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Alpelisib in the Spotlight: A Review of Its Efficacy and Safety in PIK3CA-Mutated, Hormone Receptor-Positive Advanced Breast Cancer

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Abstract:

Alpelisib, a selective inhibitor of the phosphatidylinositol 3-kinase (PI3K) alpha isoform, has emerged as a promising therapeutic option for patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer harboring PIK3CA mutations. This review provides a comprehensive overview of the clinical efficacy and safety profile of alpelisib in the treatment of PIK3CA-mutated, HR+ advanced breast cancer. We summarize key findings from pivotal clinical trials, including the SOLAR-1 trial, which demonstrated the efficacy of alpelisib in combination with fulvestrant in improving progression-free survival compared to fulvestrant alone in patients with PIK3CA-mutated, HR+ advanced breast cancer. Additionally, we discuss considerations for patient selection, treatment sequencing, and management of adverse events associated with alpelisib therapy. By synthesizing evidence from clinical trials and real-world experience, this review aims to provide oncologists, clinicians, and healthcare providers with practical insights into the use of alpelisib as a targeted therapy for PIK3CA-mutated, HR+ advanced breast cancer.

Keywords: Alpelisib, PIK3CA mutation, Hormone receptor-positive breast cancer, Advanced breast cancer, Targeted therapy, Clinical efficacy, Safety profile.

Introduction:

Advanced breast cancer remains a significant clinical challenge, particularly among patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) disease who develop resistance to endocrine therapy. Dysregulation of the phosphatidylinositol 3-kinase (PI3K) pathway, commonly driven by mutations in the PIK3CA gene, contributes to tumor growth, survival, and resistance to endocrine therapy in HR+ breast cancer. Alpelisib, a potent and selective inhibitor of the PI3K alpha isoform, represents a novel therapeutic strategy for targeting PIK3CA-mutated breast cancer. This review provides a comprehensive overview of the clinical efficacy and safety profile of alpelisib in the management of PIK3CA-mutated, HR+ advanced breast cancer.

Volume 2, Issue 01, 2023
Page 17-20
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Clinical Efficacy:

The efficacy of alpelisib in PIK3CA-mutated, HR+ advanced breast cancer has been demonstrated in the phase III SOLAR-1 trial, which evaluated alpelisib in combination with fulvestrant compared to fulvestrant alone in postmenopausal women and men with HR+, HER2- advanced breast cancer who had received prior endocrine therapy. The study showed a significant improvement in progression-free survival (PFS) with the addition of alpelisib to fulvestrant, leading to its approval by regulatory agencies for this indication. Subgroup analyses revealed consistent PFS benefits across various patient subgroups, including those with visceral metastases and those with PIK3CA mutations detected in circulating tumor DNA.

Safety Profile:

Alpelisib is associated with a distinct adverse event profile, most notably hyperglycemia, rash, diarrhea, and stomatitis, which are consistent with the mechanism of action of PI3K inhibition. Effective management of these adverse events through patient education, proactive monitoring, dose adjustments, and supportive care measures is essential for optimizing treatment tolerability and adherence. Additionally, rare but potentially severe adverse events, such as pneumonitis, hepatotoxicity, and severe cutaneous reactions, necessitate vigilant monitoring and prompt intervention to mitigate risks and ensure patient safety.

Considerations for Clinical Practice:

The integration of alpelisib into clinical practice requires careful consideration of patient-specific factors, including tumor characteristics, prior treatment history, comorbidities, and treatment goals. Molecular testing for PIK3CA mutations should be performed to identify eligible patients who may benefit from alpelisib therapy. Treatment decisions should be individualized based on the balance of clinical benefits, potential risks, patient preferences, and available treatment alternatives. Furthermore, ongoing research efforts are focused on optimizing treatment sequencing, identifying biomarkers of response and resistance, and exploring combination strategies to maximize the therapeutic efficacy of alpelisib in HR+ advanced breast cancer.

Conclusion:

Alpelisib represents a valuable addition to the treatment armamentarium for patients with PIK3CA-mutated, HR+ advanced breast cancer, offering a targeted therapeutic option that addresses an unmet medical need in this patient population. The clinical efficacy and safety profile of alpelisib, as demonstrated in pivotal clinical trials, support its use in combination with fulvestrant for the treatment of postmenopausal women and men with PIK3CA-mutated, HR+ advanced breast cancer following progression on endocrine therapy. Continued research efforts are warranted to optimize treatment strategies, elucidate mechanisms of resistance, and improve patient outcomes in this

Volume 2, Issue 01, 2023
Page 17-20
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challenging clinical setting. By integrating alpelisib into personalized treatment algorithms and multidisciplinary care approaches, clinicians can strive to improve clinical outcomes and enhance the quality of life for patients with advanced breast cancer.

References

1. André, F., Ciruelos, E., Rubovszky, G., Campone, M., Loibl, S., Rugo, H. S., ... & Diéras, V. (2019). Alpelisib for PIK3CA-mutated, hormone receptor-positive advanced breast cancer. New England Journal of Medicine, 380(20), 1929-1940.

2. Di Leo, A., Johnston, S., Lee, K. S., Ciruelos, E., Lønning, P. E., Janni, W., ... & Pivot, X. (2020). Buparlisib plus fulvestrant in postmenopausal women with hormone-receptor-positive, HER2-negative, advanced breast cancer progressing on or after mTOR inhibition (BELLE-3): a randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet Oncology, 21(3), 387-397.

3. Baselga, J., Im, S. A., Iwata, H., Cortés, J., De Laurentiis, M., Jiang, Z., ... & Dent, S. (2017). Buparlisib plus fulvestrant versus placebo plus fulvestrant in postmenopausal, hormone receptor-positive, HER2-negative, advanced breast cancer (BELLE-2): a randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet Oncology, 18(7), 904-916.

4. Hortobagyi, G. N., Stemmer, S. M., Burris III, H. A., Yap, Y. S., Sonke, G. S., Paluch-Shimon, S., ... & Campone, M. (2018). Updated results from MONALEESA-2, a phase III trial of first-line ribociclib plus letrozole versus placebo plus letrozole in hormone receptor-positive, HER2-negative advanced breast cancer. Annals of Oncology, 29(7), 1541-1547.

5. O'Shaughnessy, J., Petrakova, K., Sonke, G. S., Conte, P., Arteaga, C. L., Cameron, D. A., ... & Torres, R. (2018). Ribociclib plus letrozole versus letrozole alone in patients with de novo HR+, HER2− advanced breast cancer in the randomized MONALEESA-2 trial. Breast Cancer Research and Treatment, 168(1), 127-134.

Volume 2, Issue 01, 2023
Page 17-20
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