

Investigating associations of comorbidities and race with all-cause mortality outcomes of PI3K inhibitor use in metastatic breast cancer

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Introduction

• PI3K and AKT pathway inhibitors Alpelisib, Inavolisib, and Capivasertib (PI3K/AKTi) are FDA approved treatments with demonstrated significant clinical benefit, improving progression free survival for Hormone receptor positive (HR+) metastatic breast cancer (mBC).

•While knowledge about disparities in outcomes based on race and comorbidities in certain mBC subtypes is emerging, real world data about PI3K/AKTi is limited.

Objectives

• Identify outcomes disparities in mBC treatment with PI3K/AKTi in relation to demographic factors

• Investigate the contribution of time of comorbidity development, before or after treatment with PI3K/AKTi, to all cause mortality.

References

Sirico M, D'Angelo A, Gianni C, Casadei C, Merloni F, De Giorgi U. Current State and Future Challenges for PI3K Inhibitors in Cancer Therapy. Cancers (Basel). 2023 Jan 23;15(3):703. doi: 10.3390/cancers15030703. PMID: 36765661; PMCID: PMC9913212.

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Methods

• TriNetX Research Network was used systems to compare mortality of patients with breast cancer diagnoses treated with PI3K/AKTi across 3 raced-based cohorts of African American (AA), Asian (A), and White (W) identifying patients, male and female.

• Grouping into cohort by comorbidity was also used to examine hazard ratios for conditions developed before or after treatment.

• Cohorts were matched for age, BMI, comorbidities, and treatment lines using 1:1 matching with a greedy nearest neighbor search.

Analysis Date: September 22, 2025	African American (AA)	White (W)	Asian (A)
Number of Patients	270	1,958	144
Age at Index	60.5 ± 12.6	63.7 ± 11.7	63.7 ± 11.7
Gender (F)	262	1,933	144
DM (E08-E13) at Index	71	332	30
HTN (I10-I15) at Index	163	852	59
Median Survival (days)	692	686	754

Table 1: Demographic characteristics of race and comorbidity cohorts at time of analysis (9/22/2025).

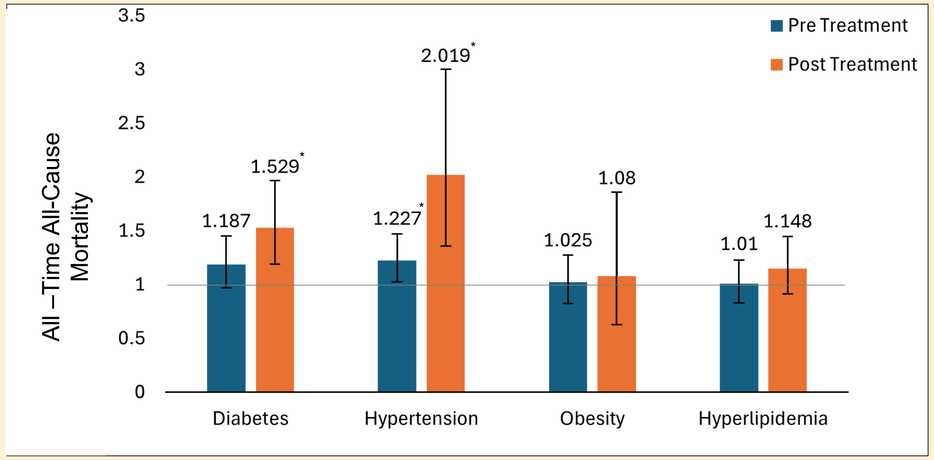


Figure 1: Odds ratios post-matching for outcomes tested using the TriNetX database comparing all-time all cause mortality amongst those diagnosed with comorbidities pre vs post treatment. Line indicates CI threshold at 1. Statistical significance with 95% confidence intervals is indicated by *.

Results

• Compared to non-diabetic patients, those diagnosed with diabetes after treatment had higher odds of mortality post-matching but those with pre-existing diabetes showed no significant difference in mortality.

• Pre-existing hypertension and hypertension diagnosed post-treatment were associated with higher mortality compared to non-hypertensive patients.

• No statistically significant difference in mortality odds was seen comparing the AA cohort to W cohort (matched OR = 0.99, 95% CI 0.70–1.39) or A cohort to W cohort post matching (OR = 0.72, 95% CI 0.45–1.16).

• Hyperlipidemia was not statistically significant after matching and no significant association was seen with obesity before or after treatment (all CI including 1).

Conclusions and Future Work

• Diagnosis with hypertension before and after treatment with PI3K/AKTi had higher odds of mortality suggesting the importance of primary prevention to reduce mortality outcomes.

• Patients diagnosed with diabetes post treatment having higher mortality odds highlights the importance of comorbidity management in the post-treatment setting.

•Future studies are needed to understand interactions between individual PI3K/AKTi agents and comorbidities to inform appropriate management strategies.

•Understanding the level of control of various comorbidities in these cohorts may also help determine if any medical intervention to address them has led, or can be trialed to lead, to significant mortality odds reduction.

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