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Cyclin inhibitors for breast cancer: a comparative real world data analysis

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Objective: This study aimed to evaluate the impact of different cyclin-dependent kinase 4 and 6 inhibitors (CDK 4/6) as first line therapy on median overall survival (mOS) in a contemporary real-world setting. **Methods:** Data from TriNetX (a global dataset of electronic medical records of patients from 111 healthcare organizations) were analyzed and queried for patients with specific terms between 2004–2024. A propensity score matching analysis balanced the cohort. Ribociclib (Rib), palbociclib (Palb), and abemaciclib (Abem) were compared using a 2x2 group selection method. Analysis 1 compared Rib vs. Abem; Analysis 2 compared Rib vs. Palb; and Analysis 3 compared Palb vs. Abem. The mOS was evaluated with the Kaplan–Meier method. Statistical comparison was performed with a stratified log-rank test. **Results:** No difference in risk for death was identified in Analysis 1 (271 patients in each arm), with a not reached mOS for both cohorts (5 years; OS 61.82% vs. 53.66%, $\chi^2=0.03$; $p=0.863$; hazard ratio [HR] 0.964; 95% confidence interval [CI] 0.634–1.467). Analysis 2 (980 patients in each arm) revealed a statistically significant increased risk of death when receiving Palb over Rib (risk ratio [RR] 2.42; 95%CI -0.202–0.280; $p\leq 0.0001$) with mOS of 1,286 vs. 1,946 days ($\chi^2=15.447$; $p<0.0001$; HR 1.441; 95%CI 1,200–1,731). Analysis 3 (318 patients in each arm), revealed a statistically significant increased risk of death when receiving Palb over Rib (RR 2.47; 95%CI -0.231–0.372; $p\leq 0.0001$) with mOS of 1,124 vs. 1,706 days ($\chi^2=9.025$; $p<0.003$; HR 1.56, 95%CI 1,165–2,091). **Conclusion:** Our study revealed that patients treated with Palb instead of Rib or Abem achieved a lower mOS with an increased risk of death from breast cancer. Additionally, when comparing Rib to Abem, despite a percentage trend favoring Rib, no difference was found in the overall survival analysis for the risk of death from breast cancer.

Keywords: breast neoplasms; metastasis; cyclin-dependent kinases; treatment outcome; survival.