Executive Summary: Interim Analysis of the NCI-MATCH Trial

National Cancer Institute-**M**olecular **A**nalysis for **T**herapy **Ch**oice (NCI-MATCH) is a phase II precision medicine trial that seeks to determine whether matching certain drugs or drug combinations in adults whose tumors have specific gene abnormalities will effectively treat their cancer, regardless of their cancer type. The trial was co-developed by the ECOG-ACRIN Cancer Research Group and the NCI.

The trial opened in August 2015 with 10 treatment arms and a goal to genetically screen 3000 patients. Patient enrollment was paused in November 2015 for a planned interim analysis. Data as of March 9, 2016 were included in the analysis.

Major Interim Analysis Findings

- The expectation was that the trial would genetically screen the tumor samples of about 50 patients per month during year one; however, enrollment far exceeded expectations with 795 people registering for screening in the first three months
- The laboratories were able to complete tumor testing for 87 percent of cases with samples submitted, a good result where the standard is about 80 percent
- Sample quality was the main issue for cases not able to be analyzed
- Nine percent of tested patients had a gene mutation matching one of the 10 available treatment arms, only one percent lower than the expected rate
- Most of the actual mutation prevalence rates found were much lower than expected based on estimates from The Cancer Genome Atlas and other sources
- Five percent of tested patients received treatment assignments (33) and 16 patients enrolled; 19 patients did not enroll in treatment for reasons including ineligibility, starting other treatment, disease progression, and death
- The following table summarizes accrual:

NCI-MATCH Accrual Summary Activated 08/12/15; Paused 11/11/15: 92 Days		
Patient cases registered for screening	795	
Cases with samples submitted	739	
Cases where labs were able to complete tumor testing	645	87% (N=739)
Cases with mutation matching 1 of 10 available treatment arms	56	9% (N=645)
Patients matching specific eligibility criteria for, and assigned to, a treatment arm	33	5% (N=645)
Patients who entered 7 of 10 available treatment arms	16	2.5% (N=645)

- Sixty-five percent of all patients who registered for screening had uncommon cancers—those other than breast, colorectal, non-small cell lung, or prostate
- One quarter of patient cases with samples submitted included optional cytology specimens, which proved to be valuable in 19 cases where the core samples were unusable but the cytology was able to be analyzed

Changes to the Trial Based on the Interim Analysis

- The overall size of the trial is increasing from 3000 to 5000 patients for genetic screening, and to 24 available treatment arms
- The overall expected mutation match rate for 24 treatment arms is 23 percent
- Laboratory capacity has been expanded to handle processing of 100 patients per week
- Prevalence expectations for gene mutations have been revised downward based on actual findings
- There is a greater focus on communication with enrolling physicians about the importance of adhering to screening eligibility criteria and selecting patients with good ECOG performance status (zero or one), adequate organ function, and ability to withstand being off treatment for a month or more while testing occurs
- Cytology will be required in all cases
- Tumor samples obtained from patients up to six months prior to registration will be allowed
- Use of data from other genetic testing platforms at cancer centers and in industry will be pursued to identify patients for the treatment arms studying rare mutations

Conclusions from the Interim Analysis

- A trial of therapy based on genetic characteristics of the tumor is feasible on a national scale in the NCI-sponsored networks
- The whole process of tumor characterization from accrual to biology read-out is feasible, having been accomplished in 87 percent of patients
- A high proportion of less common malignancies in this early analysis opens options for advances in these cancers
- The interim analysis that was applied early in the trial permitted implementation of several enhancements to the structure of the study
- The trial's early analysis permits planning for the realistic needs of additional trials/drugs that can be analyzed in specific gene abnormalities

The interim analysis was presented in April 2016 at the annual meeting of the American Association for Cancer Research (AACR). There is a slide set based on the data presented at AACR that is available for anyone to use when discussing the interim analysis. To download the interim analysis slide deck, visit **ecog-acrin.org/nci-match-eay131/interim-analysis**.

More information about the trial is also available at **cancer.gov/nci-match**.