

# Alpelisib-Associated Hyperglycemia in Metastatic Breast Cancer Treatment

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## INTRODUCTION

Metastatic Breast Cancer (MBC) presents a complex challenge to oncologists and patients alike, requiring multidisciplinary approaches and tailored treatment strategies. Among the latest advancements in MBC therapy is the introduction of targeted therapies, such as alpelisib, a selective inhibitor of the PI3K pathway. While alpelisib has shown promise in improving outcomes for certain patients, it also carries the risk of hyperglycemia, a potentially serious adverse effect. In this article, we explore the mechanism of alpelisib-associated hyperglycemia, its clinical implications and strategies for managing this complication to ensure optimal care for patients with MBC.

## DESCRIPTION

### Understanding alpelisib and the PI3K pathway

Alpelisib is a small molecule inhibitor that specifically targets the alpha isoform of the Phosphatidylinositol 3-Kinase (PI3K) enzyme, a key regulator of cell growth, survival and metabolism. Dysregulation of the PI3K pathway is common in many cancers, including breast cancer and contributes to tumor growth and progression. By selectively inhibiting the PI3K pathway, alpelisib disrupts signaling cascades that promote cancer cell proliferation, making it an attractive therapeutic option for patients with PIK3CA-mutated MBC.

### Hyperglycemia

A known adverse effect despite its therapeutic benefits, alpelisib is associated with a notable adverse effect profile, with hyperglycemia being one of the most common and clinically significant side effects. Hyperglycemia occurs as a result of alpelisib's inhibition of the PI3K pathway, which plays a crucial role in insulin signaling and glucose metabolism. By disrupting this pathway, alpelisib can lead to insulin resistance, impaired glucose uptake and ultimately elevated blood glucose levels.

### Clinical implications and management strategies

Hyperglycemia associated with alpelisib treatment can manifest as new-onset diabetes or exacerbation of pre-existing diabetes in susceptible individuals. It may present with symptoms such as

increased thirst, frequent urination, fatigue and blurred vision. Given the potential for serious complications, including diabetic ketoacidosis, it is essential for healthcare providers to monitor patients receiving alpelisib closely for signs of hyperglycemia and intervene promptly.

Management strategies for alpelisib-associated hyperglycemia typically involve a combination of lifestyle modifications, pharmacological interventions and close monitoring. Patients may be advised to adopt dietary modifications, increase physical activity and undergo regular blood glucose monitoring to optimize glycemic control. In some cases, initiation or adjustment of antidiabetic medications, such as insulin or oral hypoglycemic agents, may be necessary to manage hyperglycemia effectively while minimizing treatment interruptions or dose reductions of alpelisib.

Moreover, patient education and proactive communication between healthcare providers and patients are crucial for early detection and management of hyperglycemia. Patients should be informed about the potential risk of hyperglycemia associated with alpelisib treatment and instructed to report any concerning symptoms promptly. Healthcare providers should also remain vigilant in monitoring glycemic parameters throughout the course of treatment and adjust management strategies as needed to optimize patient outcomes.

## CONCLUSION

Alpelisib represents a valuable addition to the armamentarium of targeted therapies for metastatic breast cancer, offering new hope for patients with PIK3CA-mutated disease. However, the risk of hyperglycemia associated with alpelisib underscores the importance of vigilant monitoring and proactive management to ensure patient safety and treatment efficacy. By understanding the mechanisms underlying alpelisib-associated hyperglycemia and implementing comprehensive management strategies, healthcare providers can navigate this challenge effectively and optimize outcomes for patients with metastatic breast cancer undergoing treatment with alpelisib.

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