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Fast Facts

Molecular Analysis for Therapy Choice (MATCH)

MATCH Treatment Subprotocol H: Phase II Study of Dabrafenib and Trametinib in Patients with Tumors with BRAF V600E or V600K Mutations (Excluding Melanoma and Thyroid Cancer)

Treatment: Dabrafenib will be administered in combination with trametinib. The dose of dabrafenib is 150 mg orally twice daily, taken approximately 12 hours apart in combination with trametinib 2 mg given orally once daily for a 28 days cycle. **Drugs are provided.**

Eligibility Criteria

1. Patients must fulfill all eligibility criteria outlined in Section 3.1 of MATCH Master Protocol (excluding section 3.1.6) at the time of registration to treatment step (step 1, 3, 5, 7).
2. Patients must have a BRAF V600E or, V600K, V600R or V600D mutation as identified via the MATCH Master Protocol. See Appendix IV for a list of targeted BRAF mutations and the corresponding Levels of Evidence (LOE).
3. Patients with a diagnosis of metastatic melanoma from a cutaneous, acral, mucosal, or unknown primary site are excluded.
4. Patients with a diagnosis of papillary thyroid cancer are excluded.
5. Patients with a diagnosis of colorectal cancer are excluded.
6. Patients must have normal organ and marrow function as defined below:
   - Prothrombin time (PT)/International normalized ratio (INR) and partial thromboplastin time (PTT) ≤1.3x institutional ULN; subjects receiving anticoagulation treatment may be allowed to participate with INR established within the therapeutic range prior to randomization.
7. Patients must have an ECHO or a nuclear study (MUGA or First Pass) within 4 weeks prior to registration to treatment and must not have a left ventricular ejection fraction (LVEF) < the institutional lower limit of normal (LLN). If the LLN is not defined at a site, the LVEF must be > 50% for the patient to be eligible.
8. Patients must have an electrocardiogram (ECG) within 8 weeks prior to treatment assignment and must have NONE of the following cardiac criteria:
   - Clinically important abnormalities in rhythm, conduction or morphology of resting ECG (e.g. complete left bundle branch block, third degree heart block).
   - Treatment-refractory hypertension defined as a blood pressure of systolic >140 mmHg and/or diastolic > 90 mmHg which cannot be controlled by anti-hypertensive therapy.
9. Patients with a history of interstitial lung disease or pneumonitis are excluded.
10. Patients must not have known hypersensitivity to dabrafenib and trametinib or compounds of similar chemical or biologic composition or to dimethyl sulfoxide (DMSO).
11. Patients must not have a history or current evidence/risk of retinal vein occlusion (RVO). An eye exam is required at baseline. See Appendix III for the Trametinib Ophthalmic Exam Form.
12. Patients who previously received MEK inhibitors (including, but not limited to, trametinib, binimetinib, cobimetinib, selumetinib, RO4987655 (CH4987655), GDC-0623 and pimasertib) will be excluded.

13. Patients who previously received BRAF inhibitors (including, but not limited to, dabrafenib (Tafinlar), vemurafenib (PLX-4720) (Zelboraf), RAF265, LGX818 (encorafenib), RO5212054 (PLX3603), ARQ 736, XL281 (BMS-908662), CEP-32496, and the BRAF/MEK dual inhibitor RO5126766) will be excluded.
14. Patients with prior exposure to dabrafenib or trametinib on another treatment subprotocol of the MATCH trial are excluded.
15. Current use of a prohibited medication. Patients receiving any medications or substances that are strong inhibitors or inducers of CYP3A or CYP2C8 are ineligible. Current use of, or intended ongoing treatment with: herbal remedies (e.g., St. John's wort), or strong inhibitors or inducers of P-glycoprotein (Pgp) or breast cancer resistance protein 1 (Bcrp1) should also be excluded. See Appendix II for a list of these prohibited medications.
16. Patients who previously received monoclonal antibody therapy (eg. Ipilimumab and others) must have stopped the prior therapy for 8 or more weeks before starting on trametinib and dabrafenib.
17. Patients with a history of Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection are excluded. An exception will be patients with cleared HBV and HCV infection which will be allowed on study.
18. Patients with history of RAS mutation-positive tumors are not eligible regardless of interval from the current study. ***NOTE:*** Prospective RAS testing is not required. However, if the results of previous RAS testing are known, they must be used in assessing eligibility.

4.1 Therapeutic Parameters for Dabrafenib plus Trametinib Treatment

NOTE: In addition to the study parameters listed in the MATCH Master Protocol at Step 0, the below parameters must also be performed for patients receiving Dabrafenib plus Trametinib treatment.

NOTE: All assessments required prior to registration to treatment should be done ≤ 4 weeks prior to registration to Steps 1, 3, 5, 7, excluding the radiologic evaluation and electrocardiogram (ECG).

Test/Assessment	Prior to Registration to Treatment	Treatment		End of Treatment	Follow Up[F]
		Every Cycle, prior to treatment	Every 2 Cycles		
H&P, Weight, Vital signs[A]	X	X[J]			X
Performance status	X	X[J]			X
CBC w/diff, plts[B]	X	X[J]			X
Serum chemistry[B]	X	X[J]			X
Radiologic evaluation[D]	X		X[D]		X[F]
β-HCG[C]	X				
Toxicity Assessment[G]		X		X	X[F]
Pill Count/Diary[H]		X		X	
ECG[K,L]	X	X[L]			
Echocardiogram or Nuclear Study[L]	X	X[L]			
Dermatologic Exam	X		X[M]	X	X[M]
Eye Exam	X	X[I]			
Tumor biopsy and blood sample for MATCH Master Protocol[E]				X	

The procedures listed below are required only for this study and will be provided to the patient at no charge:

- Echocardiogram (ECHO) or nuclear study (multigated acquisition [MUGA] or similar scan), at week 5, week 13, and every 12 weeks thereafter.
- Eye exam by an ophthalmologist before patients begins the study and as clinically needed thereafter.