Cancer Research Consortium of West Michigan
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Fast Facts

Molecular Analysis for Therapy Choice (MATCH)

MATCH Treatment Subprotocol B: Phase II Study of Afatinib in Patients with Tumors with HER2 Activating Mutations

Treatment: afatinib 40mg PO daily at the same time each day continuously for each 28 day cycle until tumor progression or unacceptable toxicities. **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. Patient's tumor must have activating HER2 mutation as determined by the MATCH NGS assay. Additionally, any inframe insertions in exon 20 will be considered an activating mutation. See Appendix III for a full list of the ERBB2 mutations and the corresponding Levels of Evidence (LOE). Patients must have an electrocardiogram (ECG) within 8 weeks prior to treatment assignment and must have no clinically important abnormalities in rhythm, conduction or morphology of resting ECG (e.g. complete left bundle branch block, third degree heart block).
3. Patients must have an electrocardiogram (ECG) within 8 weeks prior to treatment assignment and must have no clinically important abnormalities in rhythm, conduction or morphology of resting ECG (e.g. complete left bundle branch block, third degree heart block).
4. Patients with known left ventricular dysfunction must have ECHO or a nuclear study (MUGA or First Pass) within 4 weeks prior to registration to treatment and must not have left ventricular ejection fraction (LVEF) < institutional lower limit of normal (LLN). If the LLN is not defined at a site, the LVEF must be >50% for the patients to be eligible. **NOTE:** Pre-treatment LVEF determination in patients without known left ventricular dysfunction is NOT otherwise required.
5. Patients must not have known hypersensitivity to afatinib or compounds of similar chemical or biologic composition.
6. Patients must have ≤ Grade 1 diarrhea at baseline.
7. Patients with a history of interstitial lung disease will be excluded.
8. Patients must not have had prior treatment with any of the following TKIs, which have known activity against HER2 kinase:

   - Neratinib
   - Afatinib
   - AC-480 (BMS-599626)
   - AEE 788
   - AST 1306
   - AZD8931
   - Canertinib (CI 1033)
   - CP-724714
   - CUDC-101
   - Dacomitinib
   - Lapatinib
   - Perlitinib
   - TAK285

9. Patients must have ≤ Grade 1 renal function as defined below:

Creatinine ≤ 1.5 x normal institutional limits **OR** Measured Creatinine clearance ≥ 60 mL/min/1.73 m2 for patients with creatinine levels above institutional normal or as calculated by the Cockcroft-Gault Equation. **The above renal eligibility criteria should be strictly followed and will override the MATCH Master Protocol requirements.**

10. Patients with non-small cell lung cancer will be excluded.

Study Parameters

4.1 Therapeutic Parameters for Afatinib Treatment

NOTE: In addition to the study parameters listed in the MATCH Master Protocol, the below parameters must also be performed for patients receiving afatinib 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]
		Cycle 1, day 8 and day 15 [G]	Every Cycle, prior to treatment	Every 2 Cycles		
H&P, Weight, Vital signs[A]	X		X[J]			X
Performance status	X	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]	X		X[I]			
Echocardiogram or Nuclear Study[K]	X[I]		X[I]			X[I]
Tumor biopsy and blood sample for MATCH Master Protocol[E]					X	