le 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Request for Letters Of Interest (LOI) for NCI-ComboMATCH Laboratories

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Cancer Institute (NCI) through its National Clinical Trials Network (NCTN) has developed a successor precision medicine trial to 'NCI-Molecular Analysis for Therapy Choice (NCI-MATCH)' entitled 'NCI-ComboMATCH'. The principle of this initiative is to overcome drug resistance to single-agent therapy by developing genomically-directed targeted agent combinations. All combinations must be supported by robust, preclinical *in vivo* evidence.

DATES: Letters Of Interest (LOIs) should be submitted to the National Cancer Institute (NCI), National Institutes of Health (NIH) on or before 5:00 P.M. EST on September 30, 2023.

ADDRESSES: Submit LOIs by e-mail to NCICOMBOMATCHLabApps@nih.gov.

9609 Medical Center Drive, 3 West, Room 360, Rockville, MD 20892.

FOR FURTHER INFORMATION CONTACT: Questions about this request for LOIs should be directed to NCICOMBOMATCHLabApps@nih.gov or Benjamin Kim at benjamin.kim@nih.gov or by phone at (240) 276-5961.

SUPPLEMENTARY INFORMATION:

NCI-ComboMATCH trial leadership invites applications for Clinical Laboratory Improvements Program (CLIA) certified/accredited laboratories that test tumor specimens from patients utilizing Next-Generation Sequencing (NGS) assays to participate in the NCI-ComboMATCH trial. These laboratories are required to have a catchment area that serves underrepresented populations and should be able to provide

documentation of the proportion of subjects seen by the lab by race/ethnic origin. Laboratories serving a large percentage (>30%) of African Americans, Native Americans, Hispanics, Asians and Pacific Islanders will be considered. In order to support this trial, the designated laboratories participating in NCI-ComboMATCH will identify patients for the specific molecular variants needed for trial eligibility. Laboratories will be asked to indicate on their report if a patient is eligible for one of the NCI-ComboMATCH subprotocols. If this is not feasible the lab is asked to contact the patients provider via letter, email or fax that the individual may be eligible for a NCI-ComboMATCH subprotocol if a specimen sent from the lab has a variant(s) that would potentially make the patient eligible for one of the treatment arms. Physicians will also be able to refer the patient directly to the NCI-ComboMATCH registration trial. In any of these cases, the laboratory will be required to provide the variant data to the NCI-ComboMATCH 'MATCHbox' which is a computer program that serves to gather information used to determine the eligibility of the particular patient to a treatment arm. In accordance with 42 U.S.C. 285, of the Public Health Service Act, as amended. Like NCI-MATCH, NCI-ComboMATCH is conceived as a signal-seeking study. The NCI-ComboMATCH team will determine whether patients with tumor mutations, amplifications or translocations in the genetic pathway(s) of interest are likely to derive clinical benefit if treated with a combination of precision medicine agents targeting those specific pathway(s). This recruitment is for laboratories in areas serving underrepresented populations that can screen at least 100 patients per month.

Patients with histologically documented solid tumors whose disease has progressed following at least one line of standard systemic therapy or for whom no standard therapy exists are eligible if they meet the eligibility criteria for the trial. Further information about the NCI-ComboMATCH trial may be found at https://ecog-acrin.org/clinical-trials/eay191-combomatch/.

The selected collaborating outside laboratories may only refer patients on any of the variant arms for which their assay reports actionable mutations of interest (aMOIs). The assay must also report all exclusionary variants for the arm unless these occur at a frequency of < 1% in cancer patients.

Only CLIA accredited/certified laboratories located in the United States may be considered for addition to the laboratory network.

Letter of interest (LOI) and Confidentiality Agreement

Candidate laboratories should submit a letter of interest to NCICOMBOMATCHLabApps@nih.gov stating:

- Statement of interest in the proposed activity
- Laboratory name
- Proportion of underrepresented groups or populations tested by the lab
- Lead contact name, address, email address, and telephone number
- CLIA certification number
- Assay name
- Brief description of assay
    - Sensitivity and specificity for SNVs, indels, CNV, fusions
    - Method of analysis
    - Platform and variant calling
- Number of assays on patients per month
- Willingness to report to or contact providers of patients who are potentially eligible for one of the subprotocols on NCI-ComboMATCH
- Willingness to sign a collaboration agreement with NCI and to share data and publication rights.

Following an acceptable eligibility review to the NCI-ComboMATCH screening committee, the laboratory would execute a confidentiality agreement with NCI and will be provided with a detailed list of eligibility and exclusion variants for arms (approved at that time). The lab would then be required to submit an application by September 30th, 2023 for review by the NCI-ComboMATCH review committee. Candidate laboratories will be required to meet the following general requirements:

- Testing must be performed in a CLIA-certified or -accredited laboratory located in the United States.
- Assays may be on tumor tissue or circulating nucleic acids
- Laboratory NGS panels must be analytically and clinically validated on DNA from human tumor tissue, with performance characteristics as follows:
    - Specificity at least 99% for single nucleotide variants, indels
    - Sensitivity at least 95% for single nucleotide variants, indels
    - Sensitivity of 90% for copy number variants (state fold of copy number variants that can be detected with 90% sensitivity)
    - 99% reproducibility between sequencers (if more than one sequencer is used) and between operators
    - Lower limit of detection for SNVs, indels, and CNVs must be stated.
    - Laboratories should also provide these parameters if they have a validated circulating tumor DNA (ctDNA) assay

Laboratories must supply the following information in their application:

- Lower limit of % tumor accepted, and whether (and which) enrichment procedures are employed
- Whether the lab archives images of slides from the tumor

    - Whether the lab runs germline as well as tumor with the assay (a simultaneous germline sequencing is not required by NCI-ComboMATCH)
    - A detailed description of assay procedures, including starting material, extraction of nucleic acids, quality assurance, quality metrics, data analysis and filters must be supplied.

- Laboratory NGS test panels must interrogate actionable mutations of interest (aMOIs) required for enrollment into the available variant arms.
- The designated lab should be willing to provide residual nucleic acid from the sample they tested if the patient enrolls on NCI-ComboMATCH
- As it is important that the dataset used for analysis in NCI-ComboMATCH be as robust as possible, the laboratory NGS test will require qualification, during which the performance of the laboratory will be compared with the NCI-ComboMATCH Central Laboratory test to ensure good agreement with that assay.
- Laboratories shall NOT advertise that they are screening laboratories for ComboMATCH eligibility without prior review by NCI and ECOG-ACRIN. Any press release or public disclosure requires clearance by NCI and NCI-ComboMATCH regulatory team.
- Laboratories must agree to use the existing workflow established by the NCI-ComboMATCH trial team to identify patients for the variant arms.
    - Laboratory results of NGS assays done for clinical care will be the subject of this initiative. There is no funding for “screening” a patient for NCI-ComboMATCH.

- Laboratories must notify NCI-ComboMATCH sites that the laboratory results would potentially allow the patient to be eligible for NCI-ComboMATCH.
- Laboratories must track how many assays per month detect variants that could make a patient eligible for NCI-ComboMATCH.
- If the clinician presents the NCI-ComboMATCH study and the patient is eligible and desires to enter the study, the laboratory must agree to enter the results into the informatics system that assigns treatment in NCI-ComboMATCH (MATCHbox).
- Laboratories must have a way to answer questions from NCI-ComboMATCH sites about their assay and must have a contact person for optimal communication with the NCI-ComboMATCH team.

- Prior to participation, laboratories must enter into a collaboration agreement with NCI. A sample agreement is available upon request and includes the requirement to participate in trial monitoring by NCI, the trial sponsor. As part of such a collaboration agreement, laboratories must agree to provide the licensing rights described in the CTEP IP Option to the Pharmaceutical Collaborators who provided agents for the NCI-ComboMATCH trial (https://ctep.cancer.gov/branches/rab/intellectual_property_option_to_collaborators.htm) (https://www.gpo.gov/fdsys/pkg/FR-2011-03-11/pdf/FR-2011-03-11.pdf) as well as agree to the data sharing and publication rights consistent with those agreements.
- No reimbursement for these activities (testing or notification of sites of NCI-ComboMATCH eligibility) exists.

Qualified laboratories serving a large component of an underrepresented population are the only ones being considered for this Federal Register Notice.

How to apply:

1. Submit letter of interest (LOI) as described above under “Letter of Interest and Confidentiality Agreement” to NCICOMBOMATCHLabApps@nih.gov
2. LOIs must be submitted to the National Cancer Institute (NCI), National Institutes of Health (NIH) on or before 5:00 P.M. EST on September 30, 2023. LOIs will be reviewed immediately upon receipt.
3. Notification of acceptance, non-acceptance or questions from Steering Committee will be sent to the designated contact person as soon as the LOI has been reviewed. This notification will include further instructions if a full application is invited.
4. Applications that have not been submitted within 6 weeks of notification of acceptance will be de-activated and not further considered.
5. DO NOT send a full application until you are invited to do so.

Review criteria for LOI:

Laboratory is a CLIA-certified laboratory within the United States.

Laboratory is able to provide evidence that its volume of patients tested is composed >30% underrepresented peoples.

Laboratory NGS assay has adequate sensitivity and specificity.

Laboratory tests tumor tissue for variants required for NCI-ComboMATCH.

Laboratory agrees to provide needed information for evaluation of the analytical validity of the test.

Laboratory agrees to contact sites regarding NCI-ComboMATCH eligibility.

Laboratory agrees to a collaboration with NCI as detailed above.

Review criteria for full application:

Laboratory supplies evidence that the assay meets analytical requirements as detailed above.

Laboratories are capable of contacting providers and tracking activity based on detection of potential variants.

Laboratories agree to execute a collaboration agreement with NCI, as well as to data sharing and sharing publication rights.

Laboratories agree to abide by the procedures in place for the NCI-ComboMATCH study and to collaborate fully with the NCI-ComboMATCH team.

For more information, contact NCICOMBOMATCHLabApps@nih.gov.

Dated: August 8, 2023.

Lyndsay N. Harris,

Associate Director,

Cancer Diagnosis Program,

Division of Cancer Treatment & Diagnosis,

National Cancer Institute.

[FR Doc. 2023-17352 Filed: 8/11/2023 8:45 am; Publication Date: 8/14/2023]