Abstract

We analyzed de-identified patients with metastatic pancreatic ductal adenocarcinoma (PDAC) (n=2,800) from the Flatiron Health Research Database from the years 2017–2024. BRCA status was classified as benign, germline pathogenic, germline variant of uncertain significance (VUS), somatic pathogenic, or somatic VUS. Outcomes included overall survival (OS), time-to-next treatment (TTNT), first-line platinum receipt and total number of lines of therapy. Statistical models adjusted for significant covariates.

Demographically, there were a large majority of benign variants in BRCA (n=2,407; 86.0%). Other categories included: germline pathogenic (n=103; 3.7%), germline VUS (n=40; 1.4%), somatic pathogenic (n=101; 3.6%), and somatic VUS (n=149; 5.3%).

Compared to benign, germline pathogenic (HR 0.56, 95% CI 0.43–0.73, p<0.001); somatic pathogenic (HR 0.61, 95% CI 0.45–0.81, p<0.001), and somatic VUS (HR 0.80 95% CI 0.64-0.99, p=0.041) mutations were associated with improved OS. Germline pathogenic carriers also had longer time to next treatment (TTNT) (6.35 vs. 4.80 months; p=0.008) and received a larger number of lines of therapy (OR 2.67 vs benign 95% CI 1.29–4.49, p=0.006). None of the groups differed in their likelihood of receiving first line platinum chemotherapy.