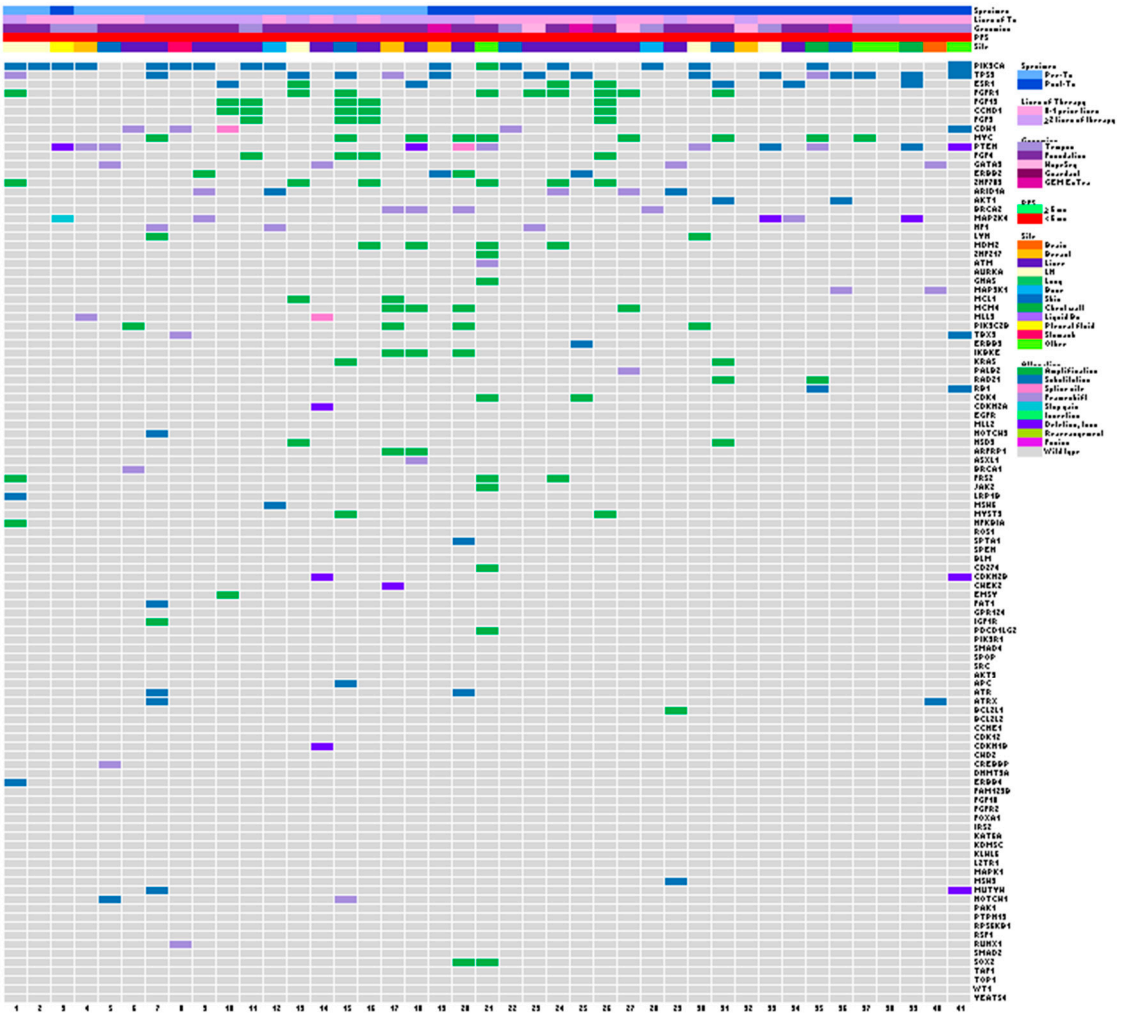
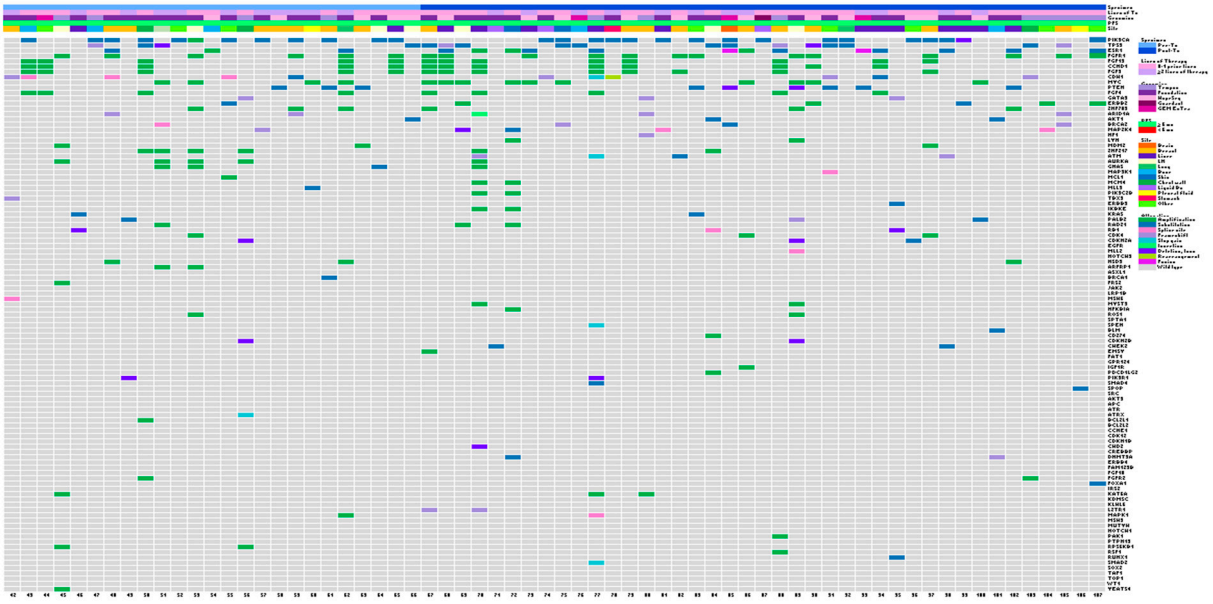
A


Specimen
Lines of Tx
Genomics
PFS
Site
PIK3CA
TP53
ESR1
FGFR1
FGF19
CCND1
FGF3
CDH1
MYC
PTEN
FGF4
GATA3
ERBB2
ZNF703
ARID1A
AKT1
BRCA2
MAP2K4
NF1
LYN
MDM2
ZNF217
ATM
AURKA
CHAS
MAP3K1
MCL1
MCM4
MLL3
PIK3CB
TBX3
ERBB3
IKBKE
KRAS
PALB2
RAD21
RB1
CDK1
CDKN2A
EGFR
MLL2
NOTCH3
NSD3
ARFRP1
ASXL1
BRCA1
FBXI
JAK2
LRP1B
MSH6
MYST3
MYO1A
ROS1
SPTA1
SPEN
SLN
CD274
CDKN2B
CHEK2
EMSY
PAT1
GPR124
IGF1R
PDCD1LG2
PIK3R1
SMAD4
SPOP
SRC
AKT3
APC
ATR
ATRX
BCL2L1
BCL2L2
CCNE1
CDK12
CDKN1B
CND2
CREBBP
DNMT3A
ERBB4
FAM123B
FGF10
FGFR2
FOXA1
IRS2
KAT6A
KDM5C
KLHL6
LZTR1
MAPK1
MSH3
MUTYH
NOTCH1
PAK1
PTPN13
RPS6KB1
RSF1
RUNX1
SMAD2
SOX2
TAF1
TOP1
WT1
YEATS4
Specimen
Pre-Tx
Post-Tx
Lines of Therapy
1-2 prior lines
≥2 lines of therapy
Genomics
Tempus
Foundation
MapSeq
Guardant
GEMCaTx
PFS
≥6 mo
<6 mo
Site
Brain
Breast
Liver
LN
Lung
Bone
Skin
Chest wall
Liquid Bx
Pleural fluid
Stomach
Other
Amplification
Substitution
Splice site
Frameshift
Stop gain
Insertion
Deletion, loss
Rearrangement
Fusion
Wild type

B



C

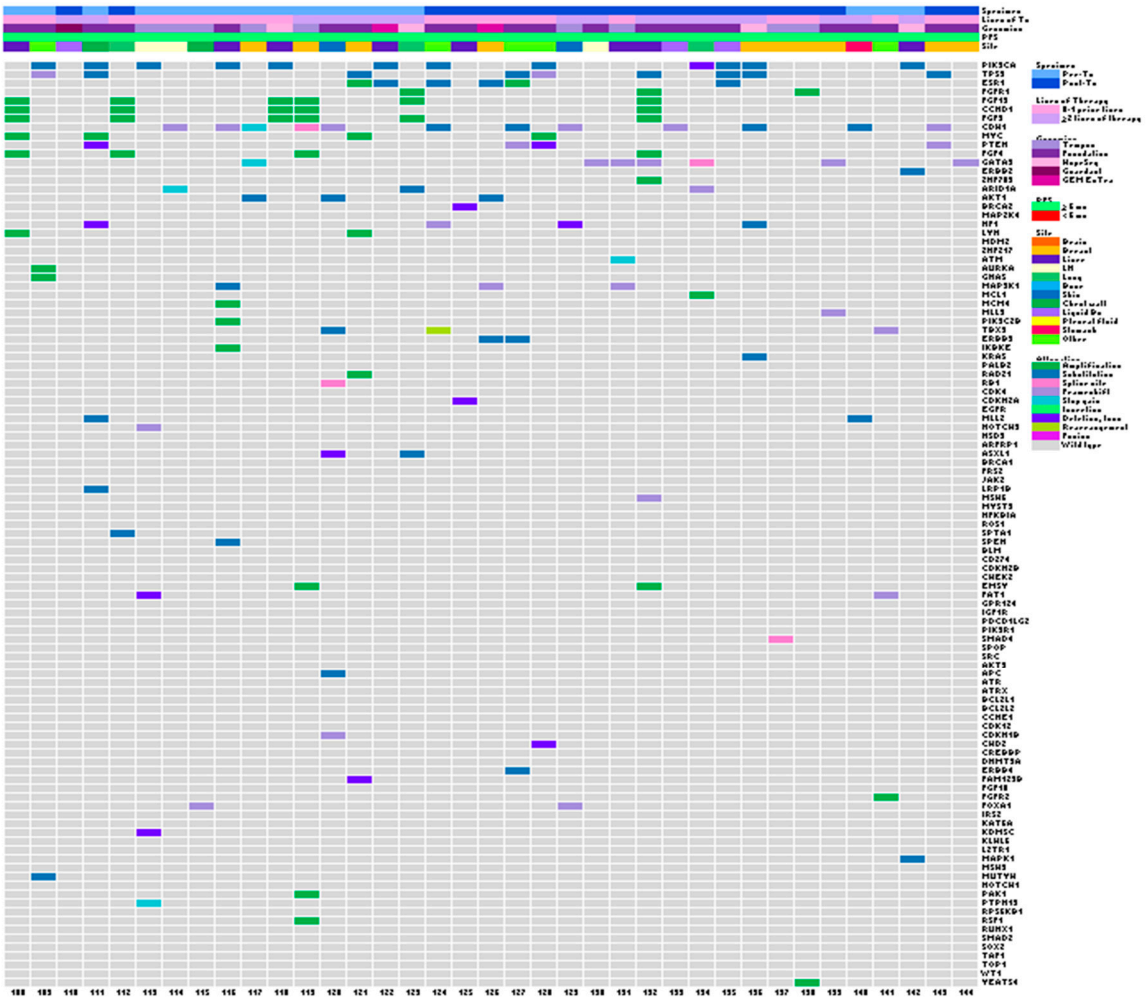
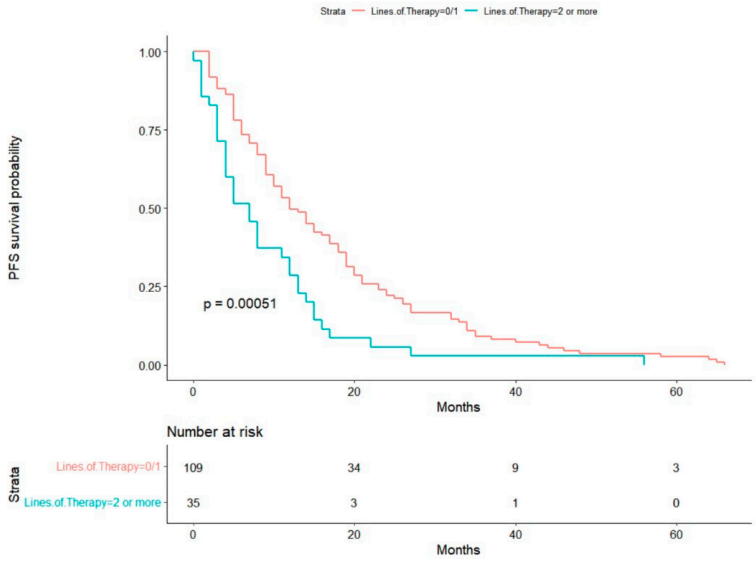


Figure S1. Tile plots of genomic alterations of each patient's tumor specimen: A) early progression (PFS < 6 months; N=41); B) intermediate progression (PFS 6-24 months for 0-1 lines; 6-9 months for 2+ lines; N=66); C) late progression (PFS >24 months for 0-1 lines; PFS >9 months for 2+ lines; N=37).

A



B

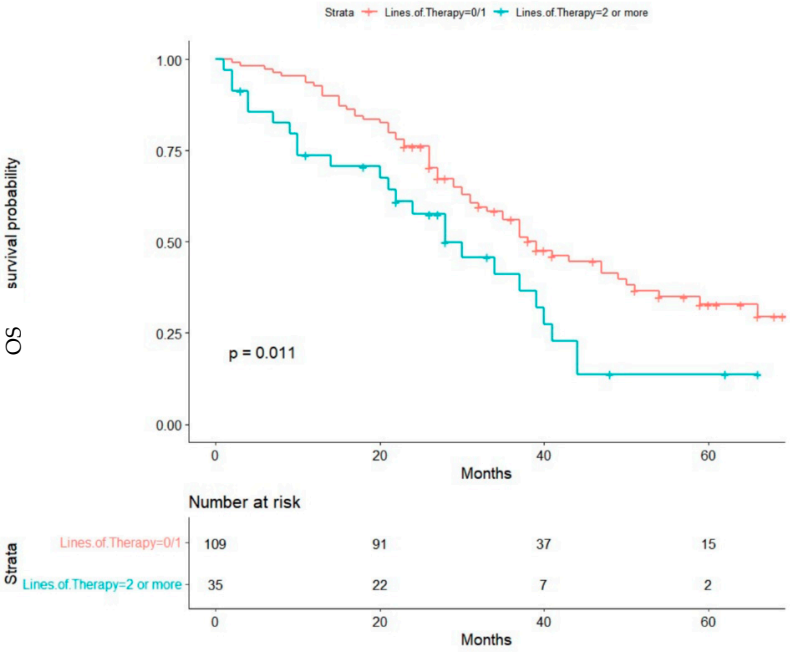


Figure S2. Kaplan-Meier survival analysis stratified by prior lines of chemotherapy: A) Median PFS for 0-1 prior lines (N=109) was 12 months (95% CI 10, 17) and for ≥ 2 lines (N=35) was 7 months (95% CI 4, 12); B) Median OS for 0-1 prior lines (N=109) was 39 months (95% CI 33, 51) and for ≥ 2 lines (N=35) was 28 months (95% CI 21, 41). Date of last follow up was used.

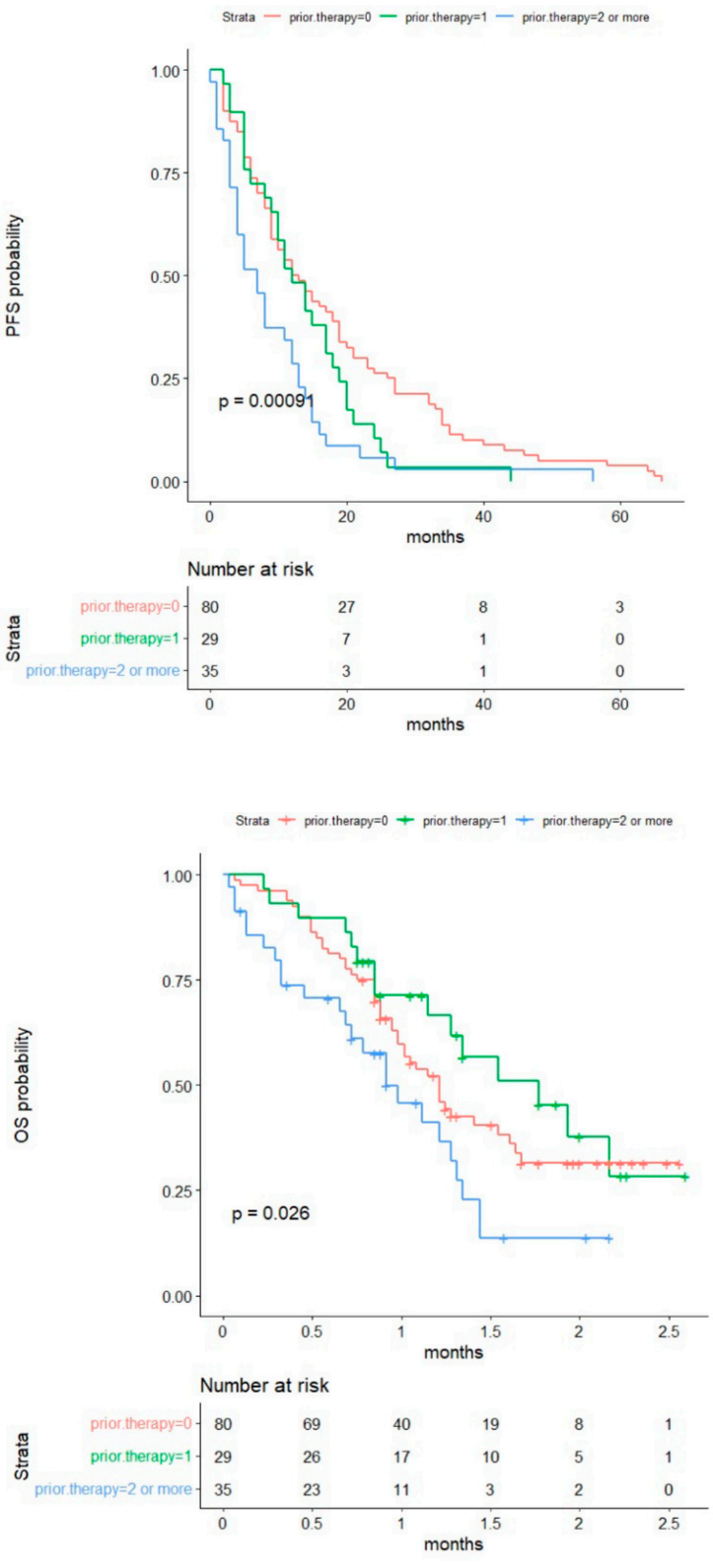


Figure S3. Kaplan-Meier survival analysis stratified by 0, 1, and ≥ 2 prior lines of chemotherapy: A) Median PFS for 0 prior lines (N=80, red line) was 12.5 months (95% CI 9—19); median PFS for 1 prior line (N=29, green line) was 12 months (95% CI 12—18);and median PFS for ≥ 2 lines (N=35, blue line) was 7 months (95% CI 4—12); B) Median OS for 0 prior lines (N=80, red line) was 37 months (95% CI 30—50);median PFS for 1 prior line (N=29, green line) was 54 months (95% CI 29—NA); and median PFS for ≥ 2 lines (N=35) was 28 months (95% CI 21—41).

Table S1. Tumor genomic analysis of patients with 0 or 1 line of prior therapy (n=109) and mutations that are present in ≥2 patients showed association with impaired PFS.

Table S2. RNA analysis for patients with 0 or 1 line of prior therapy (n=24) patients with 0-1 prior lines of therapy. 11,426 protein-coding genes were studied, and FDR was calculated to adjust for multiple comparisons. The 56 genes in the heatmap were selected with HR>4 or <0.25 with FDR <0.15. Unsupervised hierarchical clustering showed 3 clusters with distinct gene expression pattern. The 3 clusters are characterized by early, intermediate, and late PFS with the median PFS of 4.5 (n=4 range), 8.5 (n=12 range) and 29 (n=8, range) months, respectively. Statistical analysis was conducted in R (R-3.6.3, R Core Team).