Poster ID: P2-23-12

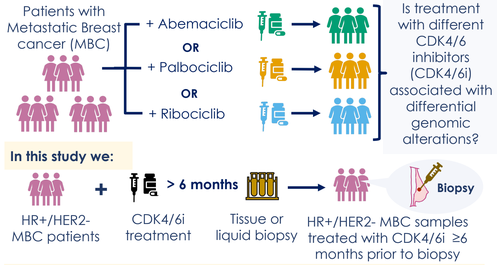
San Antonio Breast Cancer Symposium® - December 6-10, 2022

The Mutational Landscape of 1172 Patients with Hormone Receptor-Positive, HER2-Negative Metastatic Breast Cancer Treated with CDK4/6 Inhibitors

Ami N. Shah, MD[1], Bora Lim, MD[2], Monica Mita, MD[3], Elizabeth Mauer, MS[4], Kayla Viets Layng, PhD[4], Calvin Chao, MD[4], Adam Brufsky, MD, PhD[5]

[1]Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, 303 E Superior, Chicago, IL 60611, [2]Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine, 7200 Cambridge St., Houston, TX 77030, [3]Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, 127 S San Vicente Blvd, Los Angeles, CA 90048, [4]Tempus Labs, 600 W Chicago, Chicago, IL 60654, [5]Hillman Cancer Center, University of Pittsburgh Medical Center, 300 Halket St., Pittsburgh, PA 15213

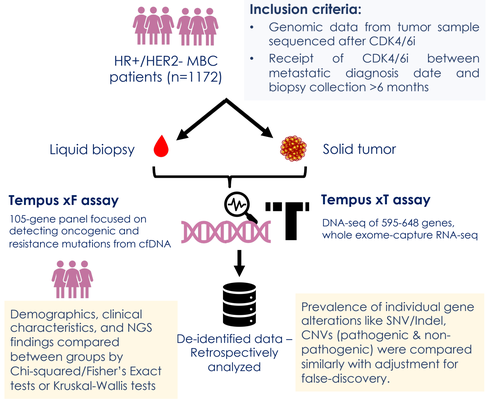
INTRODUCTION



Compare mutational landscapes and tumor mutational burden (TMB) in CDK4/6i treated HR+/HER2- MBC samples by treatment exposure

* Important previous work – PMIDS: 30205045[1], 32404308[2], 30206110[3]

METHODS



Acknowledgments: We thank Ellen Jaeger for data analysis, Emily Teslow Ph.D, and Amrita A. Iyer, Ph.D, for poster preparation and review.

Correspondence: brufskyam@upmc.edu

Cohort Characteristics

Characteristic	Overall, N = 1,172[1]	Abemaciclib N = 122[1]	Palbociclib N = 954[1]	Ribociclib N = 96[1]	p-value[2]
Age at diagnosis (yrs, IQR)	55 (45, 63)	52 (43, 60)	55 (46, 64)	51 (44, 61)	**0.015**
Unknown	1	0	1	0	
Gender					**0.2**
Female	1163 (99%)	122 (100%)	947 (99%)	94 (98%)	
Male	9 (0.8%)	0 (0%)	7 (0.7%)	2 (2.1%)	
Race					**0.2**
White	625 (81%)	71 (83%)	503 (82%)	51 (71%)	
Black /African American	87 (11%)	9 (10%)	68 (11%)	10 (14%)	
Asian	31 (4.0%)	3 (3.5%)	24 (3.9%)	4 (5.6%)	
Other Race	26 (3.4%)	3 (3.5%)	17 (2.8%)	6 (8.3%)	
Native Hawaiian or Other Pacific Islander	2 (0.3%)	0 (0%)	2 (0.3%)	0 (0%)	
American Indian/Alaska	1 (0.1%)	0 (0%)	0 (0%)	1 (1.4%)	
Unknown	400	36	340	24	
Ethnicity					**0.014**
Not Hispanic or Latino	398 (86%)	33 (87%)	339 (88%)	26 (70%)	
Hispanic or Latino	64 (14%)	5 (13%)	48 (12%)	11 (30%)	
Unknown	710	84	567	59	
Assay					**< 0.001**
xF	684 (58%)	87 (71%)	527 (55%)	70 (73%)	
xT	488 (42%)	35 (29%)	427 (45%)	26 (27%)	
Tissue Site					
Blood	684 (58%)	87 (71%)	527 (55%)	70 (73%)	
Liver	241 (21%)	15 (12%)	217 (23%)	9 (9.4%)	
Other	87 (7.4%)	5 (4.1%)	75 (7.9%)	7 (7.3%)	
Breast	61 (5.2%)	7 (5.7%)	52 (5.5%)	2 (2.1%)	
Lung	38 (3.2%)	2 (1.6%)	32 (3.4%)	4 (4.2%)	
Lymph nodes	29 (2.5%)	4 (3.3%)	22 (2.3%)	3 (3.1%)	
Bone	26 (2.2%)	2 (1.6%)	23 (2.4%)	1 (1.0%)	
CNS	6 (0.5%)	0 (0%)	6 (0.6%)	0 (0%)	

[1]Median (IQR); n (%)
[2]Kruskal-Wallis rank sum test; Fisher's exact test; Pearson's Chi-squared test

Other findings of interest:

- *ESR1* mutations occurred at similar rates among each CDK4/6i treatment group
- *RB1* mutation/*RB1* loss was seen less frequently after exposure to Palbociclib than other CDK4/6i and only in a minority of patients
- MSI-high was identified in 2.5%, 0.1%, and 1.1% of the patients who received Abemaciclib, Palbociclib, and Ribociclib, respectively, P<0.001

RESULTS

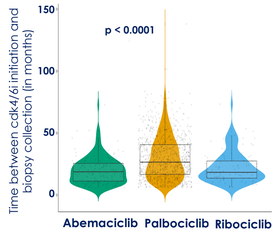


Figure 1. Distributions of times between CDK 4/6 inhibitor initiation and collection of biopsy

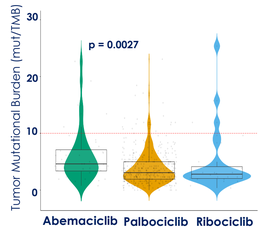


Figure 2. Distributions of TMB values for each CDK 4/6 inhibitor with medians and interquartile ranges

Table 2. TMB assessment across CDK 4/6 inhibitors *TMB assessment only included patients with xT (tissue) testing (n=488 [42%])

Biomarker	Abemaciclib, N = 122[1]	Palbociclib N = 954[1]	Ribociclib N = 96[1]	p-value[1]
TMB Median (IQR)	4.6 (3.4,7.1)	3.1 (1.9,5.0)	2.8 (2.0,4.1)	0.004
High TMB	14%	5.2%	12%	0.04

KEY TAKEAWAYS

- Results from our real-world dataset describe the genomic landscape in HR+ HER2- MBC that have been exposed to >6 months of CDK4/6i. This is the largest dataset, to our knowledge from patients in this setting, and included patients treated with all 3 approved CDK4/6i (palbociclib, ribociclib, and abemaciclib)
- The landscape was consistent with previously reported data in this setting[1,2,3], such as high prevalence of *ESR1*, *PIK3CA*, *TP53* with other noteworthy alterations in the PI3K/AKT/PTEN and DNA-repair pathway associated genes.
- Relevant alterations were detected by both Tempus tissue (xT) and liquid biopsy (xF) testing, supporting a role for either assay in identifying resistance alterations.
- *RB1* mutations were identified at a relatively low prevalence, with a trend towards lower frequency of RB1 mutations in patients treated with palbociclib. These data support studies evaluating the use of CDK4/6i after initial CDK4/6i, such as the MAINTAIN and PACE trials.
- Although infrequent, a small subset of patients were identified as TMB-H, which was more common among abemaciclib treated patients.
- This study was limited by a smaller sample size in the ribociclib, abemaciclib, TMB-H, and MSI-H groups. Additional analysis is recommended once more data is available from abemaciclib and ribociclib-treated patients, given the observed differences in frequency of gene mutations across CDK4/6i treated patients in this study.

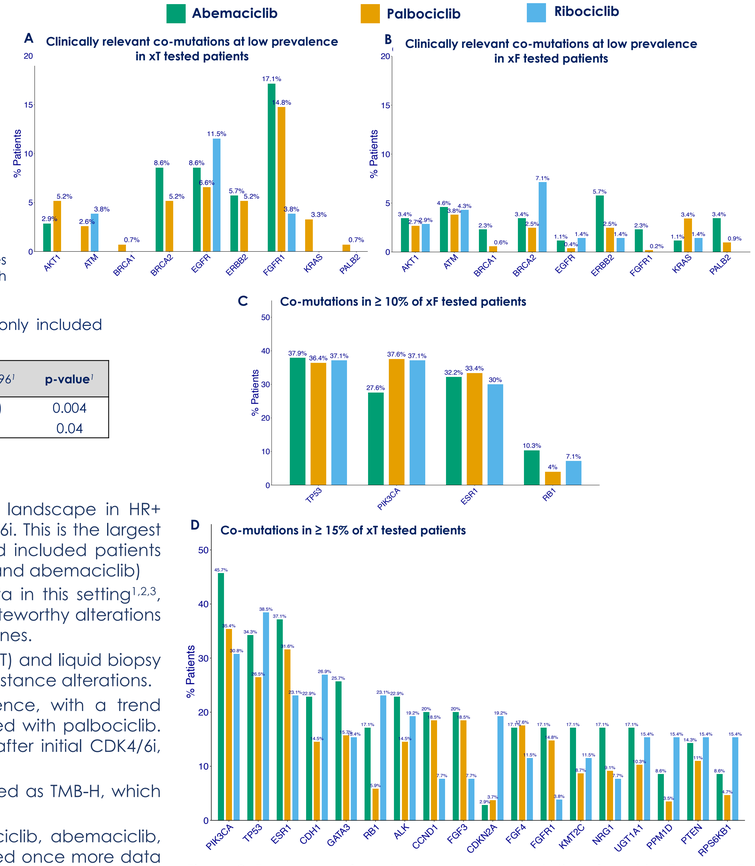


Figure 3. Frequency of most common gene mutations found by Tempus xT or xF for each CDK 4/6 inhibitor.
**Although the frequency of some gene mutations were significantly different amongst the groups in bivariate testing, all were non-significant after false-discovery correction*