Cancer Research Consortium of West Michigan
P: 616.391.1230 | 800.336.6299 | www.crcwm.org

FAST FACTS

MATCH Treatment Subprotocol Y: AZD5363 in Patients with Tumors with AKT Mutations

AZD5363 480mg PO twice a day 4 days on/3 days off on a weekly basis for each 28 day cycle until progression or toxicity

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 by the MATCH screening assessment. See Appendix II for a list of 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 AZD5363 if patient just progressed on this anti-estrogen 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 AZD5363. NOTE: SERMs, such as tamoxifen or toremifene, are not allowed, given concerns about CYPD26 and CYP3A4 metabolism, respectively.
4. 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).
5. Patients must not have known hypersensitivity to AZD5363 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 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)
   - Insulin required for routine diabetic management and control
   - More than two oral hypoglycemic medications required for routine diabetic management and control
8. Patients may not have received treatment with another inhibitor of PI3K, AKT or mTOR in the neoadjuvant, adjuvant or metastatic setting with the exception of FDA approved rapalogs. Patients with metastatic cancer, who received PI3K/AKT/mTOR inhibitors on short preoperative window trials (treatment for 4 weeks or less) will be eligible if the treatment was over 6 months prior to registration (See Appendix IV).
9. Patients may not have received strong inhibitors or potent inducers or substrates of CYP3A4 or substrates of CYP2D6 within 2 weeks before the first dose of study treatment (3 weeks for St John's Wort). See Appendix III.