Cancer Research Consortium of West Michigan
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Fast Facts

Molecular Analysis for Therapy Choice (MATCH)

MATCH Treatment Subprotocol M: Phase II Study of MLN0128 (TAK-228) in Patients with Tumors with TSC1 or TSC2 Mutations

Schema

Cycle = 28 days
Accrual Goal: 35

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 TSC1 or TSC2 mutation as determined by the MATCH screening assessment. See Appendix II for a list of the TSC1 or TSC2 mutations and corresponding Levels of Evidence.**
3. **Patients must have an electrocardiogram (ECG) within 8 weeks prior to treatment assignment and must NOT have any 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, QTc interval > 480 milliseconds).**
   - **Uncontrolled hypertension (i.e. systolic blood pressure > 180 mm Hg, diastolic blood pressure > 95 mm Hg) are not eligible. Use of anti-hypertensive agents to control hypertension before Cycle 1 Day 1 is allowed.**
   - **Pulmonary hypertension**

   Date of ECG: _____
4. **Patients must not have known hypersensitivity to MLN0128 (TAK-228) or compounds of similar chemical or biologic composition.**

5. **Patients must not have known hepatitis B surface antigen-positive, or known or suspected active hepatitis C infection, but may have had previously treated and successfully eradicated HCV.**
6. **Patients must have none of the following within six months of receiving the first dose of MLN0128 (TAK-228): ischemic, myocardial or cerebrovascular event, class III or IV heart failure, placement of pacemaker, or pulmonary embolism.**
7. **Patients must have no manifestations of malabsorption due to prior gastrointestinal (GI) surgery, GI disease, or for an unknown reason that may alter the absorption of MLN0128 (TAK-228).**
8. **Patients who have a history of brain metastasis are eligible for the study provided that all the following criteria are met:**
   - **Brain metastases which have been treated**
   - **No evidence of disease progression for ≥ 1 months before the first dose of study drug**
   - **No hemorrhage after treatment**
   - **Off-treatment with dexamethasone for 4 weeks before administration of the first dose of MLN0128 (TAK-228)**
   - **No ongoing requirement for dexamethasone or anti-epileptic drugs**
9. **Patients must meet the following criteria for concomitant medications prior to starting MLN0128 (TAK-228):**
   - **Discontinuation of strong inhibitors and/or strong inducers of cytochrome P450 (CYP) 3A4, CYP2C19 or CYP2C19 for at least 1 week preceding the first dose of study drug.**
   - **Discontinuation of daily or chronic proton pump inhibitor (PPI) use. PPI use must be discontinued for at least 7 days before receiving the first dose of study drug.**
10. **Patients must not have known treatment with systemic corticosteroid within one week prior to the first administration of study drug.**
11. **Patients must not have uncontrolled diabetes mellitus. Controlled diabetes is defined as: Glycosylated hemoglobin (HbA1c) < 7.0%, or fasting serum glucose (≤ 130 mg/dL).**
12. **Patients must not have fasting triglycerides ≥ 300 mg/dL.**
13. **Patients must not have had prior treatment with other known TORC1/2 inhibitors, including:**
    - **AZD8055, XL765, BEZ235, GSK2126458, XL388, DS3078(a), PF-05212384, SF1126, Palomid-529, GDC0980 (apitolisib), LY30223414, BKM120, OSI0127, MLN0128 (TAK-228), AZD2014**
14. **Patients must not have other clinically significant co-morbidities that, in the opinion of the investigator, would limit compliance with study requirements.**
15. **Fertility and developmental studies with MLN0128 (TAK-228) have not been conducted. On the basis of potential hazard of other mTOR inhibitors (i.e., rapamycin and other rapalogs) on the developing fetus, women of childbearing age should avoid becoming pregnant while taking MLN0128 (TAK-228). For this reason, women of child-bearing potential and men must agree to practice 1 highly effective method of contraception and 1 additional effective (barrier) method of contraception, at the same time, from the time of signing the informed consent through 120 days after the last dose of study drug, or agree to completely abstain from heterosexual intercourse. Men must agree not to donate sperm during the course of this study or within 120 days after receiving their last dose of study drug.**
16. **Patients who are known to be HIV-positive are not eligible for this study.**

Study Parameters

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
Laboratory Studies[L]	X	X[J,L]			
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]	X	X[I]			
Tumor biopsy and blood sample for MATCH Master Protocol[E]			X	X	