PICK THE BEST PATH: OPTIMIZING PIK3CA MUTATION-TARGETED HR+/HER2-PIK3CA-MUTATED THERAPY AND HYPERGLYCEMIA MANAGEMENT

Dear Colleague:

Thank you for your recent participation in the CE activity “Pick the Best Path: Optimizing PIK3CA Mutation-Targeted HR+/HER2- PIK3CA-Mutated Therapy and Hyperglycemia Management” with Drs. Kaklamani and Mortimer and developed by the Annenberg Center for Health Sciences. As you continue to advance the care you provide to these patients, here are the key concepts for you to consider:

- PIK3CA testing is currently recommended for patients with locally recurrent or metastatic HR+/HER2- breast cancer who would be candidates for a PI3K inhibitor.
- Prior to the availability of inavolisib + palbociclib + fulvestrant, PIK3CA mutation testing was typically pursued while a patient with HR-positive/HER2-negative metastatic breast cancer was receiving first-line treatment with endocrine therapy plus a CDK4/6 inhibitor to assess for eligibility for subsequent-line use with alpelisib or capivasertib. Early PIK3CA testing at the time of metastatic recurrence will be necessary in order to be able to consider PI3K inhibitor-based treatment in the first-line treatment setting.
- Current guidelines allow for either next generation sequencing of tumor tissue or ctDNA in plasma to determine eligibility for PI3K-targeted therapy. If ctDNA is negative, repeat testing of tumor tissue is recommended.
- In the SOLAR-1 trial, patients were required to have at least 1 of 11 prespecified PIK3CA mutations. It’s unknown whether other mutations are associated with response to alpelisib. In the INAVO120 and CAPItello-291 trial, there were no prespecified PIK3CA mutations, so patients with any type of PIK3CA-activating mutation were considered for treatment.
- Inavolisib + palbociclib + fulvestrant can be considered in the first-line setting for patients with high-risk HR+/HER2-/PIK3CA-mutated locally advanced or metastatic breast cancer who recur on or after completing adjuvant endocrine therapy. Alpelisib + fulvestrant and capivasertib + fulvestrant are usually reserved for the subsequent-line setting in patients with advanced or metastatic breast cancer who progressed on or after an endocrine-based regimen and have PIK3CA-activing mutations (alpelisib) or PIK3CA or AKT1 activating mutations or PTEN alterations (capivasertib).
- Prediabetes and diabetes are not contraindications to treatment with PI3K or AKT inhibitors. However, close glucose monitoring, initiation or intensification of antihyperglycemics, and the support of an interprofessional, multidisciplinary team, including endocrinology, will better ensure treatment success.
- PI3K and AKT inhibitors differ in terms of rates of hyperglycemia, rash, diarrhea, fatigue, and stomatitis. Treatment selection may also depend on patient comorbidities and preference.

We invite you to participate in other accredited activities we offer (www.Annenberg.net). Thank you.

Regards,
The Annenberg Center Team