https://doi.org/10.29289/259453942025V35S1023

Efficacy and safety of capivasertib for breast cancer patients: a systematic review and meta-analysis of randomized controlled trials

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Introduction: Capivasertib, an oral AKT inhibitor, has shown potential in treating breast cancer by targeting the PI3K/AKT pathway. **Objective:** This meta-analysis aimed to assess the efficacy and safety of capivasertib in breast cancer by summarizing high-quality evidence from randomized controlled trials. **Methods:** PubMed, Embase, and Cochrane databases were searched to identify randomized controlled trials evaluating capivasertib, an oral inhibitor of all three isoforms of the serine/threonine kinase AKT, in patients with breast cancer. The outcomes of interest included overall survival, progression-free survival, objective response rate, and grade 3–5 adverse events. When possible, subgroup analyses were performed for patients with and without PIK3CA/AKT1/PTEN alterations. Data pooling was performed using a random-effects model. Statistical analyses were conducted using the "meta" and "metaprop" packages in RStudio. **Results:** A total of 631 studies were screened. Four randomized controlled trials with a total of 548 patients were included in this meta-analysis. Among these, 124 patients received capivasertib+paclitaxel, while 424 received capivasertib+fulvestrant. A total of 236 patients were part of the PIK3CA/AKT1/PTEN-altered subpopulation, while 243 were in the non-altered subpopulation. For progression-free survival, the capivasertib group demonstrated a hazard ratio (HR) of 0.69 (0.54–0.89), heterogeneity (I^2) of 64%, and p-value (p)<0.01. For overall survival, the HR was 0.67 (0.50–0.89; I^2=0; p<0.01). No statistically significant results were observed in the subgroup analysis of PIK3CA/AKT1/PTEN mutations for overall or progression-free survival. The objective response rate was 0.34 (0.20–0.52; I^2=90.0%) for the overall population and 0.40 (0.23–0.60; I^2=83.2%) for patients with PIK3CA/AKT1/PTEN alterations. Furthermore, the incidence of adverse events of grade ≥3 was 54% (43%–65%; I^2=82.7%). **Conclusion:** This meta-analysis supports the efficacy of capivasertib in improving overall and progression-free survival in breast cancer patients. However, the high rate of grade 3–5 adverse events suggests the need for careful monitoring. Future research should focus on reducing side effects and exploring the effects of capivasertib in specific molecular subgroups.

Keywords: breast neoplasms; progression-free survival; survival.