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REVIEW

Impact of the PIK3CA mutation on breast cancer

Impacto de la mutación PIK3CA en el cáncer de mama

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ABSTRACT

Breast cancer was a health priority both globally and in Argentina, where it was the leading cause of death from tumours in women. Its molecular and genetic understanding has led to advances in diagnosis, prognosis and treatment. The luminal subtype, characterised by hormone receptors, and the PIK3CA gene mutation, involved in the PI3K/Akt/mTOR pathway, were highlighted as being associated with greater tumour aggressiveness and resistance to therapies. In Argentina, studies have shown a high prevalence of this mutation, prompting the use of targeted therapies such as Alpelisib. This personalised approach has improved the stratification and clinical management of the disease.

Keywords: PIK3CA; Breast Cancer; Targeted Therapy; Luminal Subtype; PI3K/Akt/Mtor Pathway.

RESUMEN

El cáncer de mama representó una prioridad sanitaria tanto a nivel mundial como en Argentina, donde fue la principal causa de muerte por tumores en mujeres. Su comprensión molecular y genética permitió avances en diagnóstico, pronóstico y tratamiento. Se destacó el subtipo luminal, caracterizado por receptores hormonales, y la mutación del gen PIK3CA, implicada en la vía PI3K/Akt/mTOR, la cual se asoció con mayor agresividad tumoral y resistencia a terapias. En Argentina, estudios evidenciaron una alta prevalencia de esta mutación, impulsando el uso de terapias dirigidas como Alpelisib. Este enfoque personalizado mejoró la estratificación y abordaje clínico de la enfermedad.

Palabras clave: PIK3CA; Cáncer de Mama; Terapia Dirigida; Subtipo Luminal; Vía PI3K/Akt/Mtor.

INTRODUCTION

Breast cancer is a priority challenge for global public health and, particularly, for the Argentine healthcare system, where it is the leading cause of death from tumors in women. Understanding its molecular and genetic mechanisms has led to significant advances in its diagnosis, treatment, and prognosis. Within this approach, the characterization of molecular subtypes, such as luminal breast cancer, and the identification of relevant mutations, such as the PIK3CA gene mutation, have revolutionized the clinical approach to this disease. This theoretical framework explores the relevance of this mutation in tumor progression, its impact on therapeutic response, and the role of targeted therapies as a key strategy in precision oncology.

DEVELOPMENT

Breast cancer is one of the leading causes of death in women worldwide, ranking first in Argentina in terms

of deaths from tumors, with an increasing incidence in recent decades.[1,2] This disease originates from the abnormal and uncontrolled proliferation of epithelial cells in the mammary gland, which acquire a malignant phenotype with invasive and metastatic capacity. This transformation involves genetic and epigenetic alterations that affect key pathways in cell regulation.[1]

In clinical and pathological terms, the current classification of breast cancer is decisive for both prognosis and therapeutic choice. According to Alcaide Lucena et al.[3], the most common subtype is luminal, characterized by the expression of estrogen and/or progesterone hormone receptors and HER2 negativity. This classification is complemented by clinical staging based on anatomical and functional parameters,[4,5] allowing individualized treatment strategies to be defined.

One of the most relevant findings in the molecular biology of breast cancer has been the identification of specific mutations, such as that of the PIK3CA gene, which encodes a subunit of phosphatidylinositol 3-kinase (PI3K). This enzyme participates in the PI3K/Akt/mTOR pathway, which is involved in cellular processes such as proliferation, survival, autophagy, and angiogenesis.[6] Aberrant activation of this pathway has been associated with resistance to hormone therapies, accelerated tumor progression, and shorter survival.[7,8]

In the Argentine context, Mandó et al.[9] analyzed the prevalence of PIK3CA mutations in breast cancer patients, showing a significant association between the presence of the mutation and a more aggressive clinical-pathological profile. This finding raises a new paradigm in the therapeutic approach, considering that targeted treatments such as specific PI3K inhibitors, including Alpelisib (Piqray), have shown benefits in patients with this genetic alteration.[10]

On the other hand, disease progression is defined as the appearance of new lesions or a significant increase in existing ones, which allows the efficacy of the therapeutic lines applied to be assessed.[11] In this sense, the mutational status of PIK3CA could be considered a negative prognostic marker, as it is associated with faster progression and lower survival, as recent clinical studies have shown.[6,7,12,13]

In summary, the molecular approach to breast cancer has led to progress toward a more personalized approach, where the identification of biomarkers such as PIK3CA is crucial. This allows not only for better stratification of patients based on their prognosis but also for the targeting of therapies that can improve the quality of life and the clinical course of the disease.[1,6,9]

CONCLUSIONS

The incorporation of molecular knowledge into the study of breast cancer has led to a better understanding of its biological heterogeneity, highlighting the importance of biomarkers such as the PIK3CA gene mutation in determining prognosis and therapeutic choice. Its presence is associated with a more aggressive profile and lower survival, underscoring the need for its systematic detection in advanced stages of the disease. In this context, treatments aimed at inhibiting the PI3K/Akt/mTOR pathway are emerging as a promising therapeutic alternative, contributing to the development of a more personalized, effective, and equitable approach to breast cancer management in Argentina and worldwide.

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CONFLICT OF INTEREST

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