Poster: 1059 Cell-free DNA comparative analysis of hormone-receptor positive, first-line metastatic breast cancer genomic landscapes in US and China

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Introduction

Metastatic breast cancer (MBC) is a heterogeneous disease associated with known somatic mutations of variable biological value in different subtypes. Furthermore, the clinical evolution of the disease demonstrates clonal evolution resulting in disease resistance more accurately detected using blood-based sequencing.

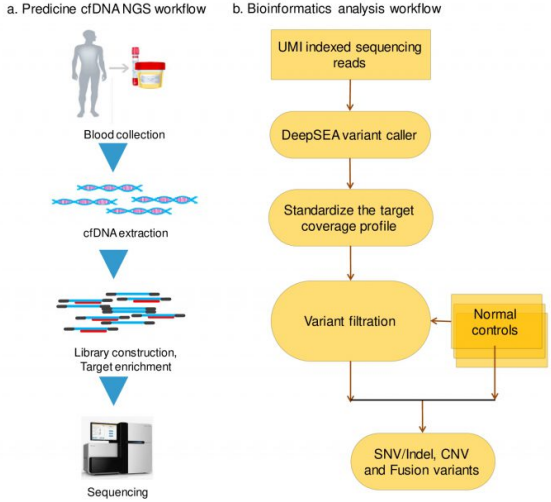
Few studies have explored differences in genomic features of tumors across populations. Here, we performed circulating tumor DNA (ctDNA) sequencing to compare the genomic landscape of patients with hormone-receptor positive MBC at time of first recurrence or de-novo metastatic diagnosis in the United States (US) and China.

Methods and Materials

Patients: Twenty-three **first recurrence HR+ MBC** US patients from Northwestern University and sixty five Chinese patients with **same characteristics** from Peking University

NGS testing: ctDNA sequencing from plasma was performed using the harmonized CLIA-certified, 152-gene PredicineCare™ NGS assay in laboratories in the US and China, respectively. The data analysis was conducted in China. Institutional Review Boards at each site approved the study. Fisher's exact test was performed to compare mutational frequencies across populations.

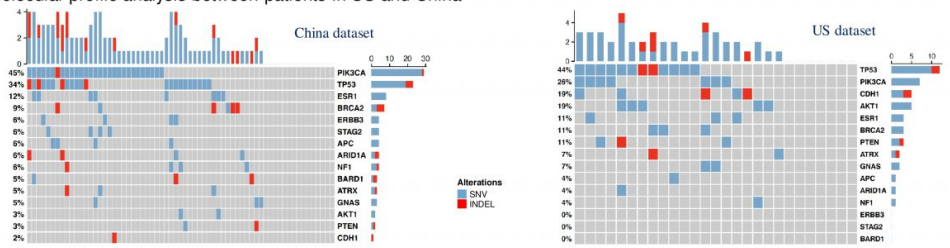
Figure 1: Workflow for Predicine's PredicineCARE liquid biopsy assay



Results

Figure 2: cfDNA mutation profiles of HR positive, first line metastatic breast patients in US and China

a. SNV/Indel molecular profile analysis between patients in US and China



b. Variant rate comparison

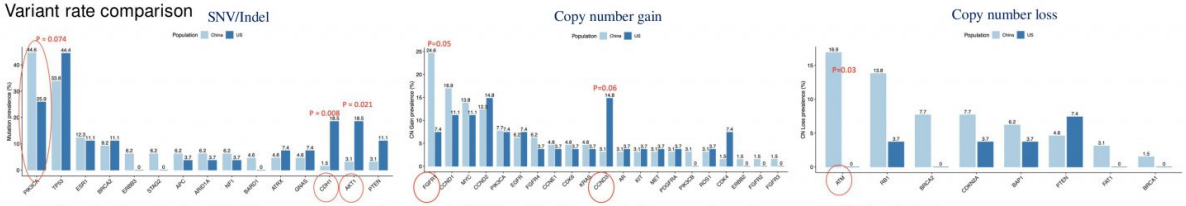
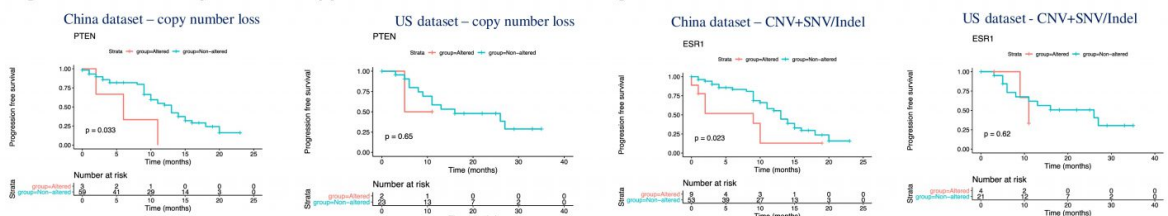


Figure 3. Survival analysis: PTEN copy number loss and ESR1 activating mutation carriers have overall short PFS



Conclusions

- This is the first study that a harmonized cfDNA assay (152-gene PredicineCARE) was used to profile plasma samples of first recurrence HR+ MBC patients in US and China.
- Most commonly mutated genes in the US and China study populations were similar. However, the occurrence of several abnormalities, including SNV/Indel of *PIK3CA*, *AKT1*, *CCND1* and CNV of *FGFR1*, *CCND2* and *ATM* were significantly different between the US and China study populations.
- *PTEN* copy number loss and *ESR1* mutations were significantly associated with PFS in the Chinese study population. Similar trends were also observed in the US study population, but were statistically underpowered due to the small sample size

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