

FAST FACTS

EAY131: Molecular Analysis For Therapy Choice (MATCH)

This checklist is for eligibility for the Master Screening Protocol only; each subprotocol will have additional eligibility criteria that will be outlined in Section 2.1 of the agent-specific subprotocol.

NOTE: Patients may not receive more than two rounds of treatment (e.g. may only be assigned 2 different treatments based on aMOIs) between biopsies.

ELIGIBILITY CRITERIA FOR SCREENING BIOPSY (STEP 0)

1. Patients must be ≥ 18 years of age. Because no dosing or adverse event data are currently available on the use of study investigational agents in patients < 18 years of age, children are excluded from this study.
2. Patients of childbearing potential must have a negative serum pregnancy test within 2 weeks prior to registration. Patients that are pregnant or breast feeding are excluded.
A patient of childbearing potential is anyone, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).
3. Patients must not expect to conceive or father children by using accepted and effective method (s) of contraception or by abstaining from sexual intercourse prior to study entry, for the duration of study participation, and for 4 months after completion of study.
Should a patient or a partner of the patient become pregnant or suspect a pregnancy while participating in this study, the treating physician should be informed immediately.
4. Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma or multiple myeloma requiring therapy and meet one of the following criteria:
 - Patients must have progressed following at least one line of standard systemic therapy and there must not be other approved/standard therapy available that has been shown to prolong overall survival (i.e. in a randomized trial against another standard treatment or by comparison to historical controls). Patients who cannot receive other standard therapy that has been shown to prolong overall survival due to medical issues will be eligible, if other eligibility criteria are met. If the patient is currently receiving therapy, the clinician must have assessed that the current therapy is no longer benefitting the patient prior to enrolling on MATCH, regardless of whether it is considered standard.

OR

- Patients for whose disease no standard treatment exists that has been shown to prolong overall survival.

NOTE: No other prior malignancy is allowed except for the following:

- a) adequately treated basal cell or squamous cell skin cancer
- b) in situ cervical cancer
- c) adequately treated Stage I or II cancer from which the patient is currently in complete remission
- d) any other cancer from which the patient has been disease-free for 5 years.

5. Patients must have measurable disease as defined in Section 6.

6. Patients must meet the criteria below

NOTE: Tumor tissue for the confirmation of “rare variant” by the MATCH assay is to be submitted, preferably from the same time of collection as that used to determine patient candidacy for treatment arm assignment, per Section 4.1.5, Section 7.2 and Section 9.

- a. Registration to Step 0 must occur after stopping prior systemic anti-cancer therapy. There is no specific duration for which patients must be off treatment prior to registration to Step 0, as long as all eligibility criteria are met.
- b. Patients may have received other non-targeted, immunotherapy or targeted treatment between the prior genetic testing at the outside lab and registration to Step 0. The decision to stop such treatment in favor of participation in MATCH, if no further clinical benefit is expected, is per the treating physician's discretion. Documentation of a lack of response to the prior treatment is not required in these cases. The requirements in Section 3.1.4 still apply.
- c. Patients with an applicable “rare variant” must be able to meet the eligibility criteria for the appropriate subprotocols within 4 weeks following notification of treatment assignment, per Section 4.2.
- d. Patient meets one of the following criteria:
 - i. Patient is a candidate for Z1M based on local CLIA assessment of MMRd by IHC or MSI status by PCR, adequate tumor tissue is available for submission for mandatory central screening IHC and the patient will be able to meet the eligibility criteria for Z1M within 4 weeks following notification of treatment assignment.
 - ii. The sites have received results from one of the designated outside laboratories indicating a “rare variant” that is an actionable Mutation of Interest (aMOI) for specific select subprotocols.

NOTE: See appendix XIV for more information on the designated laboratories and applicable arms.

NOTE: There is no particular window of time after receiving the sequencing report notification of potential eligibility from an outside lab in which the patient must be registered to Step 0, but treatment slots will be assigned on a first come, first serve basis to those who do register to Step 0, and are not held for those notified of potential eligibility who do not register to Step 0.

NOTE: Treatment assignment (and the start of the associated deadline for Step 1 registration) may occur shortly after Step 0 registration. Note that certain “rare variant” arms require submission of archival tissue for central IHC testing to determine treatment assignment. For those arms, adequate tissue for the central IHC is required to be available for submission.

NOTE: Other potential aMOIs that would be eligibility criteria for “NON RARE” arms, as determined by the designated laboratories, are not applicable for this process in MATCH. See additional requirements outlined in Section 4.1.5.4.

7. Patient must not require the use of full dose coumarin-derivative anticoagulants such as warfarin. Low molecular weight heparin is permitted for prophylactic or therapeutic use. Factor X inhibitors are permitted. **NOTE:** Warfarin may not be started while enrolled in the EAY131 study. Stopping the anticoagulation for biopsy should be per site SOP.

8. Patients must have ECOG performance status ≤ 1 , see Appendix V and a life expectancy of at least 3 months.
9. Patients must not currently be receiving any other investigational agents.
10. Patients must not have any uncontrolled intercurrent illness including, but not limited to:
 - Symptomatic congestive heart failure (NYHA classification of III/IV)
 - Unstable angina pectoris or coronary angioplasty, or stenting within 6 months prior to registration to Step 0, 2, 4, 6
 - Cardiac arrhythmia (ongoing cardiac dysrhythmias of NCI CTCAE v4 Grade ≥ 2)
 - Psychiatric illness/social situations that would limit compliance with study requirements
 - Intra-cardiac defibrillators
 - Known cardiac metastases
 - Abnormal cardiac valve morphology (\geq grade 2) documented by ECHO (as clinically indicated); (subjects with grade 1 abnormalities [i.e., mild regurgitation/stenosis] can be entered on study). Subjects with moderate valvular thickening should not be entered on study

NOTE: To receive an agent, patient must not have any uncontrolled intercurrent illness such as ongoing or active infection. Patients with infections unlikely to be resolved within 2 weeks following screening should not be considered for the trial.
11. Patients must be able to swallow tablets or capsules. A patient with any gastrointestinal disease that would impair ability to swallow, retain, or absorb drug is not eligible.
12. Patients who are HIV-positive are eligible if:
 - CD4+ cell count greater or equal to 250 cells/mm³
 - If patient is on antiretroviral therapy, there must be minimal interactions or overlapping toxicity of the antiretroviral therapy with the experimental cancer treatment; for experimental cancer therapeutics with CYP3A/4 interactions, protease inhibitor therapy is disallowed; suggested regimens to replace protease inhibitor therapy include dolutegravir given with tenofovir/emtracitabine; raltegravir given with tenofovir and emtracitabine. Once daily combinations that use pharmacologic boosters may not be used.
 - No history of non-malignancy AIDS-defining conditions other than historical low CD4+ cell counts
 - Probable long-term survival with HIV if cancer were not present.
13. Any prior therapy, radiotherapy (except palliative radiation therapy of 30 Gy or less), or major surgery must have been completed ≥ 4 weeks prior to start of treatment. All adverse events due to prior therapy have resolved to a grade 1 or better (except alopecia and lymphopenia) by start of treatment. Palliative radiation therapy must have been completed at least 2 weeks prior to start of treatment. The radiotherapy must not be to a lesion that is included as measurable disease.

NOTE: Prostate cancer patients may continue their LHRH agonist.

NOTE: For patients entering the study via the original screening process, patients may receive non-protocol treatment after biopsy (if clinically indicated) until they receive notification of results; however, lack of response (per Section 6) must be documented prior to registration to Step 1. New non-protocol treatment will NOT be permitted as intervening therapy after registration to Step 0. The only intervening treatment permitted is prior therapy that the patient already received prior to Step 0 registration.

The decision to stop the intervening non-protocol treatment will be left up to the treating physician if patient has an aMOI. However, patients will need to be off such therapy for at least 4 weeks before

receiving any MATCH protocol treatment. Please refer to Section 4.2 for additional relevant time restrictions.

NOTE: For patients entering the study via a designated outside laboratory, no intervening systemic non-protocol treatment is permitted after Step 0 registration. All other eligibility requirements still apply to these patients, including the washouts for prior therapy noted above in this section, the time restrictions outlined in Section 4.2, and the eligibility criteria for the intended subprotocol.

14. Patients with brain metastases or primary brain tumors must have completed treatment, surgery or radiation therapy ≥ 4 weeks prior to start of treatment.
15. Patients must have discontinued steroids ≥ 1 week prior to registration to Step 0 and remain off steroids thereafter, except as permitted (see below). Patients with glioblastoma (GBM) must have been on stable dose of steroids, or be off steroids, for one week prior to registration to treatment step (Step 1, 3, 5, 7).

NOTE: The following steroids are permitted (in the list below, low dose steroid use is defined as prednisone 10 mg daily or less, or bioequivalent dose of other corticosteroid):

- Temporary steroid use: e.g. for CT imaging in setting of contrast allergy
- Low dose steroid use for appetite
- Chronic inhaled steroid use
- Steroid injections for joint disease
- Stable dose of replacement steroid for adrenal insufficiency or low doses for non-malignant disease
- Topical steroid
- Steroids required to manage toxicity related to study treatment, as described in the subprotocols
- Steroids required as pre- or post-chemotherapy medication for acceptable intervening chemotherapy

NOTE: Steroids must be completed alongside last dose of chemotherapy.

16. Patients must have adequate organ and marrow function as defined below within 2 weeks prior to screening step registration and within 4 weeks prior to treatment step registration.
 - Leukocytes $\geq 3,000/ \text{mL}^*$
 - Absolute neutrophil count $\geq 1,500/ \text{mL}^*$
 - Platelets $\geq 100,000/ \text{mL}^*$

NOTE: *Patients with documented bone marrow involvement by lymphoma are not required to meet the above hematologic parameters, but must have a platelet count of at least 75,000/mcL and neutrophil count of at least 1000/mcL.

 - Total bilirubin $\leq 1.5 \times$ institutional ULN (unless documented Gilbert's Syndrome, for which bilirubin $\leq 3 \times$ institutional ULN is permitted)
 - AST(SGOT)/ALT(SGPT) $\leq 2.5 \times$ institutional upper limit of normal (ULN) (up to 5 times ULN in presence of liver metastases)
 - Creatinine clearance $\geq 45 \text{ mL/min/1.73 m}^2$ for patients with creatinine levels above institutional normal as defined by the Cockcroft-Gault Equation
17. Patients must have an electrocardiogram (ECG) within 8 weeks prior to registration to screening step and must meet the following cardiac criteria:
 - a. Resting corrected QT interval (QTc) > 480 msec.

NOTE: If the first recorded QTc exceeds 480 msec, two additional, consecutive ECGs are required and must result in a mean resting QTc \leq 480 msec. It is recommended that there are 10-minute (\pm 5 minutes) breaks between the ECGs.

The following only need to be assessed if the mean QTc $>$ 480 msec.

- Check potassium and magnesium serum levels
- Correct any identified hypokalemia and/or hypomagnesemia and may repeat ECG to confirm exclusion of patient due to QTc
- For patients with HR 60-100 bpm, no manual read of QTc is required.
- For patients with baseline HR $<$ 60 or $>$ 100 bpm, manual read of QT by trained personnel is required, with Fridericia correction applied to determine QTc.
- Patient must not have hypokalemia (value $<$ institutional lower limit of normal).

b. No factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure, congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years of age or any concomitant medication known to prolong the QT interval (For a list of these medications, please see [Appendix XIII](#))

Date of ECG: _____

NOTE: Patient must be taken off prohibited medication prior to registration to the screening Step (Step 0, 2, 4, 6) and remain off these medications thereafter, unless permitted on a subprotocol for the management of treatment related toxicity.. Patient must be off the drug for at least 5 half lives prior to registration to the treatment step (Step 1, 3, 5, 7). The medication half life can be found in the package insert for FDA approved drugs.

ELIGIBILITY CRITERIA FOR FIRST TREATMENT (STEP 1)

1. Eligibility requirements for registration onto Step 1 are outlined in Section 2.1 of the agent-specific subprotocol.

NOTE: For patients entering Step 0 with assay results from outside laboratories, no systemic treatment is allowed after Step 0 registration.

2. As MATCH is designed to add additional subprotocols, implement limited expansions of accrual for certain subprotocols, and/or amend existing arm-specific eligibility criteria, some patients entering under the original screening method may be eligible to have their results rerun in MATCHbox, even if they did not match to a treatment initially or did not receive a treatment assignment due to a lack of available assignment slots. Patients whose sequence results will be rerun through MATCHbox must also meet the following criteria:

- a. Samples must have been collected within 5 months of the activation of the addendum, as there is an additional month needed to get the patients on trial.
- b. Patient has not had treatment within the 5 months that resulted in a PR or better after the performance of the screening assessment.
- c. Patient must meet eligibility criteria, including performance status 1 or better and life expectancy of at least 3 months.

- d. Patients must meet the eligibility requirements found in Section 3.1.13, with the following exceptions:
- a. Patients may have received other non-targeted, immunotherapy or targeted treatment, which could be stopped in favor of returning to MATCH, if no response to the interim treatment has occurred and no further benefit is expected from this interim treatment, per the treating physician's discretion. Documentation of a lack of response to the interim treatment is not required in these cases.
However, the following restrictions apply:
 - Enrollment onto another investigational therapeutic study is not permitted.
 - Patient cannot be responding to interim treatment, since the benefit of the MATCH treatment is unknown and may deprive patient of an effective treatment if it were given when a patient is responding to another treatment.

NOTE: Patients meeting these criteria will NOT be biopsied at this time point. Instead, their Step 0 results will be re-interrogated to determine if another treatment is available.

ELIGIBILITY CRITERIA FOR SECOND SCREENING (STEP 2)

1. Patient's disease has progressed on Step 1 treatment (per Section 6) or could not tolerate assigned treatment.

NOTE: PATIENTS ENTERING STEP 1 WITH A RARE VARIANT FROM AN "OUTSIDE" LAB ARE NOT ELIGIBLE FOR STEP 2. SEE SECTION 3.3.3 BELOW.

2. Patients must meet one of the following criteria:
 - a. No response and progression (or inability to tolerate further treatment) occurred < 6 months from start of Step 1 treatment.

NOTE: Patients meeting these criteria will NOT be biopsied at this time point. Instead, their Step 0 MATCH assay results will be re-interrogated to determine if another treatment is available upon registration to this study step. It is not necessary to confirm the availability of another potential treatment assignment in advance. Only aMOIs detected by the MATCH assay may be used for the determination of eligibility to a relevant subprotocol.

OR

- b. Progression (or inability to tolerate further treatment) occurred after a (1) response OR (2) after ≥ 6 months from start of Step 1 treatment. Patient must have tumor amenable to percutaneous biopsy and be willing and able to undergo a tumor biopsy or bone marrow aspirate for collection and submission of tumor tissue OR patient will be undergoing a procedure due to medical necessity during which the tissue may be collected for the central determination of the presence of one or more of the specific "actionable" mutations/amplifications of interest (aMOI) (defined in Appendix VII). See Section 9. Archived specimens cannot be accepted.
3. Patients must meet eligibility criteria as defined in Section 3.1 (excluding section 3.1.6).
4. Patient must not have been assigned to Step 1 treatment based on a "rare variant" determined by a designated outside laboratory (See Appendix XIV).

ELIGIBILITY CRITERIA FOR SECOND TREATMENT (STEP 3)

1. Eligibility requirements for registration onto Step 3 are outlined in Section 2.1 of the agent-specific subprotocol. **NOTE: If screening biopsy samples were submitted during Step 2, patients may receive**

non-protocol treatment after biopsy (if clinically indicated) until they receive notification of results however, lack of response (per Section 6) must be documented prior to registration to Step 3. New non-protocol treatment will NOT be permitted as intervening therapy after registration to Step 2. The decision to stop the intervening nonprotocol treatment will be left up to the treating physician if patient has an aMOI. Waiting periods as described in Section 3.1.13 will apply. .

ELIGIBILITY CRITERIA FOR THIRD SCREENING (STEP 4)

1. Patient's disease has progressed on Step 3 treatment or patient could not tolerate assigned treatment.
 - a. If patient's disease has progressed, they must meet one of the following criteria:
 - No response and progression occurred < 6 months from start of Step 3 (second) treatment AND the latest MATCH assay results indicated >1 targeted treatments AND a biopsy was performed at Step 2 screening. **NOTE:** Patients meeting these criteria will NOT be biopsied at this time point. Instead, their results will be re-interrogated to determine if another treatment is available. **OR**
 - Progression occurred on Step 3 treatment and a biopsy was not performed at Step 2 screening (due to presence of additional aMOIs at that stage). Patient must have tumor amenable to percutaneous biopsy and be willing and able to undergo a tumor biopsy or bone marrow aspiration for collection and submission of tumor tissue OR patient will be undergoing a procedure due to medical necessity during which the tissue may be collected for the central determination of the presence of one or more of the specific "actionable" mutations/amplifications of interest (defined in Appendix VII). Biopsy must not be considered to be more than minimal risk to the patient. See Section 9.
2. Patients must meet eligibility criteria as defined in section 3.1 (excluding section 3.1.6). **NOTE:** A patient may have a maximum of 2 screening biopsies (not including re-biopsy due to assay failure), and 2 MATCH treatments per biopsy (if > 1 aMOI). See Section 4.12 for further information on biopsies.

ELIGIBILITY CRITERIA FOR THIRD TREATMENT (STEP 5)

1. Eligibility requirements for registration onto Step 5 are outlined in Section 2.1 of the agent-specific subprotocol. **NOTE: If screening biopsy was submitted on Step 4,** patients may receive non-protocol treatment after biopsy (if clinically indicated) until they receive notification of results however, lack of response (per Section 6) must be documented prior to registration to Step 5. New non-protocol treatment will NOT be permitted as intervening therapy after registration to Step 4. The therapy cannot be an arm in the MATCH trial. The decision to stop the intervening nonprotocol treatment will be left up to the treating physician if patient has an aMOI. Waiting periods as described in Section 3.1.13 will apply.

ELIGIBILITY CRITERIA FOR FOURTH SCREENING (STEP 6)

1. Patient's disease has progressed on Step 5 protocol treatment or patient could not tolerate assigned treatment.
2. Patient must have had no response, and progression (or inability to tolerate further treatment) occurred < 6 months from start of Step 5 treatment AND a biopsy was performed at Step 4 screening. **NOTE:** Patients meeting these criteria will NOT be biopsied at this time point. Instead, based on their 2nd biopsy, their results will be interrogated to determine if another treatment is available upon registration to this study step. It is not necessary to confirm the availability of another potential treatment assignment in advance.
3. Patients must meet eligibility criteria as defined in Section 3.1 (excluding Section 3.1.6). **NOTE:** For Step 6, biopsies to collect material for screening assay will NOT be performed. A patient may have a maximum of 2 successful screening assessments of submitted tissue (Steps 0 and 2 OR Steps 0 and 4), and 2 MATCH treatments per biopsy (if > 1 aMOI). See Section 4.12 for further information on biopsies.

ELIGIBILITY CRITERIA FOR FOURTH TREATMENT (STEP 7)

1. Eligibility requirements for registration onto Step 7 are outlined in Section 2.1 of the agent-specific subprotocol. **NOTE:** Patients must not receive non-protocol treatment after biopsy until they receive notification of results, as it will delay initiation of assigned treatment.

ELIGIBILITY CRITERIA FOR RESEARCH BIOPSY (STEP 8)

NOTE: ALL PATIENTS SHOULD BE ENCOURAGED TO PARTICIPATE IN STEP 8, IF SAFE; IF BIOPSY IS REFUSED OR INADVISABLE, ENCOURAGE COLLECTION OF WHOLE BLOOD FOR CIRCULATING TUMOR DNA, PER SECTION 9.3.2.

As a reminder, the submission of the Step 8 samples requires additional patient consent, as well as registration to Step 8.

NOTE: Patients who entered the study (Step 0) with a “rare variant” determined by an outside assay ARE potentially eligible and encouraged to participate in Step 8.

1. Patient has completed their most recent MATCH study treatment, will not undergo an additional screening biopsies, and will receive no additional treatment on MATCH.
NOTE: If a 2nd Screening Biopsy was performed and showed no study-actionable abnormalities, and blood samples were submitted with the screening biopsy, no additional end of treatment specimens are requested.
2. For patients who consent to undergo the optional research biopsy, patient’s disease responded to the most recent MATCH study treatment and then progressed (or unable to tolerate further treatment) OR the disease progression (or inability to tolerate further treatment) occurs > 6 months since the last screening biopsy.
NOTE: Performance of a biopsy to collect tumor tissue for research is strongly encouraged but not required. It is acceptable to submit only the optional blood specimens.
NOTE: If a biopsy will be performed solely to collect tumor specimens for research, the patient must be willing and able to undergo a tumor biopsy or bone marrow aspirate (for applicable multiple myeloma), per Section 9, for the collection and submission of tissue for research.