Cancer Research Consortium of West Michigan
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Fast Facts

Molecular Analysis for Therapy Choice (MATCH)

MATCH Treatment Subprotocol Z1K: Ipatasertib in Patients with Tumors with AKT Mutations

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 AKT mutation as determined via the MATCH Master Protocol and described in Appendix II. See Appendix II for information on the AKT mutation and corresponding Levels of
   Evidence.
3. Patients with hormone receptor positive, defined as estrogen receptor and/or progesterone receptor > 1% by immunohistochemistry19, AND HER2 negative unresectable breast cancer, with no overexpression
   by IHC or amplification by in-situ hybridization20, are allowed to continue fulvestrant or an aromatase inhibitor (anastrazole, letrozole, exemestane) with Ipatasertib if patient just progressed on this antiestrogen therapy. GnRH agonists (such as leuprolide or goserelin) are allowed. For instance, if the last treatment was letrozole plus goserelin, the patient is allowed to continue the letrozole plus goserelin with Ipatasertib.
   NOTE: SERMs, such as tamoxifen or toremifene, are not allowed, given concerns about CYPD26 and CYP3A4 metabolism, respectively.
4. Patients with castration-resistant prostate cancer should maintain castrate levels of testosterone (i.e., with GnRH agonists or through surgical castration). Patients are allowed to continue abiraterone acetate / prednisone with Ipatasertib if the patient just progressed on abirterone acetate / prednisone.
5. Patients must not have known hypersensitivity to Ipatasertib or compounds of similar chemical or biologic composition.
6. Patients with known KRAS, NRAS, HRAS, or BRAF mutations are not eligible for this protocol, as these mutations may lead to limited response due to resistance.
7. Patients with diabetes or risk for hyperglycemia are eligible. Patients with diabetes mellitus should be on a stable dose of oral hypoglycemic agents for ≥ 4 weeks and appropriate diet. Patients with diabetes mellitus may enter the study unless any of the following exclusion criteria are fulfilled:
   - Baseline fasting glucose value of >8.9 mmol/L or 160 mg/dL
     (fasting is defined as no calorific intake for at least 8 hours)
   - Patients not on a stable dose of oral hypoglycemic medication for
     ≥ 4 weeks and appropriate diet
   - Insulin required for routine diabetic management and control
   - More than two oral hypoglycemic medications required for routine

diabetic management and control
• Hemoglobin A1C ≥ 7.5%

8. Prior PI3K and mTOR inhibitors are allowed, including in the metastatic setting. Prior AKT inhibitors are excluded (See Appendix IV).
9. Patients with a history of inflammatory bowel diseases (Crohn's disease and ulcerative colitis) or active diverticulitis are not eligible.
10. Patients may not have received strong inhibitors or potent inducers or substrates of CYP3A4/5 within 2 weeks before the first dose of study treatment (3 weeks for St John's Wort). See Section 5.1.8 and Appendix III.
11. In addition to the patient contraception requirements outlined in EAY131 MATCH Master Protocol, male patients must also refrain from donating sperm for the duration of study participation, and for 4 months after completion of study.

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