THE PATHCARE NEWS

STAND ALONE MOLECULAR TESTING FOR PIK3CA/AKT1

Testing for PIK3CA and AKT1 mutations in tumors is important for several reasons, especially in the context of personalized medicine and targeted cancer therapy.

PIK3CA and AKT1 are genes involved in the PI3K/AKT/mTOR signaling pathway, which plays a crucial role in cell growth, proliferation, and survival. Mutations in these genes can lead to abnormal activation of the pathway, contributing to cancer development and progression. Identifying mutations in PIK3CA and AKT1 can help predict whether a patient is likely to respond to targeted therapies that inhibit this pathway.

BREAST CANCER:

ER+/Her2- Breast Cancer:

- Around 75% of patients with breast cancer have tumours expressing oestrogen receptor (ER) and are offered adjuvant endocrine therapy for 5–10 years, which reduces the risk of recurrence by almost 50% and the mortality by up to 30%. However, around 30% of these patients later develop endocrine resistance with progression or relapse in their disease, predominantly with sustained ER expression. Differential pathway signaling of ER and several downstream systems have been investigated, and one of the most prominent pathways is that of PI3K/AKT/mTOR.

- PIK3CA mutations are some of the most common genetic variants in the cancer genome, present in up to **40% of ER-positive and HER2-negative (ER + /HER2-) breast tumours.** PIK3CA mutations are also present in approximately **30% of early-stage HER2+ tumours.**

- Mutational activity in the PIK3CA gene, coding for the catalytic subunit p110α of PI3K, causes the constitutive activation of PI3K and is associated with **resistance to certain standard therapies in breast cancer, such as endocrine therapy.**

- Identifying PIK3CA mutations can help guide treatment decisions, as specific inhibitors targeting the PI3K/AKT/mTOR pathway (FDA-approved PI3K inhibitor **alpelisib** and/or a pan-AKT kinase inhibitor capivasertib in combination with the selective oestrogen receptor degrader (SERD) fulvestrant) have been shown to be effective in patients with these mutations for the treatment of ER+/HER2- metastatic breast cancer.

HER2+ Breast Cancer:

- Somatic activating mutations in PIK3CA have also been shown to drive therapeutic **resistance to multiple HER2- targeted agents.** Results from early phase I trials indicate that **PI3K inhibitors will likely also become essential in the treatment of HER2+ disease**, and underscore the importance of this biomarker in identifying patients with HER2+ disease who are most likely to benefit from addition of PI3K inhibitors.

Prognostic Significance:

- The presence of PIK3CA mutations has appeared to be both an **individual negative prognostic factor and a negative predictive factor to chemotherapy treatment in patients with metastatic ER + /HER2- breast cancer.**

VASCULAR NEOPLASMS & MALFORMATIONS:

- PIK3CA mutations are commonly found in vascular tumors, particularly in cases of capillary and venous malformations and some types of haemangiomas. Studies support PI3Kα inhibition as a promising therapeutic strategy in patients with PIK3CA or TEK-mutated vascular malformations when local treatment methods have had only partial or temporary effect or when the lesion is inoperable because of its location or size. Objective responses have been noted with resultant improvement in the quality of life for these patients.

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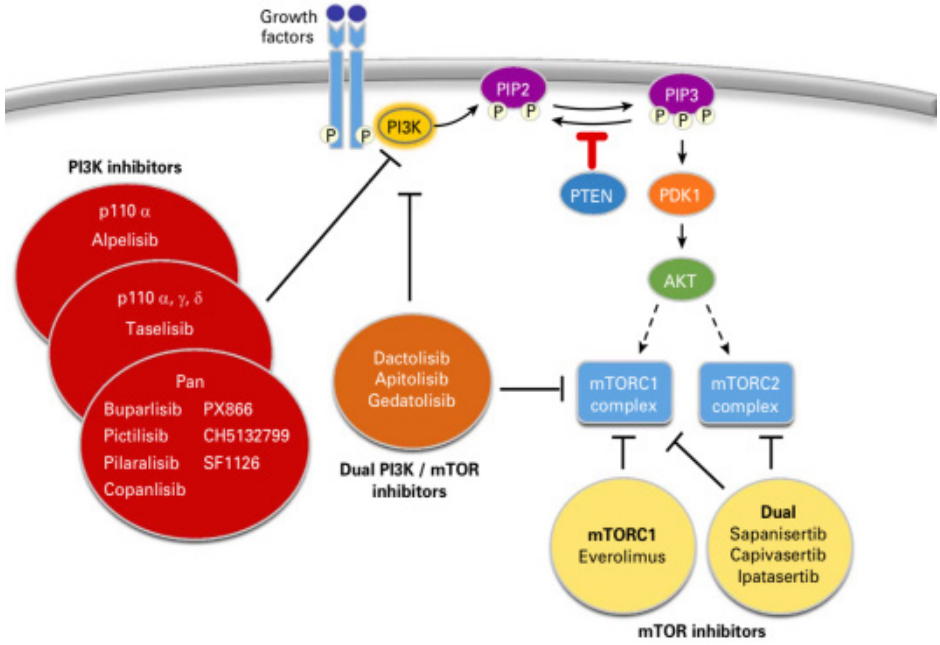
- Several questions still need to be answered, as this is an off-label, agnostic, and experimental treatment. Optimal treatment duration, dosing, and scheduling are still to be investigated further.

- Identifying these mutations can help determine if targeted therapies that inhibit the PI3K/AKT/mTOR pathway could be effective in treating these tumours/malformations.



TEST INFORMATION

The Idylla™ PIK3CA-AKT1 Mutation Assay, performed on the Biocartis Idylla™ System, is a fully automated real-time polymerase chain reaction (PCR) Assay for the qualitative detection of 13 mutations in the PIK3CA gene (N345K, C420R, E542K, E545K, E545G, E545D (c.1635G>T), E545A, Q546K, Q546R, Q546E, H1047R, H1047L, H1047Y) and one mutation in the AKT1 gene (E17K) in FFPE human tissue sections.

HOW TO REQUEST:

- Complete the PathCare molecular oncology request form and email to your local histopathologist or histopathology laboratory.
- Test mnemonic: PMPIK3CA
- Result availability: within 2 working days of specimen receipt in the molecular laboratory
- Cost - Request a quote for your patient by emailing the PathCare Molecular Oncology Helpdesk (mor@pathcare.co.za)
  For more information, email **molecularoncology@pathcare.net.**

Reference:

Schagerholm C. et al. PIK3CA mutations in endocrine - resistant breast cancer. Scientific Reports (2024) 14:12542

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