Cancer Research Consortium of West Michigan
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Fast Facts

Molecular Analysis for Therapy Choice (MATCH)

MATCH Treatment Subprotocol S1: Phase II Study of Trametinib in Patients with Tumors with NF1 mutations

Treatment: Trametinib 2mg PO once daily until progression or unacceptable toxicity / Cycle = 28 days
Drug is 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 deleterious inactivating mutations of NF-1 by the MATCH NGS assay. See Appendix III for a description of the included NF1 mutations and corresponding Levels of Evidence.
3. 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.
4. Patients with a history of interstitial lung disease or pneumonitis are excluded.
5. 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.
6. Patients must not have known hypersensitivity to trametinib or compounds of similar chemical or biologic composition or to dimethyl sulfoxide (DMSO).
7. Patients must not have a history or current evidence/risk of retinal vein occlusion (RVO). An eye exam is required at baseline. See Appendix II for the Trametinib Ophthalmic Exam Form.
8. Patients who previously received MEK inhibitors (including, but not limited to, trametinib, binimetinib, cobimetinib, selumetinib, RO4987655 (CH4987655), GDC-0623 and pimarsertib) will be excluded.
9. Patients who previously received monoclonal antibody therapy (eg. ipilimumab, nivolumab, pembrolizumab and others) must have stopped the prior therapy for 8 or more weeks before starting on trametinib.
10. Patients with glioblastoma must have histologically or radiographically confirmed recurrent or progressive WHO Grade 4 glioma (glioblastoma). **NOTE:** All baseline and post-baseline disease assessments must be performed using contrast-enhanced cranial MRI or contrast-enhanced CT for subjects who cannot have MRI performed.

Study Parameters

4.1 Therapeutic Parameters for Trametinib Treatment

NOTE: In addition to the study parameters listed in the main screening protocol, the below parameters must also be performed for patients receiving 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	X[F]
Pill Count/Diary[H]		X		X	
ECG[K,L]	X	X[L]			
Echocardiogram or Nuclear Study[L]	X	X[L]			
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 patient begins the study and as clinically needed thereafter.