Update on Adult & Pediatric MATCH Trials and Plans for Future Basket & Umbrella Trials in the NCI National Clinical Trials Network (NCTN)
Presentation Agenda

- Overview and Update on NCI NCTN Adult MATCH & Pediatric MATCH Trials

- Lessons Learned – Focus on 2 Main Areas
  - Use of Laboratory Network for Testing for Rare Mutations/Variants
  - Need for Simplification of Protocol Structure

- Future Directions
CTEP’s Role in Drug Development for National Program

- Combinations of targeted agents a high priority
  - Based on evidence that resistance to initially effective single agents often develops quite rapidly in many adult tumors
  - More than 100 combination trials initiated since 2000
  - Facilitated by the Intellectual Property (IP) language in CTEP-industry agreements

- Molecular-targeted effects:
  - Mechanism of Action/Proof of Principle
  - Biomarker assessment and evaluation, assay development & qualification
Doing Battle Against Cancer: A Collaborative Effort

DCTD-NCI
- Expedite Pivotal Trials
- Exploratory Studies
- Other Indications:
  - combination regimens of investigational agents from two or more sources
  - Alternative Methods of Drug Administration

Pharmaceutical/Biotech Company
- Pilot Studies & Pivotal Trials Leading to Licensing
- Collaborative Agreement: Common Data Sharing & IP Option Agreement Language

Investigational Anti-Cancer Agents

Clinical Investigators

IND & Clinical Trials

Plus: NCI-Sponsored Infrastructure for Clinical Trials
- Investigator Credentialing & Registration
- CTEP IND Sponsor / Monitoring
- Medidata Rave Data Mgt System
- NCI Central IRB
- CTSU Enrollment & Study Access
- CTSU Regulatory Support

Novel Cancer Therapies
CTEP/DCTD Clinical Trials
Clinical Trials Programs

**Phase 1**
- Pediatric Phase 1 Program
- Experimental Therapeutics Clinical Trials Network (ETCTN)

**Phase 2**
- National Clinical Trials Network (NCTN)

**Phase 3**
- US NCTN Groups Alliance
- Children’s Oncology Group
- ECOG-ACRIN
- NRG Oncology
- SWOG

**Basic Resources**

**Other / Specialty Resources**
- Adult & Pediatric Brain Tumor Consortia (ABTC & PBTC)
- Cancer Immunology Clinical Trials Network (CITN)
- Bone Marrow Transplant Clinical Trials Network (BMCTN)*

*BMTCTN overseen by NHLBI with collaborative support from NCI/CTEP

Other: SPORES, R21, R01, P01, Grants, etc.
High Priority Targets & CTEP/DCTD Agents

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Oncolytic

PD1
nivolumab
pembrolizumab

PD-L1
durvalumab
gateolizumab

CTLA4
ipilimumab
tremelimumab

BITE
blinatumomab

CCR4
mogamulizumab

CD27
varilumab

IDO-1
epacadostat

Dendritic Cell R
CDX-1401

IL-12 Cell R
IL-12

IL-15 Cell R
rIL-15

ATR
M6620
AZD6738

BER
methoxyamine
DNA-PK
M3814

PARP
olaparib
talazoparib
veliparib

HDAC
talinistat
entinostat
romidepsin

DNA polymerase
IPDR

EZH2
tazemetostat

DNA methylation
azacitidine
guadecitabine

IGF-1R
ganitumab
GD2
dinutuximab
HER2
trastuzumab
CD30
brentuximab
GPMB
glembatumumab
Mesothelin
anetumab ralotasisine

Other Surface Antigen-R

HGF/SF
rilometumab
FGFR
rogaratinib
E-selectin
uproleselan

tcMET
AMG-337
savoitinib
cabozaanzinib
tivotinib
PDGFR
pazopanib
cediranib
sunitinib

VEGF-R
bevacizumab
ziv-afibercept

CD-105
TRC-105

RTK-R

VEGF

VEGF-R

ATM
radiopharmaceutical
radium-223
thorium-227

DNA Replication or Repair

WEE1
RNR

Protein expression or metabolism

tripeptide

gemcitabine

Mitosis

KRT232

Migration / Invasion

MDM2
p53
RNR

Survival / Proliferation

Tripeptide
gemcitabine

Apoptosis

Angiogenesis

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Project Team-Driven Approach to NCI Early Phase Clinical Trials Associated with Drug Development Plans

New Development Cycle for NCI Experimental Therapeutics

- NExT: NCI Experimental Therapeutics
- NExT Pipeline
- Senior Advisory Committee
- Regulatory Agreements
- IDSC Review
- BRC Review
- CRADA Signed
- CRADA: Cooperative Research and Development Agreement
- IDSC: Investigational Drug Steering Committee
- BRC: Biomarker Review Committee
NCI-MATCH Objective:
A Large national “signal-finding” trial

- To determine whether matching certain drugs or drug combinations in adults whose tumors have specific gene abnormalities will effectively treat their cancer, regardless of the cancer type

- This is a signal-finding trial in patients with advanced/refractory disease; treatments that show promise can advance to larger, more definitive trials
Design of NCI MATCH
(Multiple Phase II Trials – Multiple Cancer Types)

- Master protocol w/ individual arms that open & close independently
- Genomic testing directs patients to molecularly-targeted treatments
- Each arm evaluates activity of a treatment in tumors with relevant actionable mutations in refractory malignancies (“basket” type trial)
- Goal to include at least 25% less common or rare cancers (Other than breast, colon, lung, prostate)
  - Trial started August 2015 with 10 treatment arms with a built in “pause” after 500+ patients screened for full assessment of all trial phases for feasibility
  - Trial reopened in May 2016 with a total of 24 treatment arms
  - As of 11/29/2019, screened 6,898 patients & matched 1,049 pts to 37 tx arms using Laboratory Network with high concordance in assay performance
  - If Objective Response Rate (primary endpoint) is ≥ 5/31 (16%), agent considered worthy of potential further study
NCI-MATCH Treatment Arm Overall Design
(Multiple Single-Arm Phase II Trials)

- Target 25% “rare” tumor histologies; Target Match rate of 23% to 25%
- Endpoint ORR of 5% versus 25%
### MATCH Assay Oncomine Cancer Panel gene list

<table>
<thead>
<tr>
<th>Hotspot genes (n=66)</th>
<th>Copy number variants (n=43)</th>
<th>Tumor suppressors (n=25)</th>
<th>Gene fusion drivers (n=16; 156 variants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABL1, AKT1, ALK, ALK, AR, BRAF, BTK, C15orf23, CBL, CDK4, CHEK2, CSF1R, CTNNB1, DNMT3A, EGFR, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FGFR2, FGFR3, FLT3, FOXL2, GATA2, GNA11, GNAQ, GNAS, HRAS, IDH1, IDH2, IFITM1, IFITM3, JAK1, JAK2, JAK3, KDR, KIT, KRAS, MAGOH, MAP2K1, MAPK1, MAX, MED12, MET, MPL, MTOR, MYD88, NFE2L2, NRAS, PAX5, PDGFR, PIK3CA, PPP2R1, RAF1, RET, RHEB, RH0A, SF3B1, SMO, SPOP, SRC, STAT3, U2AF1, XPO1</td>
<td>ACVRL1, AKT1, AR, APEX1, BCL2L1, BCL9, BIRC2, BIRC3, CCND1, CCNE1, CD274, CD44, CDK4, CDK6, CSN2A1, EGFR, ERBB2, FGFR1, FGFR2, FGFR3, FLT3, GAS6, IGF1R, IL6, KIT, KRAS, MCL1, MDM2, MDM4, MYC, MYCL, MYCN, NFKX2-1, PDGFR, PIK3CA, PNP, PPARG, PPS6KB1, SOX2, TERT, TIAF1, ZNF217</td>
<td>APC, ATM, BAP1, BRC1, BRC2, CDH1, CDKN2A, CDKN2A, EGFR, ERBB2, FGFR1, FGFR2, FGFR3, FLT3, GAS6, IGF1R, IL6, KIT, KRAS, MCL1, MDM2</td>
<td>AKT3, ALK, BRAF, CDK4, ERBB2, ERG, ETV1, ETV4, ETV5, FGFR3, NTRK1, NTRK3, PPARG, RAF1, RET, ROS1</td>
</tr>
<tr>
<td>Tier 3 clinical evidence highlighted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gene variants associated with clinical trial enrollment (open trials)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Highlighted genes are aMOIs which are subset of MOIs (143) with level of evidence
**NCI-MATCH Assay System & Work Flow**

~ 14 Day Turnaround Time

- Biopsy
  - Shipped to MDACC
  - Tissue Accession
  - Tissue Processing
- IHC
- NA Extraction
- NA Shipped
- Library Prep and Sequencing

**Archive**
- Tissue Blocks
- Slides
- Nucleic Acid

**MDACC**
- Ion Reporter
- MOI Annotation
- BAM File Storage

**MGH**

**MoCha**

**Yale**

**MOI**

**Clinical DB**

- Expansion of NGS capacity (S5 platform)
- Versioning of NGS assay (new variants/arms)
- Mandating needle aspiration in all cases (cytology 86->98%)
- IHC’s added (PTEN, MSH2, MLH1, Rb1)
Brief Timeline of NCI-MATCH Treatment Arms

- **Aug. 12, 2015**: Open with 10 arms
- **Mar. 13, 2017**: Expand to 30 arms
- **June 20, 2018**: Expand to 35 arms
- **July 27, 2019**: Expand to 37 arms

**Nov 2015 - May 2016**
- Pause for 6 months for interim analysis and Lab capacity increase

**Final 2 arms in development**
- 39 total arms by end 2019
NCI-MATCH Important Discovery Required an Additional Change in the Study

In the first 6,000 patients tested, the tumor gene variants we are studying occurred less frequently than expected in this study population, **ranging from 3.47 percent to zero**.

Conventional clinical trial design approach may not be feasible. Need to broaden the patient population screening process.
Current Genetic Testing Process MATCH Eligibility

• After screening fresh tumor biopsies from 6,000 patients, 19 treatment arms did not meet accrual due to low prevalence of eligibility variants.

• NCI-MATCH now identifies patients utilizing an external laboratory network of CLIA-certified academic & commercial labs that perform NGS assays as part of their routine care at NCI-MATCH participating sites.

• Candidate labs were recruited through notice in Federal Register (FRN)

• Each candidate lab submitted a letter of interest for the NCI-MATCH team review to meet baseline criteria for FRN, if so, they were invited to submit an application to become an NCI-MATCH Designated Laboratory.

• Accepted laboratories sign a collaboration agreement and undergo concordance/qualification (CQ) testing.
Patient Pathway onto NCI-MATCH - Commercial Lab

Applies only to patients at ~1100 participating trial sites

Dr. X orders test to guide pt’s care

Lab probes results; finds match; sends Dr. X a referral

Lab uploads pt info to trial database MATCHBOX verification

Dr. X evaluates pt’s eligibility for ‘arm x’

Lab runs standard test, sends results to Dr. X

Pt and Dr. X decide to enroll for screening

Trial leaders assign verified pt to ‘arm x’; notify Dr. X

Eligible pt enrolls in ‘arm x’ for treatment
## Commercial Labs Referring Patients to NCI-MATCH

<table>
<thead>
<tr>
<th>Commercial Labs Referring Patients to NCI-MATCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caris Life Sciences®</td>
</tr>
<tr>
<td>CellNetix Pathology and Laboratories</td>
</tr>
<tr>
<td>Foundation Medicine, Inc.</td>
</tr>
<tr>
<td>GenPath (BioReference Laboratories, Inc.)</td>
</tr>
<tr>
<td>NeoGenomics Laboratories, Inc.</td>
</tr>
<tr>
<td>OmniSeq, Inc.</td>
</tr>
<tr>
<td>PathGroup</td>
</tr>
<tr>
<td>Strata Oncology, Inc.</td>
</tr>
<tr>
<td>Tempus Labs, Inc.</td>
</tr>
<tr>
<td>The Jackson Laboratory</td>
</tr>
</tbody>
</table>

## Academic Labs Referring Patients to NCI-MATCH

*Generally, cancer center labs test their own patient population*

<table>
<thead>
<tr>
<th>Academic Labs Referring Patients to NCI-MATCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Augusta University</td>
</tr>
<tr>
<td>City of Hope</td>
</tr>
<tr>
<td>Cedars-Sinai Medical Center</td>
</tr>
<tr>
<td>Columbia University</td>
</tr>
<tr>
<td>Johns Hopkins University</td>
</tr>
<tr>
<td>Massachusetts General Hospital</td>
</tr>
<tr>
<td>Memorial Sloan Kettering Cancer Center</td>
</tr>
<tr>
<td>MD Anderson Cancer Center</td>
</tr>
<tr>
<td>University of Chicago</td>
</tr>
<tr>
<td>University of Colorado</td>
</tr>
<tr>
<td>University of Michigan</td>
</tr>
<tr>
<td>Weill Cornell Medicine</td>
</tr>
<tr>
<td>Yale University</td>
</tr>
</tbody>
</table>

- More labs to come
- Learn more: [ecog-acrin.org/nci-match](http://ecog-acrin.org/nci-match)
# NCI-MATCH Treatment Arms with Results

*Updated June 2019*

<table>
<thead>
<tr>
<th>Drug / Variant</th>
<th>Drug</th>
<th>Arm</th>
<th>Primary Result (ORR)</th>
<th>Publication / Presentation</th>
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<tbody>
<tr>
<td>Ado-trastuzumab emtansine HER2 amplification</td>
<td>Ado-trastuzumab emtansine</td>
<td>Q</td>
<td>8%</td>
<td>Jhaveri KL, ASCO 2018 (oral)</td>
</tr>
<tr>
<td>AZD4547 FGFR pathway aberrations</td>
<td>AZD4547</td>
<td>W</td>
<td>8%</td>
<td>Chae YK, ASCO 2018 (oral)</td>
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<tr>
<td>Taselisib PIK3CA mutations</td>
<td>Taselisib</td>
<td>I</td>
<td>0%</td>
<td>Krop IE, ASCO 2018 (oral)</td>
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<tr>
<td>GSK2636771 PTEN expr or loss by IHC</td>
<td>GSK2636771</td>
<td>N &amp; P</td>
<td>5% arm N (mut/del) 0% arm P</td>
<td>Janku FM, ESMO 2018 (poster discussion)</td>
</tr>
<tr>
<td>Capivasertib AKT mutations</td>
<td>Capivasertib</td>
<td>Y</td>
<td>23%</td>
<td>Kalinsky KM, EORTC-NCI-AACR 2018 (oral plenary)</td>
</tr>
<tr>
<td>Nivolumab dMMR status</td>
<td>Nivolumab</td>
<td>Z1D</td>
<td>24%</td>
<td>Azad N, SITC 2018 (oral plenary)</td>
</tr>
<tr>
<td>Afatinib HER2 activating mutations</td>
<td>Afatinib</td>
<td>B</td>
<td>2.7%</td>
<td>Bedard PL, AACR 2019</td>
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<tr>
<td>Palbociclib CCND1, 2, and 3 amplifications and Rb protein expression by IHC</td>
<td>Palbociclib</td>
<td>Z1B</td>
<td>0%</td>
<td>Clark AS, AACR 2019</td>
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<tr>
<td>AZD1775 BRCA1 or BRCA2 mutations</td>
<td>AZD1775</td>
<td>Z1I</td>
<td>3.2%</td>
<td>Kummar S, AACR 2019</td>
</tr>
<tr>
<td>Dabrafenib/trametinib BRAFV600</td>
<td>Dabrafenib/trametinib</td>
<td>H</td>
<td>33%</td>
<td>Salama AKS ASCO 2019</td>
</tr>
</tbody>
</table>
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
- P13K
- PIK3CA mutations
- TSC1, 2 mutations
- MTOR mutations
- PTEN LOSS
- AKT mutations

02/14/2019
NCI-MATCH Resources

Main Webpages:  
  - ecog-acrin.org/nci-match-eay131
  - cancer.gov/nci-match

Protocol Documents:  
  - ctsu.org (password required)

Spanish:  
  - cancer.gov/espanol/nci-match

Email Inquiries:  
  - match@jimmy.harvard.edu

NCI Contact Center:  
  - 1-800-4-CANCER and cancer.gov/contact
What is Pediatric MATCH?

This precision medicine clinical trial, funded by NCI and conducted by COG, matches children and adolescents with treatment based on genetic changes in their tumors.

Pediatric MATCH is for patients ages 1 to 21 who have both:

- Solid tumors, including lymphomas and brain tumors, or histiocytoses
- Tumors that no longer respond to standard treatment or that have come back after treatment

About

200-300 pediatric patients each year are expected to enroll in the screening portion of the study.

We expect to screen a total of 1,000 patients.

Tumor tissue will undergo testing for changes in more than 160 genes.
**NCI-COG Pediatric MATCH Study**

**Goal: 1,000 screened patients with ~ 300 enrolled on a treatment arm**

- Modular format
- Single stage
- N=20 per arm
- 5 to 7 arms to start
- Non-histology driven
- Estimated 300 subjects/year

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Children with relapsed and refractory solid tumors and lymphomas

- Tumor biopsy
- Genetic sequencing
- Actionable mutation detected
- Matching study agent selected

- SD, CR or PR
- Continue until progression
- PD

- Another actionable mutation detected?
  - Yes
  - No
  - Off study

MEK inhibitor
BRAF inhibitor
PI3K/mTOR inhibitor
TRK inhibitor
ALK inhibitor
FGFR inhibitor
Pediatric MATCH Specimen Work Flow Schema
Mirrors Initial Adult NCI MATCH Work

- Biopsy
  - Shipped to Nationwide
  - Tissue Accession
  - Tissue Processing
  - NA Extraction
  - NA Shipped

- Archive
  - Tissue Blocks
  - Slides
  - Nucleic Acid

- NA Shipping
  - BAM File Storage
  - MOI Annotation

- Library Prep and Sequencing
  - Ion Reporter
  - Review and Sign off

- Clinical DB
  - Final Report
  - Germline Report

- CHLA
- Baylor

- DART
- MoCha

- MDA
A similar signal finding study to NCI Adult MATCH with differences:

- Requirement for biopsy: must obtain tissue post-relapse for study eligibility except for brain stem glioma patients
  - **Rationale**: Tumor genomes evolve. To identify potential targets for therapy a “current” relapsed sample is needed
- Inclusion of agents with adult RP2D-some never tested in pediatric previously
- 20 patients enrolled/treatment arm; Activity in 3 out of 20 patients of interest; Option to expand to enroll additional patients if responses are seen
- Different administrative structure for study protocol
- Germline DNA
Germline Sequencing on Pediatric MATCH

- Blood samples being sequenced using same DNA panel
- Purpose: to identify whether mutations identified by tumor sequencing are somatic or germline (not a full evaluation)
- Interpretation by study clinical geneticists
- Results returned to treating pediatric oncologist
- MATCH study genetic resources available including genetic counseling, website and online educational materials for treating physician
Administrative Structure of NCI-COG Pediatric MATCH

1 study with multiple sub-studies or explicitly broken out with a separate Master Version Control Document

Central Coordination by COG (Group leading study)

Moderate Flexibility (around 5 to 13 sub-studies)

NCTN Group Ops/SDMC: 1 study with explicitly broken out sub-studies
CTEP PIO: 1 study with explicitly broken out sub-studies
CIRB: 1 study with explicitly broken out sub-studies
CTSU: 1 study with explicitly broken out sub-studies
CTRP / Clinicaltrials.gov: Explicitly broken out sub-studies (linked references)
FDA: 1 study with 1 IND
Sites: 1 study with explicitly broken out sub-studies

Master Version Control Document
APEC1621

Master Screening Protocol APEC1621 SC

Treatment A Sub-protocol APEC1621 A

Treatment B Sub-protocol APEC1621 B

Treatment J Sub-protocol APEC1621 J
# Treatment Subprotocols (10 activated as of 12/31/2018)

<table>
<thead>
<tr>
<th>Protocol ID</th>
<th>Agent</th>
<th>Agent Class</th>
<th>aMOI Frequency</th>
<th>Activation Date</th>
<th>Accrual as of 11/29/2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>APEC1621-A</td>
<td>Larotrectinib</td>
<td>TRK inhibitor</td>
<td>2-3%</td>
<td>7/24/2017</td>
<td>5</td>
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<tr>
<td>APEC 1621-B</td>
<td>Erdafitinib</td>
<td>FGFR inhibitor</td>
<td>2-3%</td>
<td>11/06/2017</td>
<td>11</td>
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<tr>
<td>APEC 1621-C</td>
<td>Tazemetostat</td>
<td>EZH2 inhibitor</td>
<td>2-3%</td>
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<tr>
<td>APEC 1621-D</td>
<td>LY3023414</td>
<td>PI3K/mTOR inhibitor</td>
<td>5-10%</td>
<td>7/31/2017</td>
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<tr>
<td>APEC 1621-E</td>
<td>Selumetinib</td>
<td>MEK inhibitor</td>
<td>10-20%</td>
<td>7/24/2017</td>
<td>21 Met Accrual</td>
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<td>APEC 1621-F</td>
<td>Ensartinib</td>
<td>ALK inhibitor</td>
<td>2-3%</td>
<td>7/24/2017</td>
<td>6</td>
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<tr>
<td>APEC 1621-G</td>
<td>Vemurafenib</td>
<td>BRAF inhibitor</td>
<td>5%</td>
<td>7/24/2017</td>
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<tr>
<td>APEC 1621-H</td>
<td>Olaparib</td>
<td>PARP inhibitor</td>
<td>2-3%</td>
<td>7/24/2017</td>
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<tr>
<td>APEC 1621-I</td>
<td>Palbociclib</td>
<td>CDK4/6 inhibitor</td>
<td>Variable</td>
<td>6/25/2018</td>
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<td>APEC1621-J</td>
<td>Ulixertinib</td>
<td>ERK1/2 inhibitor</td>
<td>Variable</td>
<td>10/01/2018</td>
<td>8</td>
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</table>

806 children screened as of 11/29/2019
Bolded agents-first time tested in children
### 3 Additional Treatment Subprotocols In Development

<table>
<thead>
<tr>
<th>Protocol ID</th>
<th>Agent</th>
<th>Agent Class</th>
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<tbody>
<tr>
<td>APEC1621- K</td>
<td>Ivosidenib</td>
<td>IDH 1 inhibitor</td>
<td>Fall, 2019</td>
</tr>
<tr>
<td>APEC 1621- M</td>
<td>Tipifarnib</td>
<td>Farnesyl transferase inhibitor</td>
<td>Fall, 2019</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Target HRAS</td>
<td></td>
</tr>
<tr>
<td>APEC 1621- N</td>
<td>Loxo - 292</td>
<td>RET inhibitor</td>
<td>Fall, 2019</td>
</tr>
</tbody>
</table>
Screening Protocol Enrollment Description
As of 12/32/2018, 422 patients screened
(basis for ASCO June 2019 Presentation on NCI Pediatric MATCH)

Patient sex, race, ethnicity

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>248</td>
<td>59%</td>
</tr>
<tr>
<td>Female</td>
<td>174</td>
<td>41%</td>
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<tr>
<td>Ethnicity</td>
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<tr>
<td>Hispanic or Latino</td>
<td>86</td>
<td>20%</td>
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<tr>
<td>Not Hispanic or Latino</td>
<td>320</td>
<td>76%</td>
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<td>16</td>
<td>4%</td>
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<tr>
<td>Race</td>
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<tr>
<td>White</td>
<td>284</td>
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<td>Black or African American</td>
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<tr>
<td>Native Hawaiian or Pacific Islander</td>
<td>4</td>
<td>1%</td>
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<tr>
<td>Asian</td>
<td>19</td>
<td>5%</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>2</td>
<td>1%</td>
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<tr>
<td>Multiple Races</td>
<td>7</td>
<td>2%</td>
</tr>
<tr>
<td>Not Reported or Unknown</td>
<td>51</td>
<td>12%</td>
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</table>

Patient age
- Age range 1 to 21 years (median = 13)
- 40% of patients from 15-21 years

Patients enrolled

Age at enrollment (years)
Screening protocol diagnoses

ALL DIAGNOSES

- CNS tumors (24%)
- Non-CNS solid tumors (71%)
- Lymphomas and histiocytoses (5%)

NON-CNS TUMORS

- OS (29%)
- RMS (15%)
- ES (13%)
- Sarcoma, other (14%)
- Renal (9%)
- NB (6%)
- Carcinoma (4%)
- Liver (3%)
- Other (6%)

OS, osteosarcoma; RMS, rhabdomyosarcoma; ES, Ewing sarcoma; NB, neuroblastoma
Screening protocol diagnoses

ALL DIAGNOSES

- Lymphomas and histiocytoses (5%)
- CNS tumors (24%)
- Non-CNS solid tumors (71%)

CNS TUMORS

- EPN (17%)
- MB (12%)
- AT/RT (7%)
- PNET (4%)
- Other (10%)
- Mixed glial/GNT (4%)
- Astrocytoma (47%)

EPN, ependymoma; MB, medulloblastoma; AT/RT; atypical teratoid/rhabdoid tumor; GNT, glioneuronal tumor; PNET, primitive neuroectodermal tumor
Tumor testing and matching

- Tumor sample was received for 390/422 (92%) enrolled patients

Median turnaround time (tumor receipt to assignment): 15 days

Parsons DW et al. ASCO 2019
Actionable mutation detection – all tumors

An aMOI was detected in 112/357 (31%) tumors

- 31% (112/357) of all tumors
- 26% (67/255) of Non-CNS solid tumors
- 46% (39/85) of CNS solid tumors
- 35% (6/17) of Lymphomas/histiocytoses

n=357 tumors with testing completed as of 12/31/18
Actionable mutation detection - genes

Gene

# tumors With aMOI

n=357 tumors with testing completed as of 12/31/18
Non-actionable mutations—recurrent genes

With aMOI

n=357 tumors with testing completed as of 12/31/18
Challenges in Developing Pediatric MATCH

- Risk determination
- Analytical performance of assay on pediatric tissues
- Incorporation of germline testing and validation
- Process for interpreting germline results and sharing with families
- Specimen processing at NCH and incorporation within the lab system
- Agents available for treatment arms and formulations
- Developing Pediatric MATCHBox to support a new study design and workflow
- Approach to NY state regulations
- Standardizing procedures across labs
- Education and reassurance of advocates
- Managing expectations with families
- Timing with NCI-MATCH
- Efficient and timely PedCIRB protocol reviews
- Building a cohesive informatics team with multiple partners
- Protocol configuration
Conclusions on Pediatric MATCH to Date

• NCI-COG Pediatric MATCH has created a collaborative framework for collection, processing, and sequencing of refractory pediatric cancers

• The modular format of the overall study (Master Control Version document with individual subprotocols) has made it easier for the sites to manage the study locally

• Study enrollment has exceeded projections, with participation from a large and diverse (and growing) group of COG institutions

• Approximately 25% of study patients with tumor submitted have been assigned to a treatment arm, with 10% enrolled on those trials to date

• The study is successfully facilitating the evaluation of molecularly-targeted agents in biomarker positive pediatric cohorts
Future Directions
National Trials to Succeed NCI-MATCH

3 potential successor trials in development

- **ComboMATCH:** Drug combinations are more likely to provide clinical benefit than single agents in most scenarios, so the successor trial to focus on drug combinations using pre-clinical data from *in vivo* models of drug combinations that predict clinical benefit in defined patient groups.

- **AML/MDS Precision Medicine Initiative:** Focus on matching AML molecular subtypes to targeted therapies in different age/fitness groups as well as throughout the course of the disease.

- **iMATCH:** Focus on providing prospective immunologic profiling to feed IO study arms defined by histology or molecular subgroups.

- **Coordination:** Via a Network of laboratories to provide lab support for the trials and a Precision Medicine Analysis & Coordination Center to provide screening data coordination, decision-making and communications support for the trials.
Alternative Administrative Design for Umbrella/Basket Trials Instead of Single Protocol

1 master screening protocol and then multiple “cassettes” of Separate sub-protocols over time. The screening master is independent of the “cassettes” – but it is all centrally operated/harmonized and is under 1 or multiple INDs.
Summary

• Design as well as scientific & administrative conduct of umbrella/basket trials is challenging, but efficiencies can be identified and exploited to maintain flexibility & accelerate clinical research

• Need for study of rare gene variants requires a large network of laboratories for identifying patients

• Programmatic expansion of additional large, national, umbrella/basket trials requires coordinated use of similar administrative, laboratory, and IT systems that can be shared across trials
NCI-MATCH (Adult) Study

• There is widespread participation across the NCI scientific community
  — About 120 treatment arm chairs and co-chairs
  — Nearly 1100 participating sites nationwide
  — Over 150 individuals on 10 steering committees and working groups
**NCI-COG Pediatric MATCH Study**

**Study committees**
- **Study design and logistics:** Stacey Berg, Beth Fox
- **Target/agent prioritization:** Katie Janeway (COG vice chair), Jae Cho
- **Sequencing platform/analysis:** Jim Tricoli
- **Germline result reporting:** Sharon Plon, Steven Joffe
- **Biospecimens:** Julie Gastier-Foster
- **Informatics:** Hema Chaudhary, David Patton

**COG leadership and staff**
- Peter Adamson, Thalia Beeles, Rita Tawdros, Jon Bennet, Wendy Martinez, Lauren Saguilig, Olga Militano, Todd Alonzo, Jin Piao, Renee Klenke, Joel Reid, Marilyn Siegel, Joyce Mhlanga, Alok Jaju, Anne Gill et al.

**NCI/CTEP leadership and staff**
- Nita Seibel (NCI study chair), Malcolm Smith, Mickey Williams, Naoko Takebe, Bhanu Ramineni, Brent Coffey, Cindy Winter, Jennifer Lee, adult NCI-MATCH leadership (Conley, Chen) et al.

**MATCH laboratories**
- Stan Hamilton, Ryan Pepper, Greg Tsongalis, Brianna Houde, Vivekananda Datta, Shahanawaz Jiwani, David Sims, Mark Routbort, Divya Panditi, Shountea Stover, Erik Zmuda et al.

**FDA leadership**
- Martha Donoghue, Greg Reaman