Cancer Research Consortium of West Michigan
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Fast Facts

Molecular Analysis for Therapy Choice (MATCH)
MATCH Treatment Subprotocol N: Phase II Study of PI3K Beta Specific Inhibitor, GSK2636771, in Patients with Tumors with PTEN Mutation or Deletion, with PTEN Expression on IHC

Treatment: GSK2636771 400mg PO daily until progression / cycle =28 days

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 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 not have known hypersensitivity to GSK2636771 or compounds of similar chemical or biologic composition.
4. Patients must have PTEN gene mutation/deletion.
   a. A PTEN mutation will be defined as a mutation reported at greater than 25% variant allele frequency after adjustment for viable tumor cell content. See Appendix II (Section A) for a list of the PTEN inclusion mutations and corresponding Levels of Evidence.
   This threshold was selected based on a review of sequencing data from 1000 patients tested at MD Anderson Cancer Center, which demonstrated that about 70% of patients with PTEN mutations have variant allele frequency higher than 25% and about 50% of patients with PTEN mutations have variant allele frequency higher than 25% in the absence of simultaneous alterations in the PI3K/mTOR and MAPK pathways.
   b. There must be evidence of PTEN expression by IHC (any amount of staining will be considered positive for expression).
      - Patients with complete loss of PTEN by IHC, regardless of PTEN mutations/deletion status, will be enrolled into MATCH subprotocol EAY131-P, not this subprotocol (EAY131-N).
5. Patients must not have tumors harboring co-existing aberrations activating the PI3K/MTOR and MAPK pathways, such as PIK3CA, PIK3R1, BRAF, KRAS and AKT1, TSC1/2, mTOR, RHEB, NF2, NRAS, HRAS, NF1 (See Appendix II, Section B, for exclusion mutations and corresponding Levels of Evidence).
6. Patients must not have received prior treatment with agents targeting the PI3K beta, AKT, or mTOR pathways:
   a. This includes (but is not limited to):
      - mTOR inhibitors: temsirolimus, everolimus, ridaforolimus, sirolimus, salirasib, CC-223, INK128, DS-3078, CC-115, AZD-2014
      - dual PI3K/mTOR inhibitors: BEZ235, XL-765, GDC 0980, PF-04691502, GSK 2126458, Quinacrine, PKI-587, P-P7170, LY3023414, GDC 0084, DS 7423, CBLC-137
      - pan-PI3K inhibitors: BKM-120 (buparlisib), PX-866, XL-147, GDC-0941 (pictilisib), BAY-806946, ZSTK-474, WX 037, SRX5000, SRX2523, AMG511, PQR308, BAY 94-9343
      - PI3K inhibitors with β isoform activity: prior GSK2636771 is not allowed, nor is GS-9820, PQR3XX, KAR4139

b. The following treatments are allowed:
   - BYL719 (PI3Kα inhibitor)
   - GDC-0032 (PI3Kα inhibitor)
   - INK1117 (PI3Kα inhibitor)
   - Idelalisib (PI3Kδ inhibitor)
   - IPI-125 (PI3K γδ inhibitor)
   - TGR1202 (PI3Kδ inhibitor)
   - SRX2558 (PI3Kδ inhibitor)
   - RP6530 (PI3K γδ inhibitor)
   - PWT143 (PI3Kδ inhibitor)
   - IPI443 (PI3K γδ inhibitor)
   - GNE293 (PI3Kδ inhibitor)

7. Patients with a history of interstitial lung disease or pneumonitis are excluded.
8. Patients must have hemoglobin ≥ 9 g/dL.
9. Patients must have a serum creatinine that ≤ 1.5 x ULN or have a 24-hour creatinine clearance of ≥ 50 mL/min.
10. Patients must not have any congenital platelet function defects and cannot be on any of the following anti-platelet drugs: clopidogrel, ticlopidine, prasugrel, that act at platelet purinergic receptors.
    a. Any need for starting anti-platelet therapy in a patient enrolled to this arm will have to be evaluated by the subprotocol chair.

Study Parameters

4.1 Therapeutic Parameters for GSK2636771 Treatment

NOTE: In addition to the study parameters listed in the MATCH Master Protocol, the below parameters must also be performed for patients receiving GSK2636771 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]	X	X[I]			
Urinalysis	X[I]	X[I]			
Tumor biopsy and blood sample submission for MATCH Master Protocol[E]				X	