

List of Abbreviations

µl	Micro liter
ABL1	<i>Abelson murine leukemia viral oncogene homolog 1</i>
AKT1	AKT Serine/Threonine Kinase 1
Ala	Alanine
APC	Adenomatous polyposis coli
Arg	Arginine
Asn	Asparagine
Asp	Aspartic acid
ATM	Ataxia telangiectasia mutated
BC	Breast cancer
BRAF	v-raf murine sarcoma viral oncogene homolog B1
CSF1R	Colony-Stimulating Factor 1 Receptor
CTNNB1	Catenin Beta 1
Cys	Cysteine
FFPE	Formalin-Fixed Paraffin-Embedded
FuPa	Fragmentase Universal Primer Assay
Gln	Glutamine
Glu	Glutamic acid
Gly	Glycine
HER2	Human epidermal growth factor receptor 2
His	Histidine
HRAS	Harvey Rat sarcoma viral oncogene homolog
IHC	Immunohistochemistry
Ile	Isoleucine
JAK2	Janus Kinase 2
JAK3	Janus Kinase 3

KRAS	Kirsten rat sarcoma viral oncogene homolog
Leu	Leucine
Lys	Lysine
M	Million
Met	Methionine
MPL	myeloproliferative leukaemia virus oncogene
ng	<i>Nanogram</i>
NGS	Next generation sequencing
NOTCH1	Neurogenic locus notch homolog protein 1
NRAS	Neuroblastoma RAS viral oncogene homolog
P value	Probability value
pCR	Pathological complete response
PDK	Phosphatidylinositol-dependent kinase 1
Phe	Phenylalanine
PI3K/ AKT/ mTOR	Phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT)/mammalian target of rapamycin (mTOR)
PIK3CA	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha
pM	Picomolar
Pro	Proline
PTEN	Phosphatase and TENsin homolog
PTPN11	Tyrosine-protein phosphatase non-receptor type 11
Ras-Raf-MEK-ERK	Rat sarcoma / <i>Rapidly Accelerated Fibrosarcoma</i> /MEK (mitogen-activated protein kinase/ERK kinase)/ERK (extracellular-signal-regulated kinase)
RB1	Retinoblastoma protein
Ser	Serine

SNVs	Single nucleotide variants
SRC	Proto-oncogene tyrosine-protein kinase Src
STK11	Serine/threonine kinase 11
Thr	Threonine
TP53	Tumor protein p53
Trp	Tryptophan
Tyr	Tyrosine
USA	United states of America
Val	Valine

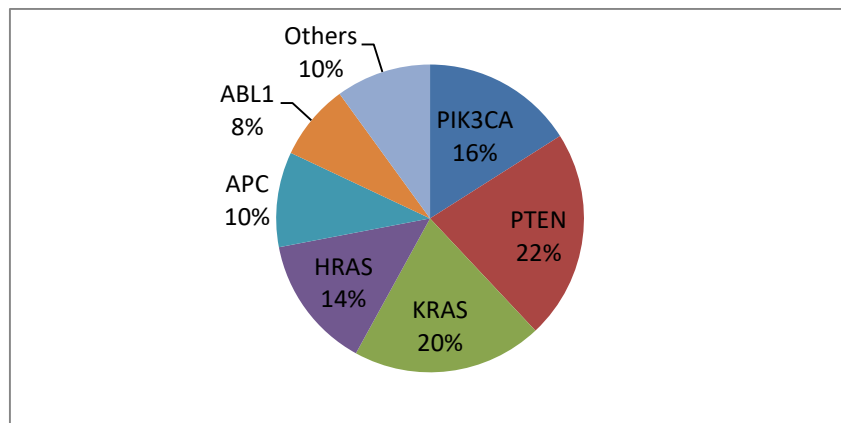


Fig. S1 Pie chart showing distribution of the studied genes variants (n=50) in the 12 responsive patients.

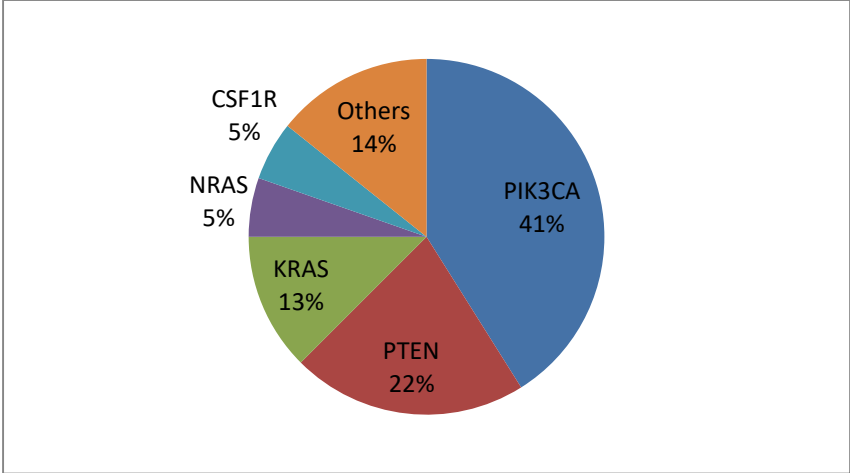


Fig. S2 Pie chart showing distribution of the studied genes variants (n = 56) in the 12 resistant patients.

Table (S1): Distribution of the studied genes variants in the total number of patients and in each group.

Genes	Total (n = 106)	Responsive (n = 50)	Resistant (n = 56)	P
PIK3CA	31(29.2%)	8(16%)	23(41%)	0.004*
PTEN	23(21.7%)	11(22%)	12(21.4%)	0.943
KRAS	17(16%)	10 (20%)	7(12.5%)	0.293
HRAS	8(7.5%)	7(14%)	1(1.7%)	^{FE} p=0.025*
APC	6(5.6%)	5 (10%)	1(1.7%)	^{FE} p=0.097
NRAS	4(3.7%)	1 (2%)	3(5.3%)	^{FE} p=0.620
ABL1	5(4.7%)	4 (8%)	1(1.7%)	^{FE} p=0.185
CSF1R	4(3.7%)	1 (2%)	3(5.3%)	^{FE} p=0.620
SRC	3(2.8%)	1 (2%)	2(3.5%)	^{FE} p=1.000
BRAF	3(2.8%)	1 (2%)	2(3.5%)	^{FE} p=1.000
JAK3	2(1.8%)	1 (2%)	1(1.7%)	^{FE} p=1.000

FE: **Fisher Exact**, p: p value for comparing between responsive and resistant

*: Statistically significant at $p \leq 0.05$

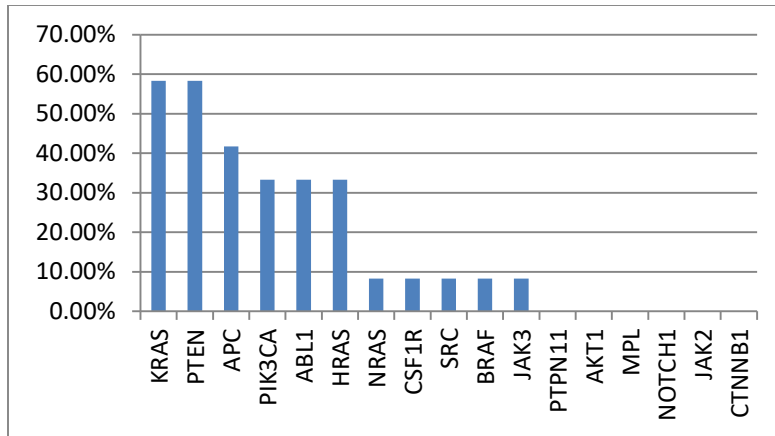


Fig. S3 The mutational frequency of the studied genes for responsive patients (n = 12)

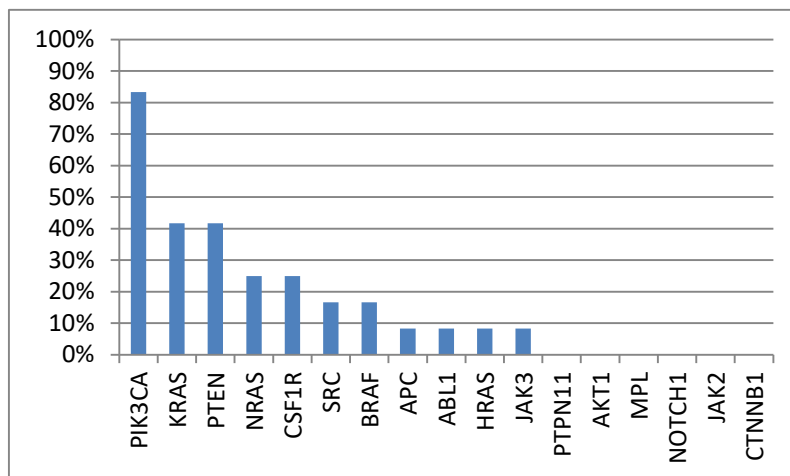


Fig. S4 The mutational frequency of the studied genes for resistant patients (n = 12)

Table (S2): Mutational frequency of the studied genes for total sample and in each group.

Prevalence of Genes	Total (n = 24)		Responsive (n = 12)		Resistant (n = 12)		p
	No.	%	No.	%	No.	%	
PIK3CA	14	58.3	4	33.3	10	83.3	^{FE} p=0.036*
PTEN	12	50.0	7	58.3	5	41.7	0.414
KRAS	12	50.0	7	58.3	5	41.7	0.414
APC	6	25.0	5	41.7	1	8.3	^{FE} p=0.155
ABL1	5	20.8	4	33.3	1	8.3	^{FE} p=0.316
HRAS	5	20.8	4	33.3	1	8.3	^{FE} p=0.316
NRAS	4	16.7	1	8.3	3	25.0	^{FE} p=0.590
CSF1R	4	16.7	1	8.3	3	25.0	^{FE} p=0.590
SRC	3	12.5	1	8.3	2	16.6	^{FE} p=1.000
BRAF	3	12.5	1	8.3	2	16.6	^{FE} p=1.000
JAK3	2	8.3	1	8.3	1	8.3	^{FE} p=1.000

FE: Fisher Exact

p: p value for comparing between responsive and resistant

Table S3: The detected *PIK3CA* variants in the 2 studied groups in relation with variants detected by thescreen *PIK3CA* test.

Exon	Region	Mutation	Frequency in our study
Exon 7	C2 domain	Cys420Arg	1
Exon 9	Helical domain	Glu542Lys	3
		Glu545Lys	3
		Glu545Ala	NA
		Glu545Asp	NA
		Glu545Gly	NA
		Gln546Arg	NA
		Gln546Glu	NA
Exon 20	Kinase domain	His1047Arg	6
		His1047Leu	NA
		His1047Tyr	3

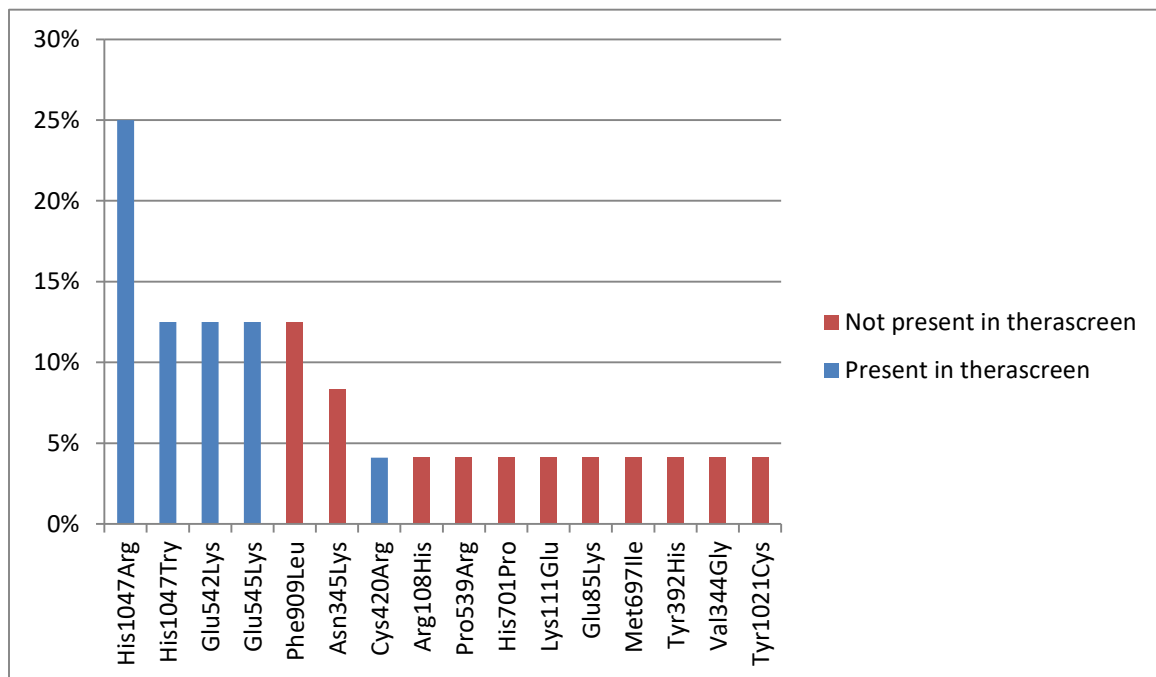


Fig. S5 The detected *PIK3CA* variants in the 2 studied groups in relation with variants detected by thescreen *PIK3CA* test.