Supplementary Figure:

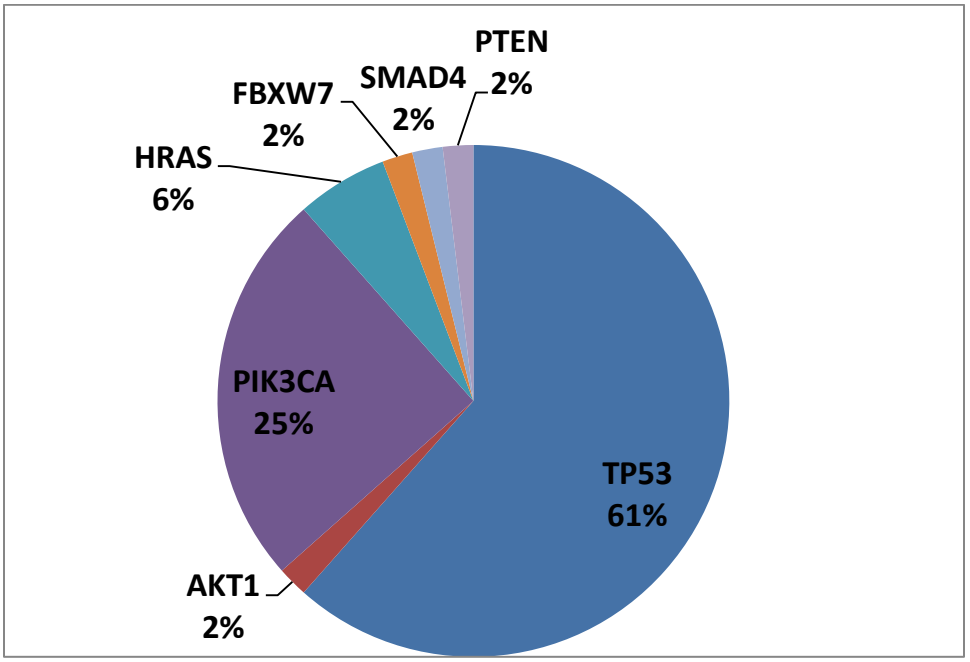

Figure S1: Proportions of different pathogenic genetic alterations detected in MBCs using Illumina TruSeq amplicon cancer hotspot panel (total number of pathogenic alterations identified= 52, denominator).

**BRCA1* mutations are not included.

Supplementary Tables:

Patient #	ALTERATIONS SEEN IN MBC CASES AND THEIR CLINICAL SIGNIFICANCE	
1	*TP53* (I195T)	pathogenic/presumed pathogenic
2	*TP53* (C242fs); *AKT1* (E17K)	pathogenic/presumed pathogenic; pathogenic/presumed pathogenic
3	*TP53* (S241C)	pathogenic/presumed pathogenic
4	*TP53* (E198X); *PIK3CA* (K111del)	pathogenic/presumed pathogenic; pathogenic/presumed pathogenic
5	*TP53* (R248Q)	pathogenic/presumed pathogenic
6	*TP53* (R282W); *STK11* (F354L)	pathogenic/presumed pathogenic; likely benign
7	*PIK3CA* (H1047R); *HRAS* (Q61L); *APC* (I1307K glm)	pathogenic/presumed pathogenic; pathogenic/presumed pathogenic; other
8	*TP53* (V216M)	pathogenic/presumed pathogenic
9	*FBXW7* (Q508X)	pathogenic/presumed pathogenic
10	*TP53* (S241C)	pathogenic/presumed pathogenic
11	*c-KIT** (T67S); *TP53* (R248W); *SMAD4* (D415fs)	likely benign; pathogenic/presumed pathogenic; pathogenic/presumed pathogenic
12	*TP53* (C242X)	pathogenic/presumed pathogenic
13	*HRAS* (Q61L)	pathogenic/presumed pathogenic
14	*TP53* (D281E)	pathogenic/presumed pathogenic
15	*TP53* (Y163C)	pathogenic/presumed pathogenic
16	*PIK3CA* (H1047L)	pathogenic/presumed pathogenic
17	*TP53* (S106R); *PIK3CA* (H1047R); *MLH1* (S406N)	pathogenic/presumed pathogenic; pathogenic/presumed pathogenic; likely benign
18	*PIK3CA* (H1047L)	pathogenic/presumed pathogenic
19	*TP53* (G244S)	pathogenic/presumed pathogenic
20	*cMET* (T1010I)	likely benign
21	*TP53* (V173M); *HRAS* (L52R)	pathogenic/presumed pathogenic; variant of unknown significance
22	*PTEN* (R233X); *PIK3CA* (H1047R)	pathogenic/presumed pathogenic; pathogenic/presumed pathogenic
23	*HRAS* (G13V); *BRAF* (N581I)	pathogenic/presumed pathogenic; variant of unknown significance
24	*PIK3CA* (H1047R)	pathogenic/presumed pathogenic
25	*TP53* (R273H)	pathogenic/presumed pathogenic
26	*TP53* (R33fs); *JAK3* (V722I)	pathogenic/presumed pathogenic; variant of unknown significance
27	*TP53* (R273C); *FBXW7* (T463S)	pathogenic/presumed pathogenic; variant of unknown signifcance
28	*TP53* (R213X)	pathogenic/presumed pathogenic
29	*PIK3CA* (H1047R)	pathogenic/presumed pathogenic
30	*PIK3CA* (N345K)	pathogenic/presumed pathogenic
31	*TP53* (C242fs)	pathogenic/presumed pathogenic
32	*TP53* (I195T)	pathogenic/presumed pathogenic
33	*TP53* (R110fs)	pathogenic/presumed pathogenic
34	*TP53* (Q165X)	pathogenic/presumed pathogenic
35	*TP53* (C242fs); *JAK3* (V722I)	pathogenic/presumed pathogenic; variant of unknown significance

36	*TP53* (R273C)	pathogenic/presumed pathogenic
37	*TP53* (C242X)	pathogenic/presumed pathogenic
38	*PIK3CA* (H1047R)	pathogenic/presumed pathogenic
39	*TP53* (Y220C); *cMET* (T1010I)	pathogenic/presumed pathogenic; likely benign
40	*PIK3CA* (H1047R)	pathogenic/presumed pathogenic
41	*STK11* (F354L)	likely benign
42	*TP53* (R175H)	pathogenic/presumed pathogenic
43	*TP53* (C238Y); *PIK3CA* (H1047R)	pathogenic/presumed pathogenic; pathogenic/presumed pathogenic
44	*TP53* (C176F)	pathogenic/presumed pathogenic
45	*STK11* (F354L)	likely benign
46	*PIK3CA* (P539R); *RET* (Y719F)	pathogenic/presumed pathogenic; likely benign
47	*TP53* (V274F); *PTEN* (K13E & R15fs)	pathogenic/presumed pathogenic; pathogenic/presumed pathogenic
48	*TP53* (R273H)	pathogenic/presumed pathogenic
	*other- mild mutation that is a common germline variant in the Ashkenazi Jewish population. Carriers have a slightly increased risk of colon cancer.	
	The row highlighted in yellow shows patients with non-pathogenic mutations and were not counted during the discussion	

Table S1: Specific alterations in genes and their clinical significance in all interpretable cases of MBCs.

PATHOGENIC ALTERATIONS IN MBCS	
Altered pathogenic gene	Frequency
TP53	32
AKT1	1
Wild Type	9
PIK3CA	13
HRAS	3
FBXW7	1
SMAD4	1
PTEN	1
Total number of mutations	52

Table S2: Pathogenic/presumed alterations and frequency seen in MBCs.

PATHOGENIC ALTERATIONS IN TNBCs	
Total number of patients with pathogenic mutations	94
Altered gene	Frequency
TP53	83
PIK3CA	13
AKT1	4
STK11	2
BRCA1	4
BRCA2	3
HRAS	1
KRAS	1
APC	2
FGFR2	2
FGFR3	1
MAPK1	1
PTEN	1
ERBB2	3
ERBB3	1
CDKN2A	1
KDR	1
ABL1	1
DDR2	1
ARAF	1
FGF10	1
CCNE1	1
MCL1	1
Total number of mutations	130

Table S3: Pathogenic alterations and their frequency in TNBCs.

PATHOGENIC ALTERATIONS IN HORMONE POSITIVE (HER2/NEU NEGATIVE) BREAST CANCERS	
Total number of patients with pathogenic mutations	58
Altered gene	Frequency
BRCA2	2
BRCA1	4
ERBB2	3
CDH1	1
TP53	25
PIK3CA	34
SMAD4	1
AKT1	4
PTEN	3
MYC	1
ATM	1
APC	1
Total number of mutations	80

Table S4: Pathogenic alterations and their frequency in Luminal breast cancer cases.

PATHOGENIC ALTERATIONS IN HER2 POSITIVE BREAST CANCERS	
Total number of patients with pathogenic mutations	20
Altered gene	Frequency
TP53	18
PIK3CA	11
PTEN	1
ERBB2	1
Total number of mutations	32

Table S5: Pathogenic alterations and their frequency in HER2+ breast cancer cases.

Subtype		Next Generation Sequencing		
		TP53 mutation	other mutations	Total
	Metaplastic carcinoma	32 (71%)	16 (29%)	45
	TNBC NOS	83 (88%)	11 (12%)	94
	HER2+	18 (95%)	2 (5%)	20
	Hormone positive breast carcinoma	25 (43%)	33 (57%)	58
Total		159 (73%)	61 (28%)	217

Table S6: Cases with pathogenic *TP53* mutation versus pathogenic mutations in other genes.