NCI-MATCH: Molecular Analysis for Therapy Choice (EAY131)
Site Participation Presentation

A Joint ECOG-ACRIN / NCI Clinical Trial

Brenda McCalister-Afflick
ECOG-ACRIN Project Manager

NRG Oncology
Clinical Trials Nurses/Clinical Research Associates Educational Session
Thursday, July 16, 2015
2pm – 6pm

Presentation Topics

- ✓ NCI-MATCH / EAY131Trial Overview
- ✓ Eligibility
- ✓ Pathology & Biopsies
- ✓ CIRB Site Participation
- ✓ Registration
- ✓ Important Tips
- ✓ Funding Information
- ✓ Study Contacts

What is the NCI-MATCH / EAY131 trial?

- National Clinical Trials Network study co-developed by NCI and ECOG-ACRIN
- Master screening protocol with multiple, small, phase 2 treatment arms (subprotocols)
  - Genomic pre-screening study that will assign patients with tumors that have specific molecular abnormalities to relevant targeted treatments.
- NCI-MATCH / EAY131 (aka MATCH) will be open to US site members of Alliance, COG, ECOG-ACRIN, NRG,SWOG

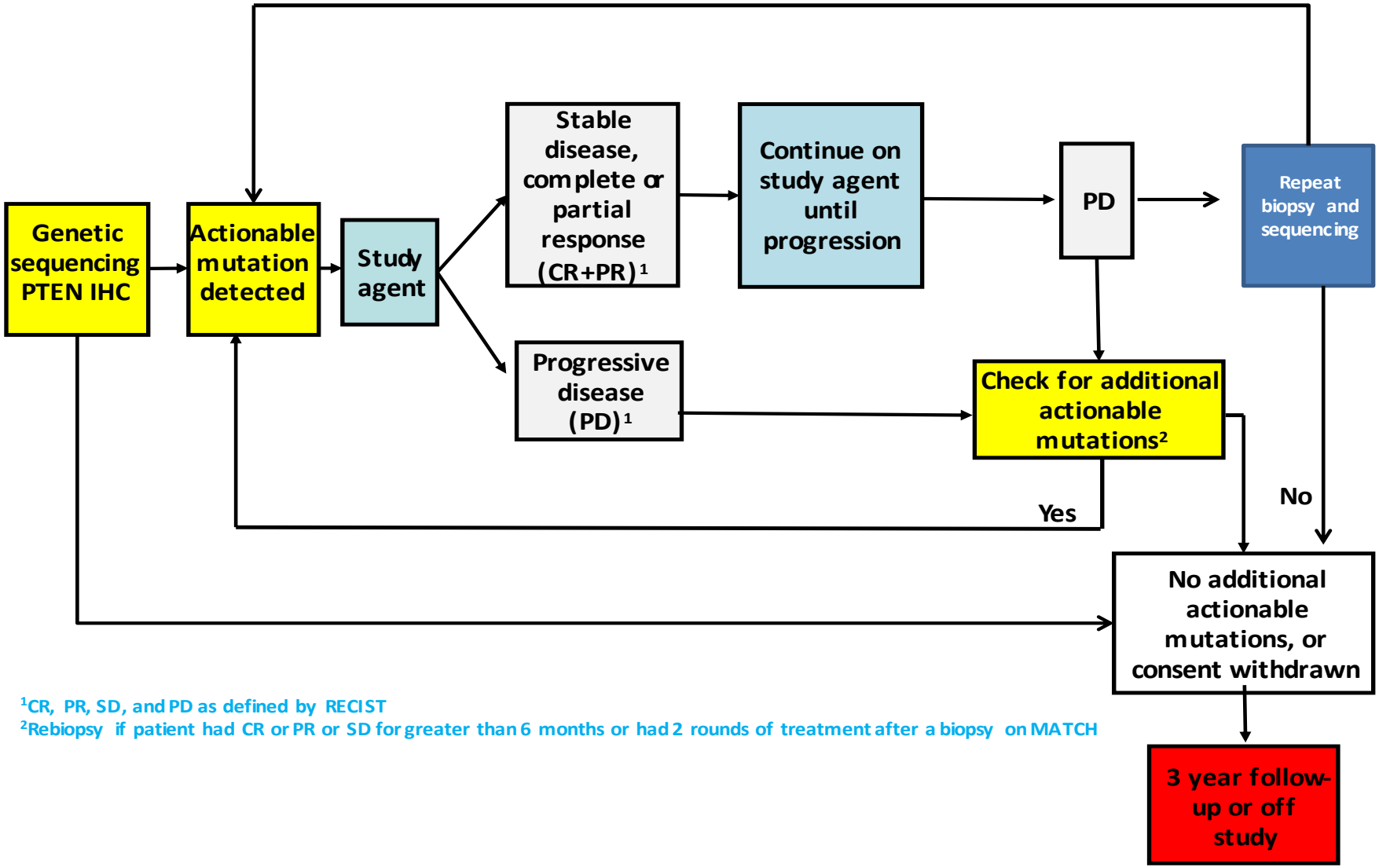
What is the NCI-MATCH / EAY131 trial, Cont'd?

- NCI-MATCH / EAY131 and associated subprotocols (treatment arms) operate as one study.
  - Once EAY131 opens, all available arms will be open.
- MATCH is not limited to specific disease sites
  - A slight overlap in patient populations could occur if another study is open for a similar population; e.g., patients with BRAF.
  - Disease site focused trial that will be open to all eligible patients who have the actionable mutation of interest (aMOI).

Subprotocols / Treatment Arms

- Screening protocol plus ten subprotocols (treatement arms) planned for activation shortly
  - Patient enrollment to begin at end of July 2015
  - Additional subprotocols in development to be added via amendment over time.
  - More than 20 subprotocols anticipated to be available for patient enrollment by end of 2015.
- Treatment arms are being developed in waves
  - Next wave is anticipated to have 7 arms; followed by an additional 4-5 arms
- Accrual to each subprotocol will be 35 patients

NCI-MATCH / EAY131 SCHEMA

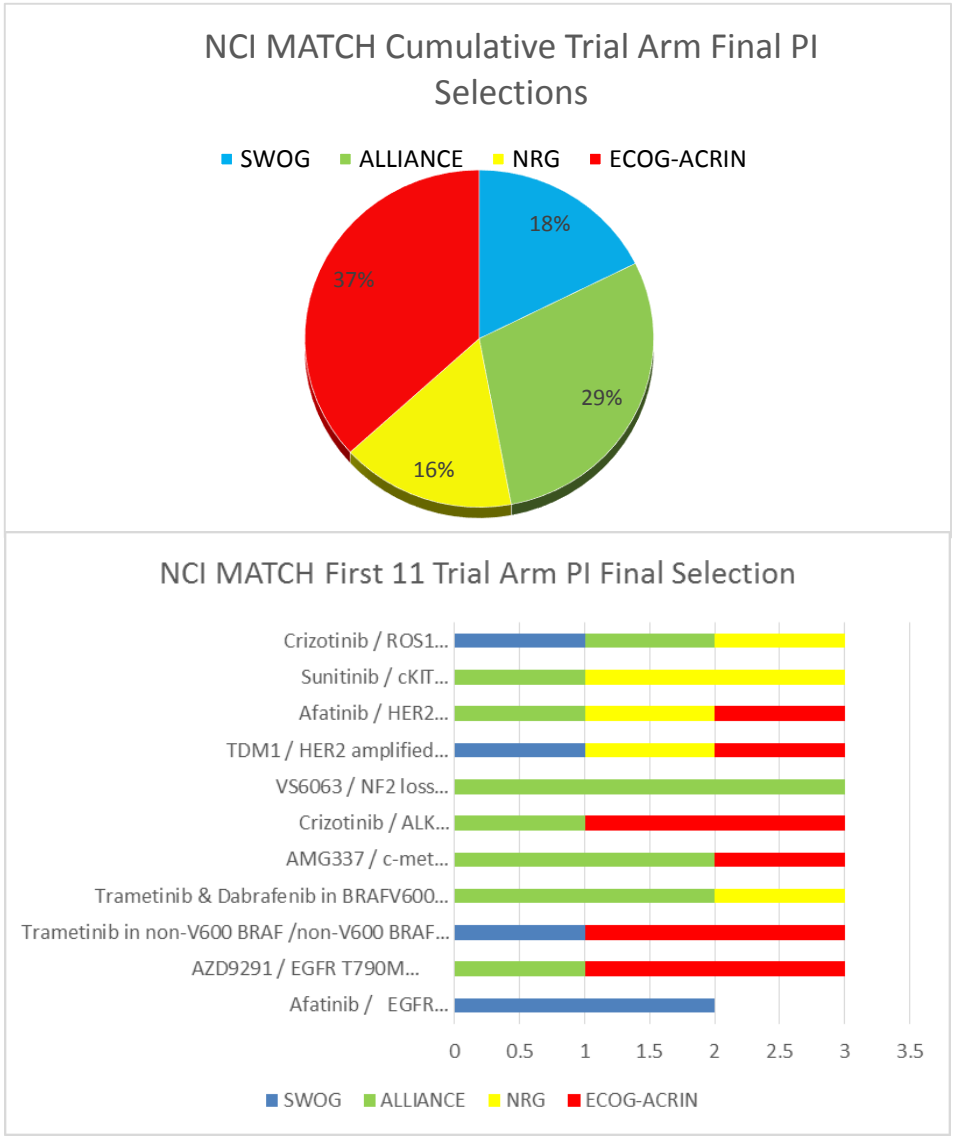


[1]CR, PR, SD, and PD as defined by RECIST
[2]Rebiopsy if patient had CR or PR or SD for greater than 6 months or had 2 rounds of treatment after a biopsy on MATCH

ECOG-ACRIN cancer research group
Reshaping the future of patient care

NATIONAL CANCER INSTITUTE

NCTN Subprotocol Investigator Participation



ECOG-ACRIN cancer research group
Reshaping the future of patient care

NATIONAL CANCER INSTITUTE

General Patient Eligibility

- Adult patients with advanced solid tumors or lymphoma; (including up to 25% rare cancers) whose tumors have begun to grow and are no longer responding to standard therapy *or* do not have a standard therapy.
  - Histologies approved by the FDA or that have shown lack of efficacy with an agent are excluded
- Tumor accessible to biopsy and patient willing to undergo biopsy
- Performance status ECOG 0-1
- Adequate organ function

Patient Registration

- Eligible patients are consented and entered onto screening step
  - Biopsy kit automatically generated
- Specimen is sent within 48 hrs to ECOG-ACRIN Central Biorepository & Pathology Facility (CBPF) at MD Anderson Cancer Center (MDACC) in provided collection kit
- If a treatment assignment is available for the patient, email notification that the treatment assignment is available in Rave is sent to the Data Administrator, Registrar and Treating physician.
  - Eligibility check form will become available in Rave for the assigned subprotocol.
  - CRA must log into Rave to see the treatment assignment and complete the eligibility form.
  - Patient eligibility is immediately evaluated in Rave.
- If patient is eligible for an assignment, return to OPEN to register patient to next step.

Patient Registration, cont'd

- If patient is not eligible for assigned treatment, screening results are re-evaluated for possible second treatment assignment.
- An email alert will be sent if another treatment assignment is available and an eligibility check form for the selected subprotocol will become available in Rave.
- Site obtains signed consent and completes eligibility check form in Rave to confirm patient consent and eligibility for assigned treatment arm.
- All treatments must start within 7 working days after registration to subprotocol.

Study Assays and Biopsies

- Eligible patients must consent and undergo a fresh biopsy at screening for sequencing of the tumor.
- Treatment assignments are based on the results generated by the four designated reference labs only.
- First biopsy (initial screening) is mandatory for participation.
  - Performed after registration to screening Step 0
- Subsequent screening biopsies may be progression samples or required if > 6 months since the initial screening biopsy was performed.
- Optional progression biopsy requested at completion of all MATCH treatment.
  - Expected turn-around time from receipt of adequate tissue at MDA to notification of treatment assignment is ~14 days.
    - Could be longer if submitted specimen is deemed inadequate
    - If additional biopsy is performed, treatment assignment would be ~14 days from MDACC receipt of that biopsy.

Specimen Submission

- Specimen kits will include all materials needed for collection and shipment:
  - including tubes, labels, cassettes, shippers, packaging supplies, and slides.
- If an aMOI is detected,
  - the treatment assignment will be posted in Medidata RAVE
  - a treatment assignment notice will be sent within 24 hours after distribution of the assay results to the site
- A generic specimen submission form will be used if the Sample Tracking System is unavailable.

Pathology

- FNA: Local pathology review (slides, onsite evaluation, rapid read etc.) is not required.
  - Sites are encouraged, at a minimum, to generate slides:
    - For documentation purposes and review
    - If deemed necessary, to determine that intact tumor is present in the FNA specimen
- Extra cores for internal pathology review are not required but are encouraged for the possibility of future local review and assessments
  - May also prevent patient from having an additional procedure.
- Splitting of cores is not permitted.
- For more information, pathology questions should be directed to the MATCH / EAY131 MDACC Pathology Coordinator at:
  - 1-844-744-2420, 1-713-745-4440 international or eacbpf@mdanderson.org

Disease Modality

- Accruals are anticipated from across the various disease groups within cancer centers and practices.
- Differing approaches to operationalize the trial are anticipated; e.g., some sites plan to utilize their Phase I group.
- Sites are encouraged to share ideas and suggestions

EAY131 Trial Pre-Activation

- Screening protocol EAY131 plus 4 subprotocols (identified by letter suffix) were CIRB reviewed and approved.
- Study will open to accrual once the current protocol amendment that includes the 6 add'l subprotocols is approved.
  - Anticipated at end of July 2015
- Protocol documents are available on the CTSU website to assist sites with initiating local regulatory processes and also allowing time to begin set up of electronic monitoring systems.

NCI-MATCH / EAY131 10 Trial Arms Planned for July 2015 Activation

Agent(s)	Molecular Target(s)	Estimated Prevalence	Trial ID
Crizotinib	ALK Rearrangement	4%	EAY131-F
Crizotinib	ROS1 Translocations	5%	EAY131-G
Dabrafenib and Trametinib	BRAF V600E or V600K Mutations	7%	EAY131-H
Trametinib	BRAF Fusions, or Non-V600E, Non-V600K BRAF Mutations	2.8%	EAY131-R
Afatinib	EGFR Activating Mutations	1 – 4%	EAY131-A
Afatinib	HER2 Activating Mutations	2 – 5%	EAY131-B
AZD9291	EGFR T790M Mutations and Rare EGFR Activating Mutations	1 – 2%	EAY131-E
TDM1	HER2 Amplification	5%	EAY131-Q
VS6063	NF2 Loss	2%	EAY131-U
Sunitnib	cKIT Mutations	4%	EAY131-V

ECOG-ACRIN cancer research group
Reshaping the future of patient care

NATIONAL CANCER INSTITUTE

Investigational Brochures

- Current study drugs are CTEP and CIRB approved
- Crizotinib, dabrefenib and trametinib (IND#126200) are Investigational agents.
- Copies of the Investigator's Brochures (IBs) can be obtained by calling PMB at 240-276-6575 or via email request to ibcoordinator@mail.nih.gov.
  - Your investigator's NCI # will be needed.
- The IB provides relevant and current scientific information about the investigational product.
- Please submit to your IRB/EC according to GCP regulations.
- The IB and any correspondence to the IRB should be kept in the study files of EAY131.

Site Participation and the CIRB

- NCTN participating sites (US only): Alliance, COG, EA, NRG, SWOG and NCORP
- Sites who utilize the NCI Central Institutional Review Board (CIRB)
  - CIRB must be the IRB of record for EAY131
  - Sites will only need to submit to the CIRB and if required, to their local review boards
- Study arms will open and close throughout the duration of the trial
  - can be added / replaced faster with the use of the CIRB
- Sites will already be CIRB approved when amendments are released with new therapeutic drugs/treatment arms,.
  - Use of the CIRB will allow sites to activate amendments immediately upon announcement
- Facilitates logistics of study start up, opening, closing and making changes to subprotocols.
  - Additional administrative resources could be needed if local IRBs used
  - Reduces potential treatment delays since separate protocol amendments won't be needed
- CIRB requirement will be re-evaluated later in the trial.
- Sites are encouraged to join the CIRB, if not current members

CIRB Participation

- The following criteria must be met to participate in the CIRB:
  - Investigators at the Signatory Institution must be members of NCTN groups or programs or networks who coordinate NCI-sponsored clinical trials.
  - The Signatory Institution must provide independent oversight of the conduct of the local research.
    - Current participation of ~ 400 signatory institutions represented by ~ 1500 component and affiliate sites nationwide
    - www.ncicirb.org can be accessed for a list of signatory institutions
- All new NCTN sponsored trials are anticipated to eventually transition to the CIRB model.

Site Participation – General Information

- The CIRB will forward regulatory approvals directly to the CTSU Regulatory Office on behalf of all member sites.
  - CTSU will process contingent upon having the list of participating institutions.
  - Can be provided in advance; currently via email is acceptable
- Site regulatory status can be checked at www.ctsu.org
- CIRB Assistance is available by accessing the CIRB HelpDesk at NCICIRBContact@emmes.com or 1-888-657-3711 (8am-4pm Eastern)
  - Questions can be directed to the CIRB administrators, John Horigan or Laura Covington
  - CIRB FAQ can be obtained via the website
- Per the CIRB, operational expertise and print materials will also be available during the NRG meeting at a CIRB informational table

Suggested Tips for Successful Enrollments

- Arrange to meet with affiliated surgeons and interventional radiologists to make proactive plans for rapid scheduling of biopsies
  - E.g., possibly block weekly or other routine slots on the interventional radiology schedule
  - Discuss with surgeons how to facilitate timely scheduling
    - Goal is to ensure biopsies are completed as timely as possible.
  - Draft trial tissue requirements and make available to the various disease site groups in preparation for when cases come through for potential approval.
  - Pre-activation period will allow time for operational set up
- EAY131 is a single, non-disease specific study
  - Meet with research staff to assess how will this be handled at your site.

Biopsies and Subprotocol Treatments

- Maximum number of possible study biopsies = 5
  - Maximum of 2 screening biopsies
  - Maximum of 2 possible re-biopsies due to assay failure
  - 1 research biopsy performed at progression to understand mechanisms of resistance
    - Must have completed their most recent treatment and no further treatment will be given
- Patients can have up to 2 treatment assignments per biopsy (if > 1 aMOI was identified)
  - Consent is required for all registrations

Registration Process Flow at a Glance

1. Site registers eligible patient into the CTSU OPEN system to screening STEP 0 - triggers automatic distribution of biopsy kit within 24 hours

Tissue must be submitted within 48 hours of collection.

Samples are only accepted Tuesday – Saturday for processing at MD Anderson.

2a. Site sends the biospecimens to the ECOG-ACRIN Central Biorepository & Pathology Facility (CBPF) at the MD Anderson

2b. Site enters the date of the biospecimen(s) sent to MD Anderson in the EA Sample Tracking System

2c. Site completes the MATCH Patient Screening Form in Rave for Step 0

3a. If a treatment assignment is available for selected patient, Rave eligibility check form becomes available in Rave for the assigned subprotocol.

Sample processing time ~14 days.

Treatment assignment automatically loaded into Rave.

3b. If the patient is not eligible, the specimen is reevaluated for possible second treatment assignment. Same Rave check form roll out will apply.

4. Site reviews treatment assignment with patient and obtains signed consent for the applicable targeted agent / subprotocol.

5. Site completes eligibility check form in Rave to confirm patient eligibility and consent for the assigned treatment arm.

6. Patient eligibility is evaluated in Rave instantaneously

7. If the patient is eligible, the site registers the subject to Step 1 in OPEN

8. Treatment must start within 7 working days after registration to treatment.

ECOG-ACRIN cancer research group
Reshaping the future of patient care

NATIONAL CANCER INSTITUTE

Available Per Case Funding / Case Credit

- Step 0 Screening = $500 of base intervention funding
  - i.e., $2,250 NCTN Standard, $2,500 NCORP Standard, $4,000 LAPS/NCORP HP, as applicable) will be paid.
- Remaining $1,750 (NCTN Standard), $2,000 (NCORP Standard) and $3,500 (LAPS/NCORP HP), as applicable, will be paid once patient is registered to a sub-protocol through OPEN.
- Maximum of 4 possible treatment registrations to sub-protocols.
- Payments for up to 3 additional registrations through OPEN for individual sub-protocols will be $2,250 (NCTN Standard), $2,500 (NCORP Standard) or $4,000 (LAPS/NCORP HP), as applicable.
- Accrual credits are given each time patients are enrolled on a therapeutic sub-study.

Available Per Case Funding Summary

- Total potential federal funds (standard / LAPS/NCORPS*) = $2250 (enrollment payment) for a maximum of up to 4 treatments or $9,000
- Biopsy Reimbursement = $3,000 per biopsy for a maximum N=5 or $15,000
  - Reimbursements for research biopsies will be made according to current NCTN processes.
  - NCORP credit as determined by the Division of Cancer Prevention
- Study funding sheet will be posted to the CTSU web site outlining reimbursement information once the trial activates.

Medidata Rave / Data Collection

- Standard patient enrollment forms are set up in Rave and will be populated with the enrollment data from OPEN
  - No paper data forms
- An invitation to join iMedidata will be automatically sent to those with Rave roles in CTSU
  - EAY131 can be added once site registration is approved, study is active and all learnings are completed
- If you have completed the elearnings for another ECOG-ACRIN led study, then you will not need to complete again for MATCH.
- Contact the CTSU Help Desk at 1-888-823-5923 or via e-mail at ctsucontact@westat.com or access directely on the CTSU website under the Rave tab http://www.ctsu.org/RAVE/.

NCI-MATCH / EAY131 Study Lead Contacts

NCI Study Chair: Alice Chen, MD Developmental Therapeutic Clinic DCTD/NCI 301-496-4291 chenali@mail.nih.gov	**NCI Study Co-Chair:** Barbara A. Conley, MD Associate Director Cancer Diagnosis Program 240-276-6505 conleyba@mail.nih.gov
ECOG-ACRIN Study Chair: Keith T. Flaherty, MD EA Chair of Developmental Therapeutics Committee 617-726-4800 kflaherty@partners.org	**ECOG-ACRIN Study Co-Chair:** Peter O'Dwyer, MD EA Chair of Gastrointestinal Cancer Committee 215-662-7606 Peter.odwyer@uphs.upenn.edu
NCI Imaging Co-Chair: Frank Lin, MD	**ECOG-ACRIN Imaging Co-Chair:** Marl Rosen, MD, PhD
NCI Laboratory Lead: Mickey Williams, PhD	**Pathology Co-Chair & ECOG-ACRIN Laboratory** Stanley R. Hamilton, MD

Additional Resources

- For general study questions: match@jimmy.Harvard.edu
- ECOG-ACRIN website http://www.ecog.org
- CTSU website http://www.ctsu.org
- Cancer.gov website URL
  - www.cancer.gov/nci-match
  - www.cancer.gov/nci-match (with Spanish translations at http://www.cancer.gov/espanol/noticias/comunicados-de-prensa/2015/nci-match)
- www.clinicaltrials.gov
- For questions about general trial requirements, contact the EA Protocol Liaison
- For clinical questions (i.e. patient eligibility), contact the NCI MATCH Treatment ARM PI listed on the subprotoc
- Other contacts as listed on the protocol

NCI-MATCH: Molecular Analysis for Therapy Choice (EAY131)

A Joint ECOG-ACRIN / NCI Clinical Trial

ECOG-ACRIN cancer research group
Reshaping the future of patient care

NATIONAL CANCER INSTITUTE®

With Participation From

CHILDREN'S ONCOLOGY GROUP
The world's childhood cancer experts

SWOG Leading cancer research. Together.

Alliance for Clinical Trials in Oncology

NRG ONCOLOGY
Advancing Research. Improving Lives.™

Through

NCTN NCORP

Questions?