INTRODUCTION

• The preclinical and clinical benefit of targeted and immunologic therapies is highly dependent on the tumor’s genetic landscape.

• Divergent genomic features within breast cancer subtypes have been reported.

• Previous studies of ctDNA in breast cancer patients have focused on a small panel and did not account for the dynamics of tumors across subtypes.

• We examined the differences in gene alteration frequency across subtypes in ctDNA.

METHODS

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RESULTS

• Differences in baseline genomic profiles were observed across intrinsic subtypes:

• A total of 336 patients (43.9%) had LumB subtypes, 210 (26.5%) had LumA subtypes, 123 (15.3%) had HER2E subtypes, and 147 (17.9%) had Basal-like subtypes.

• Gene amplifications were more frequent in the LumB, HER2E, and Basal-like subtypes vs. LumA subtypes (24.7% vs. 14%, 16.2% vs. 10.4%, and 12.5% vs. 2.5%, respectively).

• Gene deletions were more frequent in the LumA, HER2E, and Basal-like subtypes vs. LumB subtypes (16% vs. 5.6%, 12.5% vs. 8.6%, and 10% vs. 6.6%, respectively).

• There was a trend for higher copy number alterations in the Basal-like subtypes; there was no difference in the LumA, LumB, HER2E, and HER2 enriched subtypes.

• Differences across subtypes for tumor mutational burden (TMB) were observed, with the highest TMB observed in the HER2 enriched subtypes.

• For each gene, a Fisher exact test was used to test for differences in frequency across the subtypes.

• A false discovery rate (FDR) correction was used to adjust for multiple testing; for genes with FDR = 0.05, a singlegene nominal result was used to identify the bioinformative loci associated with survival status.

• We evaluated differences across subtypes for tumor mutational burden (TMB) using analysis of variance.

• The Kruskal-Wallis test was used to measure the differences across subtypes for cDNA fraction (an estimate of the amount of tumor DNA in the circulation and the intensity of progressive).

• The clinical and biological perspective of the Basal-like subtype is particularly relevant in the luminal B and HER2E subtypes, which show divergent genomic features.

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