blood/CTCs
Tumor

Blood/CTCs
Tumor

3D Culture, 3D Pharmacodynamics

Increasing Drug Concentration

2D and Organoid Cultures

Preclinical Trial Modeling

Live Tumor Imaging
NCI Patient-Derived Models Repository (PDMR) Initial Distribution Types

Distribution Groups (N=100 Models)

- **Colorectal Adenocarcinoma**
- **Head & Neck Squamous Cell Carcinoma**
  - Pharyngeal, Laryngeal, Lip/oral cavity, NOS
- **Urothelial/Bladder**
- **Melanoma**
- **Pancreatic Adenocarcinoma**
- **Lung Squamous Cell Carcinoma**
- **Adult Soft Tissue Sarcoma**
  - Ewings, Leiomyosarcoma, Malignant fibrohistiocytoma, Fibrosarcoma, Non-Rhabdosarcoma NOS, Rhabdosarcoma NOS
- **Renal**
- **Upper GI**
  - Stomach, Sm. Intest, GIST, Appendiceal

- PDX Pathology Confirmed
- Whole Exome Sequence, NCI Cancer Gene Panel, and RNASeq Available
- Human Pathogen Screening and STR Profile Available
- Confirmed Re-growth from Cryopreserved Fragments
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; As of May 2017: 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
Cancer Clinical Investigator Team Leadership Awards
Recognize and support outstanding clinical investigators at NCI-designated Cancer Centers who are actively engaged in NCI-funded collaborative clinical trials.

Promote the retention of clinical investigators in academic clinical research careers.
Cancer Clinical Investigator Team Leadership Awards

- $60,000 per year for 2 years
- 15% effort; time protected by sponsoring institution
- Candidate nominated by NCI Cancer Center Director
- 10 to 13 new awards per year
- First awards made in 2009; 102 recipients to date
- 93% (43/46) remain at NCI-Designated Cancer Center 5 years after award
Supported Activities Include, but Not Limited to:

- Engaging fellows and new faculty in collaborative clinical research efforts
- Mentoring
- Organizing courses, lecture/seminar series, educational sessions, or workshops related to clinical trials
- Participating on cancer center committees related to clinical trials
- Developing a clinical trial
- Designing and implementing initiatives to better coordinate, support and integrate clinical trials efforts at the institution
Eligibility

- Engaged in conducting NCI-funded cancer clinical trials
- Practicing at least 3 years but no more than 8 years post-fellowship
- Currently practicing in the oncology clinical setting; board certified
- Full-time faculty member, assistant or associate professor level
- Physician or oncology nurse, clinical psychologist, or similarly qualified clinician with a doctoral degree
2017 Cancer Clinical Investigator Team Leadership Award Recipients
2017 Recipients’ Focus Areas

- Breast cancer
- Gastrointestinal cancers
- Genitourinary cancers
- Gynecological cancers
- Leukemia
- Melanoma
- Palliative care/symptom science
- Inclusion of underserved populations in clinical trials
2017 CCITLA Recipients
2017 CCITLA Recipients

Ajjai Alva, M.D., M.S.
University of Michigan Comprehensive Cancer Center
Focus: Genitourinary cancers

Lisa Barroilhet, M.D.
University of Wisconsin Carbone Cancer Center
Focus: Gynecologic cancers
2017 CCITLA Recipients

Ursa Brown-Glaberman, M.D.
University of New Mexico Comprehensive Cancer Center
Focus: Breast cancer

Shira Dinner, M.D.
Robert H. Lurie Comprehensive Cancer Center
Northwestern University
Focus: Leukemia
2017 CCITLA Recipients

Jean Hoffman-Censits, M.D.
Sidney Kimmel Cancer Center
Thomas Jefferson University
Focus: Bladder and prostate cancers

Kevin Kalinsky, M.D., M.S.
Herbert Irving Comprehensive Cancer Center
Columbia University
Focus: Breast cancer
2017 CCITLA Recipients

Christopher Lieu, M.D.
University of Colorado Comprehensive Cancer Center
Focus: Colorectal cancer

Rahul Parikh, M.D., Ph.D.
University of Pittsburgh Cancer Institute
Focus: Bladder cancer
2017 CCITLA Recipients

Eric Roeland, M.D.
Moores Comprehensive Cancer Center
University of California, San Diego
Focus: Symptom intervention / palliative care (all cancers), gastrointestinal cancers

April Salama, M.D.
Duke Cancer Institute, Duke University Medical Center
Focus: Melanoma
Congratulations to the 2017 NCI Cancer Clinical Investigator Team Leadership Award Recipients