Molecular Analysis for Therapy Choice (MATCH)

MATCH Treatment Subprotocol U: VS-6063 (defactinib) in Patients with Tumors with NF2 Loss

Fast Facts

Treatment: VS-6063 (defactinib) 400 mg BID until progression or unacceptable toxicity. ***Drug is provided.***

Eligibility Criteria

1. Patients must fulfill all eligibility criteria outlined in Section 3.1 of MATCH screening protocol.
2. Patients must have a tumor that harbors an inactivating mutation in NF2. See Appendix III of this sub-protocol for a list of the NF2 mutations and corresponding Levels of Evidence.
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 treatment assignment 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 patient to be eligible.

NOTE: Pre-treatment LVEF determination in patients without known left ventricular dysfuction is NOT otherwise required.

5. Patients must not have known hypersensitivity to VS-6063 (defactinib) or compounds of similar chemical or biologic composition.
6. Patients must not have a history of upper GI bleeding, ulceration, or perforation within 12 months prior to the first dose of study drug.
7. Patients must not have known history of Gilbert's Syndrome.
8. Patient must not have a known history of stroke or cerebrovascular accident within 6 months prior to the first dose of VS-6063 (defactinib).
9. Patients with history of hypertension should be adequately controlled (BP < 140/90) with appropriate anti-hypertensive therapy or diet.
10. Patients must not have prior treatment with a FAK inhibitor (eg. VS-6063 (defactinib) or GSK2256098) and must not be participating or have participated in the COMMAND trial of maintenance therapy of VS-6063 (defactinib) vs. placebo, for mesothelioma.
11. Patients must not be using drugs or foods that are known potent CYP3A4 or CYP2C9 inhibitors or inducers (See Appendix II of this subprotocol).

Actionable Mutations for Sub-Protocol EAY131-U

1. NF2 is a tumor suppressor gene. Inactivating deleterious mutations could occur anywhere in the coding regions. Instead of listing all possible deleterious mutations, we have implemented a function in MATCHBOX that can identify any point mutations creating stop codons that will lead to premature truncations or any insertions/deletions causing frameshifts, which are predicted to result in a non-functional or absent protein. Variants, including missense mutations, were not included for eligibility if there was a lack of adequate evidence that such variants resulted in loss of function in NF2 gene.

Pre-Study Parameters:

1. History/Physical, Weight, Vitals, Performance Status

2. CBC/Diff/Plts, CMP
3. Pregnancy Test
4. ECHO/Nuclear Study
5. Radiologic Evaluation
6. Concomitant Medication