The Evolution of NCI-MATCH: What's Next for SWOG and the NCTN

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Conflict of Interest Disclosure

• Advisory: Genentech, BMS, Boehringer

• Clinical Trials support: Genentech, BMS, AZ, Celgene, Merck, Syndax, GSK, Abbvie, Incyte, Minneamrata, Pharmacyclics, Five Prime, Fortyseven
NCI-MATCH Timeline

MATCH Planning

Screening Accrual, N = 6000

Designated Lab Accrual N = 392 (to 4/21/19)

MATCH Successor Planning

Combo-MATCH

Leuk-MATCH

I-MATCH

Getting to There

• NCI-MATCH – design and structure

• MATCH with commercial and academic lab network to identify patients – “outside assay”

• Preliminary Results Summary

• Daughters of MATCH
NCI-MATCH – Design and Structure
A Disease Agnostic Basket Trial: NCI-MATCH

**THIS PRECISION MEDICINE TRIAL EXPLORES TREATING PATIENTS BASED ON THE MOLECULAR PROFILES OF THEIR TUMORS**

**NCI-MATCH IS FOR ADULTS WITH:**
- solid tumors (including rare tumors), lymphomas, and myeloma
- tumors that no longer respond to standard treatment
Hypothetical Framework for a Genomically-Driven Trial 2013

• Derived from early successes of targeted drugs:
  • Imatinib in CML, GIST
  • RAFi in BRAF-mutated melanoma
  • ALKi in Non-small cell lung cancer

• But also from failures
  • RAFi in BRAF-mutated colon cancer
  • MEKi in all KRAS-mutated cancers

• Begs questions
  • What is utility of targeted therapy broadly
  • Feasibility of addressing that issue
  • Does matching drug-mutation outweigh tissue of origin?
Key Considerations in Molecular Triage Trial Design

Tumor biopsy
- Archival tissue vs. fresh tumor biopsy
- Primary lesion vs. metastatic site
- Biopsy while on treatment or at progression for biomarkers of response and resistance

Biomarker platform
- Multiple institutional platforms or single platform
- Reproducible and reliable

Availability of drugs
- Are drugs available for the most frequent aberrations expected
- Are mutations found frequently enough to warrant testing in this setting

Treatment setting
- Early vs. late stage
- First vs. subsequent lines of therapy
Design

- Metastasis biopsy addresses concern of heterogeneity
- Uniform platform applied across all patient samples
- Desirable to have treatment allocation for as many as possible
# Customized Thermo Fisher Oncomine™ Assay

Reproduced with accuracy by MATCH laboratory network

<table>
<thead>
<tr>
<th>Hotspot Genes, N=73</th>
<th>Full-Gene Coverage, N=26</th>
<th>Copy Number Variants, N=49</th>
<th>Fusion Drivers, N=22</th>
</tr>
</thead>
</table>
| ABL1 ALK AR ARAF BRAF BTK CBL CDK4 CHEK2 CSF1R CTNNB1 DDR2 DNNMT3A EGFR ERBB2 ERBB3 ERBB4 ESR1 EZH2 FGFR1 FGFR2 FGFR3 FLT3 FOXL2 GATA2 GNA11 GNAQ GNAQ HNF1A HRAS IDH1 IDH2 IFITM1 IFITM3 JAK1 JAK2 JAK3 KDR KIT KITNSTRN KRAS MAGOH MAP2K1 MAP2K2 MAPK1 MAX MED12 MET MLH1 MPL MTOR MYD88 NFE2L2 NPM1 NRAS PAX5 PDGFRα PIK3CA PPP2R1A PTPN11 RAC1 RAF1 RET NOTCH1 PIK3R1 PTCH1 PTEN RB1 SMAD4 SMARCB1 STK11 TET2 TP53 TSC1 TSC2 VHL WT1 | APC ATM BAP1 BRCA1 BRCA2 CDH1 CDK2A2 FBXW7 GATA3 MSH2 NF1 NF2 NOTCH1 PIK3R1 PTCH1 PTEN RB1 SMAD4 SMARCB1 STK11 TET2 TP53 TSC1 TSC2 VHL WT1 | ACVR1L ATM APEX1 AR ATP1B1 BRCA1 BRCA2 CDH1 CDK2A2 FBXW7 GATA3 MSH2 NF1 NF2 NOTCH1 PIK3R1 PTCH1 PTEN RB1 SMAD4 SMARCB1 STK11 TET2 TP53 TSC1 TSC2 VHL WT1 | ALK RET ROS1 NTRK1 NTRK3 FGFR1 FGFR2 FGFR3 BRAF RAF1 Raf ERG ETV1 ETV4 ETV5 ABL1 AKT3 AXL EGFR ERBB2 FGFR1 FGFR2 FGFR3 XPO1 | **143 genes** **2530 amplicons in DNA panel** **207 amplicons in RNA panel**

Each mutation/variant was credentialed

Lih et al, *The Journal of Molecular Diagnostics* 2017
NCI-MATCH Laboratory Network

- ECOG-ACRIN Central Biorepository and Pathology Facility at MD Anderson Cancer Center (Stan Hamilton)
  - Intake of biospecimens and accompanying documentation
- Network of four CLIA-approved molecular diagnostics laboratories provides capacity
  - NCI Molecular Characterization Laboratory (Mickey Williams)
  - Massachusetts General (John Iafrate)
  - MD Anderson (Stan Hamilton)
  - Yale (Jeffrey Sklar)

![Diagram showing the workflow of biospecimen intake, processing, and characterization.]

**Biopsy** → **Shipped to MDACC (Central Pathological Lab)** → **Tissue Accession** → **Tissue Processing** → **PTEN IHC** → **NA Extraction** → **Archive**
- Tissue Blocks
- Slides
- Nucleic Acid

**4 Lab Network**
- MDACC
- MGH
- MoCha
- Yale

**NGS Library Prep and Sequencing**

**MATCHBox**
- Treatment Selection Final Report
- Clinical DB
Screening (Step 0) Overall Design

- ≥ 18 y.o.
- ECOG PS 0-1
- Solid tumor, Lymphoma or Myeloma
- ≥ 1 prior standard therapy
- Measurable disease
- Tumor amenable to biopsy OR FFPE obtained within 6mo

Tumor genomic testing with Thermo Fisher Oncomine™ Assay & IHC (PTEN, MLH1, MSH2, Rb)

Actionable Mutation of Interest (aMOI)?

Yes = Treatment assignment

No = Off study

Arm A Arm B Arm C Arm D Etc...

Each drug-target couple was credentialed
NCI-MATCH Treatment Arm Objectives

• Primary:
  – Estimate the proportion of patients with refractory solid tumor, lymphoma or myeloma who had an objective response (OR)

• Secondary:
  – Progression-free survival (PFS)
  – PFS at 6 months (PFS6)
  – Time to progression/death
  – Toxicity
  – Potential predictive biomarkers
NCI-MATCH Statistical Assumptions for Individual Arms

• Accrual goal per arm: 35
  • Some arms targeting more common gene variants were expanded to accommodate the higher numbers of patients with matches who came into the trial through central screening

• Reporting of primary and secondary endpoints to occur once there is complete response and toxicity data for at least 31 patients per arm
  • Accrue at least 35 to obtain at least 31 evaluable (10% ineligibility rate)
    – Need ~8 months of follow-up after accrual is complete

• If the OR is ≥ 5/31 (16%), agent worthy of further study

• Secondary analyses will examine response by a variety of factors
Treatment Arms in NCI-MATCH by Molecular Pathway

- MAP Kinase: EGFR mut: rare and T790M
- HER2 mutation and HER2 ampl
- ALK, ROS translocations
- RAF mutations, fusions
- NF2 loss, NF1 mutation
- NRAS mutations
- SMO, PTCH1, KIT mutations

- DDR2 BRCA 1, 2 mutations
- MLH1, MSH2 LOSS
- NTRK fusions
- CCND1 AMP
- CDK4 OR 6 AMP
- FGFR ampl, mut, fusion
- MET exon 14 skipping
- MET amplification
- PI3K
- PIK3CA mutations
- TSC1, 2 mutations
- MTOR mutations
- PTEN LOSS
- AKT mutations

MAP kinase
PI3Kinase
DNA repair
Immuno-onc
cell cycle
FGFR
LOXO
MET
Brief History of NCI-MATCH

• Opened on August 12, 2015, with 10 treatment arms and a goal to have 3000 patients submit tumor samples for central testing

• 795 patients were screened in the first three months
  – Screening reached >100/week by the end of this period
  – Far surpassed original estimate of 50 screens/month

• Paused enrollment on November 11, 2015, for a planned interim analysis

• Resumed enrollment of new patients on May 31, 2016, with 24 treatment arms and more laboratory capacity to handle rapid pace of enrollment, and new goal of 6000 patients for central testing

• Expanded to 30 treatment arms on March 13, 2017

• Completed central screening of ~6000 patients in July 2017, nearly two years ahead of schedule

• Continued accrual since then using outside labs
## Enrollment and Screening Activity – Screening Cohort

<table>
<thead>
<tr>
<th>Step 0/1</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients Enrolled</strong></td>
<td>6391</td>
</tr>
<tr>
<td><strong>Cases with Samples Submitted</strong></td>
<td>5961 (93.3%)</td>
</tr>
<tr>
<td><strong>1st Sample Analyzed</strong></td>
<td>5407</td>
</tr>
<tr>
<td><strong>1st Sample Fail</strong></td>
<td>554</td>
</tr>
<tr>
<td><strong>2nd Sample Submitted</strong></td>
<td>170</td>
</tr>
<tr>
<td><strong>2nd Sample Analyzed</strong></td>
<td>141</td>
</tr>
<tr>
<td><strong>Total Cases Analyzed for Match Assay</strong></td>
<td>5548</td>
</tr>
<tr>
<td><strong>Patients Assigned to Rx</strong></td>
<td>987(17.8%)</td>
</tr>
<tr>
<td><strong>Patients Enrolled on Arm</strong></td>
<td>686(69.5%)</td>
</tr>
</tbody>
</table>
NCI-MATCH – with commercial and academic lab network to identify patients – “outside assay”
10 Commercial Labs Referring Patients to NCI-MATCH

*Inquire with the lab directly — no need to contact ECOG-ACRIN or NCI*

<table>
<thead>
<tr>
<th>Lab Name</th>
<th>Contact Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caris Life Sciences®</td>
<td><a href="mailto:NCIMATCHTrial@CarisLS.com">NCIMATCHTrial@CarisLS.com</a></td>
</tr>
<tr>
<td>CellNetix Pathology and Laboratories</td>
<td><a href="mailto:cnx-trials@cellnetix.com">cnx-trials@cellnetix.com</a></td>
</tr>
<tr>
<td>Foundation Medicine, Inc.</td>
<td><a href="mailto:smarttrials@foundationmedicine.com">smarttrials@foundationmedicine.com</a></td>
</tr>
<tr>
<td>GenPath (BioReference Laboratories, Inc.)</td>
<td><a href="mailto:Kbarber@bioreference.com">Kbarber@bioreference.com</a></td>
</tr>
<tr>
<td>OmniSeq, Inc. <em>(not referring until further notice)</em></td>
<td><a href="mailto:trials@omniseq.com">trials@omniseq.com</a></td>
</tr>
<tr>
<td>The Jackson Laboratory</td>
<td><a href="mailto:CGL_NCI-MATCH@jax.org">CGL_NCI-MATCH@jax.org</a></td>
</tr>
<tr>
<td>NeoGenomics Laboratories, Inc.</td>
<td><a href="mailto:NCI-MATCH@neogenomics.com">NCI-MATCH@neogenomics.com</a></td>
</tr>
<tr>
<td>PathGroup</td>
<td><a href="mailto:oncologysupport@pathgroup.com">oncologysupport@pathgroup.com</a></td>
</tr>
<tr>
<td>Strata Oncology, Inc.</td>
<td><a href="mailto:ncimatch@strataoncology.com">ncimatch@strataoncology.com</a></td>
</tr>
<tr>
<td>Tempus Labs, Inc.</td>
<td><a href="mailto:nci-match@tempus.com">nci-match@tempus.com</a></td>
</tr>
</tbody>
</table>
16 Academic Labs Referring Patients to NCI-MATCH

*Generally, cancer center labs test their own patients*

<table>
<thead>
<tr>
<th>Augusta University</th>
<th>Memorial Sloan Kettering Cancer Center</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brigham and Women’s Hospital</td>
<td>MD Anderson Cancer Center</td>
</tr>
<tr>
<td>City of Hope</td>
<td>Stanford</td>
</tr>
<tr>
<td>Cedars-Sinai Medical Center</td>
<td>University of Chicago</td>
</tr>
<tr>
<td>Columbia University</td>
<td>University of Colorado</td>
</tr>
<tr>
<td>Frederick National Laboratory for</td>
<td>University of Michigan</td>
</tr>
<tr>
<td>Cancer Research (MoCha)</td>
<td></td>
</tr>
<tr>
<td>Johns Hopkins University</td>
<td>Weill Cornell Medicine</td>
</tr>
<tr>
<td>Massachusetts General Hospital</td>
<td>Yale University</td>
</tr>
</tbody>
</table>
# Enrollment and Screening Activity – Outside Assay

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Last Week</th>
<th>Weekly Average 1/7/18 to 6/16/18</th>
<th>Weekly Average Since 7/28/18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Enrolled</td>
<td>392</td>
<td>5</td>
<td>1.96</td>
<td>6.45</td>
</tr>
<tr>
<td>Outside Assay Processing Complete</td>
<td>382</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients Assigned to Rx</td>
<td>338(88%)</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eligibility Review Pending</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eligibility Evaluation Complete</td>
<td>333</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients Enrolled on Arm</td>
<td>273(82%)</td>
<td>2</td>
<td>1.65</td>
<td>4.45</td>
</tr>
</tbody>
</table>
## New NCI-MATCH Arms in Development

<table>
<thead>
<tr>
<th>Tumor Gene Abnormality</th>
<th>Prevalence Rate %</th>
<th>Drug</th>
<th>Arm ID</th>
<th>Opens (Pending Approval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKT mutations</td>
<td>0.77</td>
<td>Ipatasertib</td>
<td>Z1K</td>
<td>Late Spring 2019</td>
</tr>
<tr>
<td>Non-V600 BRAF mutations</td>
<td>0.80</td>
<td>Ulixertinib (BVD-523)</td>
<td>Z1L</td>
<td></td>
</tr>
<tr>
<td>dMMR status and LAG-3 expression</td>
<td>1.51</td>
<td>Nivolumab + relatlimab (BMS-986016)</td>
<td>Z1M</td>
<td>Fall 2019</td>
</tr>
<tr>
<td>TP53 mutations and MYC amplification</td>
<td>Not available</td>
<td>AZD1775</td>
<td>Z1J</td>
<td></td>
</tr>
</tbody>
</table>
NCI-MATCH – Preliminary Results
NCI-MATCH Brings Genomics to the Community

- Availability at over 1100 sites
- 56% of accrual in community
- Broad general interest in the promise of genomics

Open in every state, the District of Columbia, and Puerto Rico
Accessing targeted drugs and developing treatment options were the most salient motivations for participating in future trials

- Very/extremely important for 90% or more of respondents:
  - Access to targeted drugs
  - Generating evidence that leads to treatment options
  - Identifying treatment options based on profiling
- Very/extremely important to 70-80% of respondents
  - Help getting reimbursement for off-label drugs
  - Increasing confidence in treatment recommendations (even more important to non-AMC with 83% very/extremely, vs 64% of AMC)

Importance of objectives/motivations in considering participation in future tumor profiling clinical trials (n=171)
## NCI-MATCH Central Screening by Cancer Type

### Less Common Disease Type

<table>
<thead>
<tr>
<th>Less Common Disease Type</th>
<th>% of Total Screened (N=5560)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian</td>
<td>9.5</td>
</tr>
<tr>
<td>Uterine</td>
<td>6.2</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6.1</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>4.6</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>3.9</td>
</tr>
<tr>
<td>Neuroendocrine</td>
<td>3.3</td>
</tr>
<tr>
<td>Gastroesophageal</td>
<td>3.2</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>2.8</td>
</tr>
<tr>
<td>Liver and Hepatobiliary other than Cholangio.</td>
<td>1.9</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>1.7</td>
</tr>
<tr>
<td>Bladder/Urinary Tract</td>
<td>1.6</td>
</tr>
<tr>
<td>Cervical</td>
<td>1.6</td>
</tr>
<tr>
<td>Small Cell Lung</td>
<td>1.4</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1.4</td>
</tr>
<tr>
<td>Kidney</td>
<td>1.2</td>
</tr>
<tr>
<td>Anal</td>
<td>0.8</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>0.8</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>0.7</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>9.7</td>
</tr>
<tr>
<td><strong>Less Common Cancers</strong></td>
<td><strong>62.5%</strong></td>
</tr>
</tbody>
</table>

### Common Disease Type

<table>
<thead>
<tr>
<th>Common Disease Type</th>
<th>% of Total Screened (N=5560)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>15.3</td>
</tr>
<tr>
<td>Breast</td>
<td>12.4</td>
</tr>
<tr>
<td>Non-Small Cell Lung</td>
<td>7.3</td>
</tr>
<tr>
<td>Prostate</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Common Cancers</strong></td>
<td><strong>37.5%</strong></td>
</tr>
</tbody>
</table>

**Goal: 25% Far exceeded**
NCI-MATCH – Status of 39 Treatment Arms

- 11 with findings
- 6 in follow-up
- 7 suspended to enrollment
- 12 open to enrollment
- 4 new in development
- 12 new in development
### Eleven of the 35 subprotocols have reported out: 3/11 positive (27%)

<table>
<thead>
<tr>
<th>Subprotocol</th>
<th>Drug/molecular</th>
<th>Reported out</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z1D</td>
<td>Nivolumab for MMRd</td>
<td>SITC 2017; manuscript pending</td>
<td>Positive</td>
</tr>
<tr>
<td>Y</td>
<td>Capivasertib/AKT mutations</td>
<td>Nov 2018</td>
<td>Positive</td>
</tr>
<tr>
<td>H</td>
<td>Trametinib/Dabrafenib/BRAFV600</td>
<td>June 2019</td>
<td>Positive</td>
</tr>
<tr>
<td>I</td>
<td>Taselisib/PIK3CA mutations</td>
<td>June 2018 (ASCO)</td>
<td>Neg</td>
</tr>
<tr>
<td>Q</td>
<td>Ado-trastuzumab emtansine/ERRB2 amplification</td>
<td>June 2018 (ASCO)</td>
<td>Neg (8% RR)</td>
</tr>
<tr>
<td>W</td>
<td>AZD4547/FGFR amplification, mutation, fusion</td>
<td>June 2018 (ASCO)</td>
<td>Neg (8% RR)</td>
</tr>
<tr>
<td>N/P</td>
<td>GSK2636771/PTEN mut or loss</td>
<td>October 2018 (ESMO)</td>
<td>Neg</td>
</tr>
<tr>
<td>B</td>
<td>Afatinib/ERRB2 activating mutations</td>
<td>April 2019 (AACR)</td>
<td>Neg (2.7%)</td>
</tr>
<tr>
<td>Z1-B</td>
<td>Palbociclib/CCND1, 2, or 3 amplifications</td>
<td>April 2019 (AACR)</td>
<td>Neg</td>
</tr>
<tr>
<td>Z1-I</td>
<td>AZD1775/BRCA 1 or BRCA2 mutations</td>
<td>April 2019 (AACR)</td>
<td>Neg (3.2%)</td>
</tr>
</tbody>
</table>
**Capivasertib** in Patients with Tumors with AKT Mutations: NCI-MATCH Subprotocol EAY131-Y: Kevin Kalinsky, Fangxin Hong, Carolyn K McCourt, Jasgit C Sachdev et al.

- Oral presentation EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics November 2018.
- Concurrent fulvestrant or aromatase inhibitor allowed for hormone receptor (HR+)/HER2- breast cancer, if last metastatic regimen included that hormonal therapy (capivasertib 400 mg)
- Excluded KRAS, NRAS, HRAS, or BRAF mutations
- No prior PI3K, AKT or mTOR inhibitor
Capivasertib: in 27 patients evaluable, positive study

Confirmed PR rate (n=35): 23% (90% CI 12-38%)

p-value = 0.0003 (<0.018)
Ado-trastuzumab emtansine (T-DM1) in patients with HER2 amplified tumors excluding breast and gastric/gastro-esophageal junction (GEJ) adenocarcinomas: Results from the National Cancer Institute (NCI) - Molecular Analysis for Therapy Choice (MATCH) trial.

Komal L. Jhaveri, Vicky Makker, Xin Victoria Wang, Alice P. Chen, Keith Flaherty, Barbara A. Conley, Peter J. O'Dwyer, Paul M. Williams, Stanley R. Hamilton, Lyndsay Harris, Lisa McShane, Lawrence Rubinstein, Robert James Gray, Shuli Li, Edith P. Mitchell, David Patton, Jeffrey Moscow, James A. Zwiebel, Carlos L. Arteaga, Shiuh-Wen Luoh

Oral presentation at ASCO 2018
Arm Q Efficacy: Best % Change from Baseline (n=26)

<table>
<thead>
<tr>
<th>Best Response</th>
<th>ITT (37) n (%)</th>
<th>Evaluable (26) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed Partial response</td>
<td>3 (8%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>16 (43%)</td>
<td>16 (62%)</td>
</tr>
<tr>
<td>Progression of Disease</td>
<td>12 (32%)</td>
<td>12 (46%)</td>
</tr>
</tbody>
</table>

Komal Jhaveri, MD FACP

- Excluded breast, gastric, GEJ cancers
- ERBB2 AMPL ≥ 7 per NCI –MATCH NGS assay (2%)
- 37 patients, 65% female, 50% ≥ 3 prior treatments
- Confirmed PR in 3 patients: 8% (95% CI 2-20%)
- Responses were in rare tumors: mucoepidermoid carcinoma of salivary gland (2) and Pagets disease scrotum (1).
- 6 months PFS 25.4% (95% CI 16-41%)
- 1 patient lost ERBB2 amplification on progression (salivary gland)
Arm W: AZD4547 IN PATIENTS WITH FGFR ABNORMALITIES

YK Chae, C Vaklavas, H Cheng, F Hong et al. ASCO oral 2018

• 1.3% of screened patients
• Exclusions: patients with gastric or NSCLC cancer and FGFR amplifications
• 50 patient treated; 50% had ≥ 3 prior treatments
• FGFR1 ampl: 18; FGFR2 ampl: 3, mutations: 20; fusions 9
• PR in 4/42 patients (9.5%): 2 with FGFR3 fusions (urothelial cancer and SCC cervix, and 2 with mutations (extrahepatic cholangiocarcinoma and urothelial carcinoma bladder)
• PRs were long lasting: 156-334 days
NCI-MATCH Treatment Arms Open and Enrolling

<table>
<thead>
<tr>
<th>Variant</th>
<th>Prevalence Rate %</th>
<th>Drug(s)</th>
<th>Arm</th>
<th>Accrual As of 04/21/19</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTEN loss</td>
<td>1.93</td>
<td>Copanlisib</td>
<td>Z1G</td>
<td>4</td>
</tr>
<tr>
<td>PTEN (deleterious) seq. result + expr.</td>
<td>1.75</td>
<td>Copanlisib</td>
<td>Z1H</td>
<td>10</td>
</tr>
<tr>
<td>HER2 amplif.</td>
<td>1.49</td>
<td>Trastuzumab + pertuzumab</td>
<td>J</td>
<td>31</td>
</tr>
<tr>
<td>TSC1 or TSC2</td>
<td>1.11</td>
<td>TAK-228</td>
<td>M</td>
<td>33</td>
</tr>
<tr>
<td>FGFR</td>
<td>1.00</td>
<td>Erdafitinib</td>
<td>K2</td>
<td>22</td>
</tr>
<tr>
<td>MET exon 14 del.</td>
<td>0.61</td>
<td>Crizotinib</td>
<td>C2</td>
<td>18</td>
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- Since end of screening, accrual based on outside lab results
- Confirmation of results using MATCH platform
- 6 new arms
Daughters of MATCH
NCI-MATCH Timeline

- MATCH Planning
- Screening Accrual, N = 6000
- Designated Lab Accrual N = 392 (to 4/21/19)
- MATCH Successor Planning
- Combo-MATCH
- Leuk-MATCH
- I-MATCH

Timeline:
- April 2013
- August 2015
- November 2015
- May 2016
- July 2017
- March 2019
- June 2020
ComboMATCH protocol organization

ECOG-ACRIN administrative coordination

EA ComboMATCH master protocol (Contains rules for assignment of patients to treatment arms)

ECOG ACRIN cassette
- Substudy 1
- Substudy 2
- Substudy 3
- Substudy 4

Alliance cassette
- Substudy 1
- Substudy 2
- Substudy 3
- Substudy 4

SWOG cassette
- Substudy 1
- Substudy 2
- Substudy 3
- Substudy 4

NRG cassette
- Substudy 1
- Substudy 2
- Substudy 3
- Substudy 4
ComboMATCH treatment arm development

- **Premise:** Drug combinations are more likely to provide clinical benefit than single agents in most scenarios, so the successor trial to MATCH will focus on drug combinations

- **Hypothesis:** Pre-clinical data from *in vivo* models of drug combinations can predict clinical benefit in defined patient groups

- C-AGWG will review drug combination data presented by investigators and Pharma, prioritize substudies for development, and work with NCTN groups to distribute substudies for incorporation into cassettes

- Drug combinations without RP2D will be assigned to ETCTN for phase 1 study

- Drug combinations with promising but inconclusive data will be assigned for further study to PDXNet
ComboMATCH Steering Committee: Overall PI’s – (Drs Meric-Bernstam, Hyman and Ford), EA operations, NCTN representatives, NCI

- Protocol logistics committee (operational issues, IT, PR, data access)
- Agents and Genes Working Group (Substudy arm approval)
- Molecular Pathology/Specimen Management Committee
- Precision Medicine Analysis and Coordination Center (PMACC) (assignment of patients to treatment arms)
- Representatives from NCTN groups, EA operations, NCI
- MDNet laboratories Qualified lab tests
What have we learned....

- Feasibility established, especially at the scale needed, protocol structure works
- Robust platform and pathology analysis
- Established a different and highly collaborative way of working together between EA/NCTN and NCI, especially CTEP
- Too early to judge benefit of approach, but there are “hits” that suggest disease-agnostic activity
- Trials needed to understand both tissue-specific and tumor microenvironment influences in targeted therapy
- Combi-MATCH, Leukemia-MATCH, I-MATCH – early in development, broad Group involvement, scientific opportunity
- Reach into the community, great enthusiasm
Credit…

• Colleagues at ECOG-ACRIN who have given boundless energy to thinking then doing – especially Stan Hamilton, Keith Flaherty, Bob Comis, Bob Gray, Edith Mitchell, Mary Lou Smith, Donna Marinucci, Pam Cogliano

• Colleagues at NCI who have worked closely on MATCH: Barb Conley, Alice Chen, Jeff Abrams, Lyndsay Harris, Mickey Williams, Lisa McShane, and whole MATCHBOX team

• Individuals thinking about next iteration: Jim Doroshow, Ignacio Wistuba, Mitch Schnall