

Supplementary Table S1: *BRCA1/2* unclassified variants identified on tumor testing and their respective LOH analysis.

Patient	Gene	Variant	Protein	Functional domain	Impact	Allelic frequency	LOH	Germine variant	TP53 associated mutation	Allelic frequency	Other associated variants
P2	BRCA2	c.8645A>C	p.Lys2882Thr	Tower	Missense	0,14	No	No	c.711G>A ;p.Met237Ile	0,54	No
P3	BRCA2	c.6322C>T	p.Arg2108Cys	-	Missense	0,48	No	No	c.832 ; p.Pro278Ser	0,59	No
P4	BRCA2	c.8351G>A	p.Arg2784Gln	OB1	Missense	0,86	Yes	No	c.517G>A;p.Val173Met	0,89	UV ATR:c.7167T>G;p.Ile2389Met
P9	BRCA1	c.5096G>A	p.Arg1699Gln	BRCT1/AD2	Missense	0,79	Yes	Yes	c.722G>T;p.Glu258*	0,72	No
P12	BRCA1	c.287_292del	p.Asp96_Gly98de	Ring finger ° NES2	Small deletion	0,57	No	No	c.833_834insC; p.Gly279fs.	0,87	No
P15	BRCA2	c.6757C>G	p.Leu2253Val	-	Missense	0,15	No	No	c.702C>A; p.Tyr234*	0,68	UV ATM: c.4388T>G;p.Phe1463Cys UV ATM:c.6919C>T;p.Leu2307Phe
P20	BRCA1	c.1616C>T	p.Thr539Met	-	Missense	0,45	No	Yes	Non-contributory	Non-contributory	NR
P23	BRCA2	c.955A>T	p.Asn319Tyr	-	Missense	0,19	Yes	Yes	c.518T>G;p.Val173Gly	0,44	NR
P25	BRCA2	c.8435G>T	p.Gly2812Val	OB2	Missense	0,10	inconclusive	No	NR	NR	NR
P28	BRCA2	c.1096T>G	p.Leu366Val	-	Missense	0,18	Yes	No	c.202G>T ; p.Glu68*	0,45	NR
P31	BRCA2	c.122C>T	p.Pro41Leu	-	Missense	0,42	No	No	c.814G>A;p.Val272Met	0,66	No
P38	BRCA1	c.5165C>T	p.Ser1722Phe	BRCT1/AD2	Missense	0,41	Yes	Yes	c.782+1G>A	0,21	NF1:c.6854_6855insA,p.Tyr2285_Asn2286fs
P39	BRCA2	c.1607C>A	p.Ser536Tyr	-	Missense	0,50	inconclusive	Oui	No	WT	NR
P40	BRCA2	c.9586A>G	p.Lys3196Glu	-	Missense	0,45	No	Yes	c.309C>G ; p.Tyr103*	0,14	No

P43	BRCA1	c.508C>T	p.Arg170Trp	-	Missense	0,16	Yes	Yes	c.645T>G ; p.Ser215Arg	0,70	No
P54	BRCA1	c.300G>A	p.Glu100=	-	synonymous	0,08	inconclusive	inconclusive	c.584T>C;p.Ile195Thr	0,30	UV ATM:c.6068G>T;p.Gly2023Val UV NF1:c.4749A>G;p.Glu1583Glu
P55	BRCA2	c.7534C>T	p.Leu2512Phe	Helical domain	Missense	0,46	No	Yes	c.657_668del;p.Pro219_Pro223del	0,32	No
P56	BRCA2	c.7791A>T	p.Lys2597Asn	Helical domain	Missense	0,03	Yes	NR	c.464C>A;p.Thr155Asn	0,0211	No
P59	BRCA2	c.1275A>G	p.Glu425=	-	Missense	0,57	inconclusive	NR	c.670G>T; p.Glu224*	0,87	UV ATM:c.4258C>T; p.Leu1420Phe
P11	BRCA2	c.856T>C	p.Ser286Pro	-	Missense	0,3	Yes	No	c.351delG; p.Gly117fs	0,29	BRCA1:c.5266_5267insC; p.Gln1756_Asp1757fs
P61	BRCA2	c.6317T>C	p.Leu2106Pro	-	Missense	0,49	inconclusive	NR	c.856_861del; p.Glu286_Glu287del	0,19	UV ATM:c.1118C>G;p.Thr373Arg
P62	BRCA2	c.4928T>C	p.Val1643Ala	-	Missense	0,40	Yes	Yes	c.224delC;p.Pro75fs	Not reported	
P50	BRCA2	c.2133C>T	p.Cys711=	-		0,72	Yes	No	c.403T>G; p.Cys135Gly	0,62	UV NF1:c.369C>G;p.Thr123Thr BRCA1:c.4072G>T ; p.Glu1358*
P47	BRCA2	c.10121C>T	p.Thr3374Ile	-	Missense	0,71	inconclusive	NR	c.1010G>T ; p.Arg337Leu	0,52	BRCA1 c.3008_3009del
P64	BRCA2	c.7719A>G	p.Leu2573=	Helical domain		0,57	inconclusive	inconclusive		No	ATM:c.609C>T;p.Asp203Asp

NR : not reported

Supplementary Table S2: List of *TP53* pathogenic mutations identified on tumor testing and their corresponding allelic frequency.

Patient	<i>TP53</i> mutation	Variant localization	Variant type	Variant frequency	Immunohistochemistry
P1	c.743 G>A;p.Arg248Gln	Exon 7	Missense	0,8	NR
P2	c.657_668del;p.Pro219_Pro223del	Exon 6	Frameshift	0,32	Positive
P3	c.375+1G>T; p.?	Intron 4	Splicing	0,45	NR
P4	c.97-1G>C ; p.?	Intron 3	Splicing	0,15	NR
P5	c.468_469insCCGGCACCCGC;p.Arg156_Val157fs	Exon 5	Frameshift	0,32	Negative
P6	c.711G>A p.Met237Ile	Exon 7	Missense	0,54	Positive
P7	c.517G>A;p.Val173Met	Exon 5	Missense	0,59	Positive
P8	c.672+1G>A; p.?	Intron 6	Splicing	0,15	Negative
P9	c.527G>A;p.Cys176Tyr	Exon 5	Missense	0,89	Positive
P10	c.976G>T;p.Glu326*	Exon 9	Nonsense	0,73	Positive
P11	c.394A>G ; p.Lys132Glu	Exon 5	Missense	0,63	NR
P12	c.809T>C; p.Phe270Ser	Exon 8	Missense	0,53	NR

P13	c.673-1G>C; p.?	Intron 6	Splicing	0,55	Negative
P14	c.464C>A;p.Thr155Asn	Exon 5	Missense	0,0211	NR
P15	c.307_308insGAAAACCT;p.Tyr103_Gln104fs	Exon 4	Frameshift	0,32	Negative
P16	c.262delG; p.Ala88fs	Exon 4	Frameshift	0,68	Negative
P17	c.742C>T;p.Arg248Trp	Exon 7	Missense	0,57	Positive
P18	c.587G>C;p.Arg196Pro	Exon 6	Missense	0,68	Positive
P19	c.764T>G; p.Ile255Thr	Exon 7	Missense	0,48	NR
P20	c.120_126del; p.Met40fs	Exon 4	Frameshift	0,59	Negative
P21	c.742C>T; p.Arg248Trp	Exon 7	Missense	0,91	Positive
P22	c.722G>T;p.Glu258*	Exon 7	Nonsense	0,72	Positive
P23	c.638G>T;p.Arg213Leu	Exon 6	Missense	0,52	NR
P24	c.406C>T;p.Gln136*	Exon 5	Nonsense	0,39	NR
P25	c.524 G>A;p.Arg175His	Exon 5	Missense	0,66	Positive
P26	c.743 G>A;p.Arg248Gln	Exon 7	Missense	0,64	Positive
P27	c.338T>C;p.Phe113Ser	Exon 4	Missense	0,32	Positive
P28	c.257_279del;p.Ala86fs	Exon 4	Frameshift	0,52	NR
P29	c.455_456insC; p.Pro152_Pro153fs	Exon 5	Frameshift	0,47	Negative
P30	c.670G>T; p.Glu224*	Exon 6	Nonsense	0,87	NR
P31	c.524 G>A;p.Arg175His	Exon 5	Missense	0,92	Positive
P32	c.578A>T;p.His193Leu	Exon 6	Missense	0,24	NR
P33	c.559+1G>T ; p.?	Intron 5	Splicing	0,1	Negative
P34	c.863del;p.Asn288fs	Exon 8	Frameshift	0,42	Positive
P35	c.775_776insG;p.Asp259_Ser260fs	Exon 7	Frameshift	0,8	NR
P36	c.351del; p.Gly117fs	Exon 4	Frameshift	0,29	NR
P37	c.701A>G;p.Tyr234Cys	Exon 7	Missense	0,7	NR
P38	c.464C>A;p.Thr155Asn	Exon 5	Missense	0,59	NR
P39	c.581T>C;p.Leu194Pro	Exon 6	Missense	0,59	Positive
P40	c.713G>A;p.Cys238Tyr	Exon 7	Missense	0,5	Positive
P41	c.393_395del;p.Asn131_Lys132del	Exon 5	Frameshift	0,6	NR
P42	c.833_834insC ; p.Gly279fs	Exon 8	Frameshift	Not reported	Negative
P43	c.542G>C;p.Arg181Pro	Exon 5	Missense	0,93	Positive
P44	c.766A>C;p.Thr256Pro	Exon 7	Missense	0,57	Positive
P45	c.569del;p.Pro190fs	Exon 6	Frameshift	0,60	NR

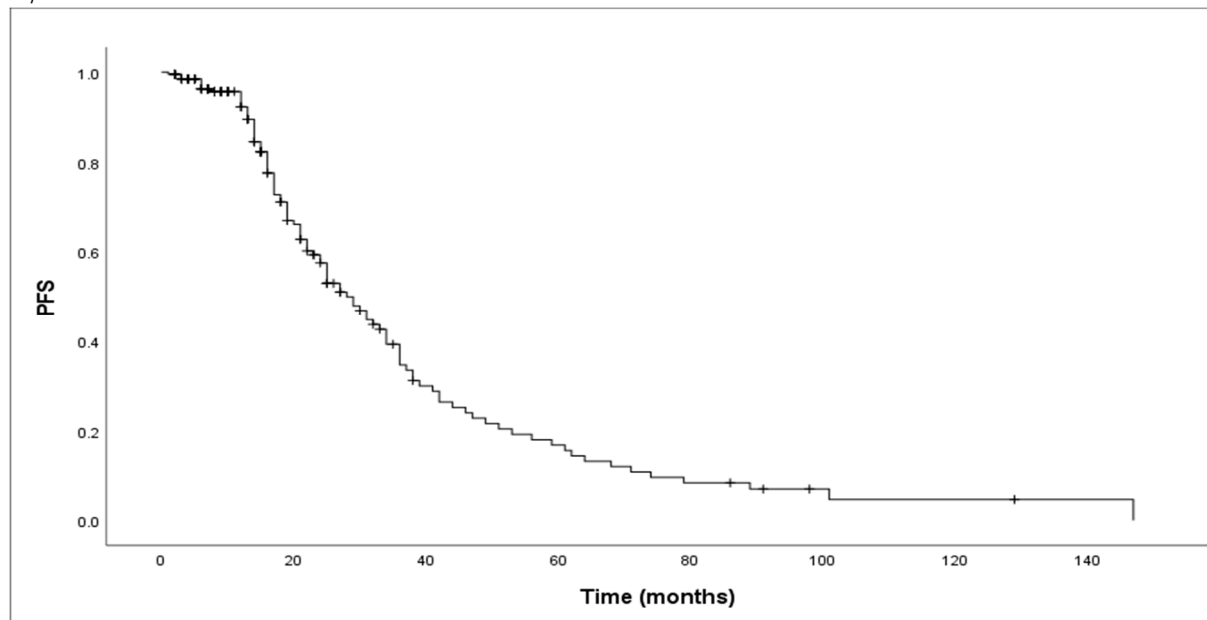
P46	c.856_861del;p.Glu286_Glu287del	Exon 8	Frameshift	0,19	Positive
P47	c.403T>C;p.Cys135Arg	Exon 5	Missense	0,18	Positive
P48	c.840A>C;p.Arg280Ser	Exon 8	Missense	0,62	NR
P49	c.702C>A;p.Tyr234*	Exon 7	Nonsense	0,68	Negative
P50	c.526T>A;p.Cys176Ser	Exon 5	Missense	Not reported	Positive
P51	c.613T>G;p.Tyr205Asp	Exon 6	Missense	0,38	NR
P52	c.646G>A;p.Val216Met	Exon 6	Missense	0,22	Positive
P53	c.375+5del;p.?	Intron 4	Splicing	0,057	Positive
P54	c.475G>C;p.Ala159Pro	Exon 5	Missense	0,07	Positive
P55	c.518T>C;p.Val173Ala	Exon 5	Missense	0,09	NR
P56	c.527G>A;p.Cys176Tyr	Exon 5	Missense	0,01	Positive
P57	c.672+1G>A;p.?	Intron 6	Splicing	0,75	Negative
P58	c.743G>A;p.Arg248Gln	Exon 7	Missense	0,61	Positive
P59	c.517G>T;p.Val173Leu	Exon 5	Missense	0,43	Positive
P60	c.422G>A;p.Cys141Tyr	Exon 5	Missense	0,29	NR
P61	c.224del;p.Pro75fs	Exon 4	Frameshift	Not reported	Negative
P62	c.743 G>A;p.Arg248Gln	Exon 7	Missense	0,22	NR
P63	c.1049T>C;p.Leu350Pro	Exon 10	Missense	0,48	NR
P64	c.517G>A;p.Val173Met	Exon 5	Missense	0,82	Positive
P65	c.832C>T;p.Pro278Ser	Exon 8	Missense	0,59	Positive
P66	c.713G>A;p.Cys238Tyr	Exon 7	Missense	0,71	NR
P67	c.527G>T;p.Cys176Phe	Exon 5	Missense	0,44	Positive
P68	c.518T>G;p.Val173Gly	Exon 5	Missense	0,44	Positive
P69	c.625A>T;p.Arg209*	Exon 6	Nonsense	0,61	Negative
P70	c.490A>G; p.Lys164Glu	Exon 5	Missense	0,35	Positive
P71	c.455_456insC;p.Pro152_Pro153fs	Exon 5	Frameshift	0,63	NR
P72	c.983del;p.Phe328fs	Exon 9	Frameshift	0,47	Negative
P73	c.824G>T;p.Cys275Phe	Exon 8	Missense	Not reported	Positive
P74	c.711G>A;p.Met237Ile	Exon 7	Missense	0,62	Positive
P75	c.146delA;p.Asp49fs	Exon 4	Frameshift	0,36	Positive
P76	c.742 C>T;p.Arg248Trp	Exon 7	Missense	0,40	Positive
P77	c.742C>T;p.Arg248Trp	Exon 7	Missense	0,15	NR
P78	c.470T>G;p.Val157Gly	Exon 5	Missense	0,35	Positive

P79	c.856G>T;p.Glu286*	Exon 8	Nonsense	0,78	NR
P80	c.916C>T ; p.Arg306*	Exon 8	Nonsense	0,48	Positive
P81	c.373A>C;p.Thr125Pro	Exon 4	Missense	0,74	NR
P82	c.395A>G;p.Lys132Arg	Exon 5	Missense	0,27	Positive
P83	c.818G>A;p.Arg273His	Exon 8	Missense	0,2	Positive
P84	c.488_489insTA;p.Lys164fs	Exon 5	Frameshift	0,79	NR
P85	c.150T>A;p.Ile50Ile p.Glu51Lysfs*67	Exon 4	Nonsense	0,14	Negative
P85	c.151_166delGAACAATGGTTCACTG;p.Glu51fs	Exon 4	Frameshift	0,14	Negative
P86	c.202G>T ; p.Glu68*	Exon 4	Nonsense	0,45	Negative
P87	c.1024C>T ; p.Arg342*	Exon 10	Nonsense	0,59	Negative
P88	c.584T>C;p.Ile195Thr	Exon 6	Missense	0,30	NR
P89	c.583A>T;p.Ile195Phe	Exon 6	Missense	0,07	NR
P90	c.402T>G;p.Phe134Leu	Exon 5	Missense	0,84	NR
P91	c.994-1G>A;p.?	Intron 9	Splicing	0,11	NR
P92	c.839G>C;p.Arg280Thr	Exon 8	Missense	0,47	Positive
P93	c.833C>T;p.Pro278Leu	Exon 8	Missense	0,76	Positive
P94	c.586C>T;p.Arg196*	Exon 6	Nonsense	0,67	Positive
P95	c.707A>G;p.Tyr236Cys	Exon 7	Missense	0,48	Negative
P96	c.542_559+6del;p.?	Exon 5	Splicing	0,26	Positive
P97	c.934dup ; p.Thr312fs	Exon 9	Frameshift	0,61	Negative
P98	c.711G>A ; p.Met237Ile	Exon 7	Missense	0,39	NR
P99	c.388C>T;p.Leu130Phe	Exon 5	Missense	0,02	NR
P100	c.524 G>A ; p.Arg175His	Exon 5	Missense	0,83	NR
P101	c.586C>T, p.Arg196*	Exon 6	Nonsense	0,20	Positive
P102	c.614A>G;p.Tyr205Cys	Exon 6	Missense	0,54	NR
P103	c.844C>T;p.Arg282Trp	Exon 8	Missense	0,81	Positive
P104	c.574C>T; p.Gln92*	Exon 6	Nonsense	0,85	Positive
P105	c.747G>T;p.Arg249Ser	Exon 7	Missense	0,04	NR
P106	c.681_682insT;p.Ser227_Asp228fs	Exon 7	Frameshift	0,42	Positive
P107	c.216_217insC;p.Pro72fs	Exon 4	Frameshift	0,69	Negative
P108	c.403T>G;p.Cys135Gly	Exon 5	Missense	0,62	Negative
P109	c.818_827del; p.Arg273fs	Exon 8	Frameshift	Not reported	NR
P110	c.450_473del;p.Thr150_Arg158del	Exon 5	Frameshift	0,53	Positive

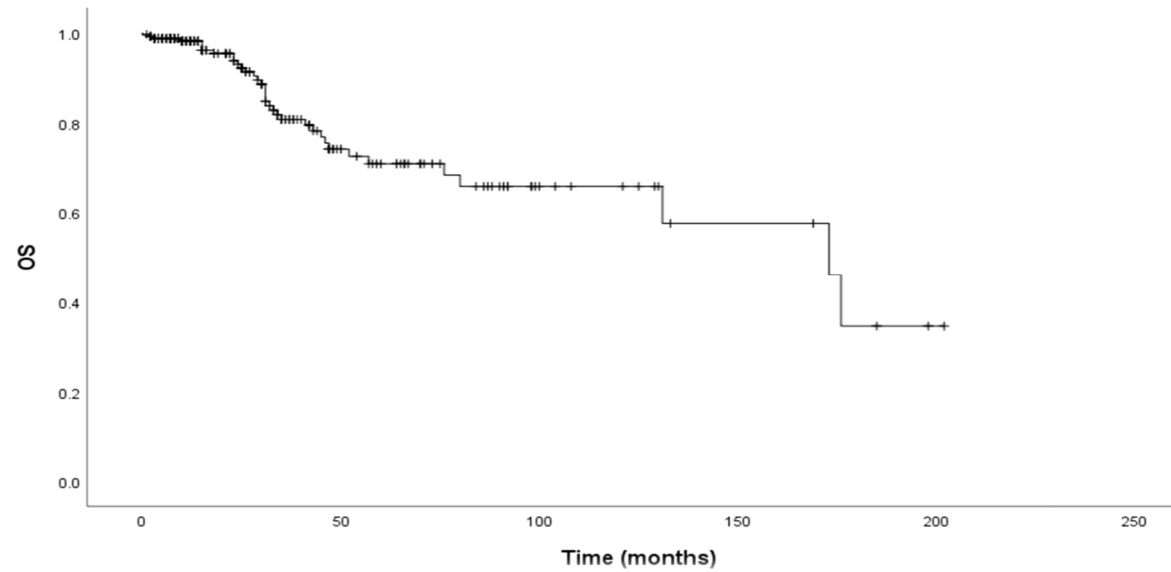
P111	c.783-1_784delinsCTT;p.?	Intron 7	Splicing	0,20	NR
P112	c.818_827del;p.Arg273fs	Exon 8	Frameshift	0,25	Negative
P113	c.380C>T;p.Ser127Phe	Exon 5	Missense	0,62	NR
P114	c.814G>A;p.Val272Met	Exon 8	Missense	0,66	Positive
P115	c.824G>A;p.Cys275Tyr	Exon 8	Missense	0,62	NR
P116	c.524G>A;p.Arg175His	Exon 5	Missense	0,47	Positive
P117	c.644G>T;p.Ser215Ile	Exon 6	Missense	0,05	NR
P118	c.422G>A;p.Cys141Tyr	Exon 5	Missense	0,68	NR
P119	c.517G>T ; p.Val173Leu	Exon 5	Missense	0,02	Positive
P120	c.586C>T;p.ARG196*	Exon 6	Nonsense	0,26	NR
P121	c.659A>G;p.Tyr220Cys	Exon 6	Missense	0,22	NR
P122	c.151delG;p.Glu51fs	Exon 4	Frameshift	0,52	NR
P123	c.817 C>T; p.Arg273Cys	Exon 8	Missense	0,16	Negative
P124	c.394A>G;p.Lys132Glu	Exon 5	Missense	0,15	Positive
P125	c.159_198del;p.Trp53fs	Exon 4	Frameshift	0,15	NR
P126	c.782+1G>A	Intron 7	Splicing	0,21	NR
P127	c.742 C>T;p.Arg248Trp	Exon 7	Missense	0,27	NR
P128	c.461G>T;p.Gly154Val	Exon 5	Missense	0,71	NR
P129	c.526T>G ; p.Cys176Glu	Exon 5	Missense	0,72	Positive
P130	c.309C>G ; p.Tyr103*	Exon 4	Nonsense	0,14	Positive
P131	c.711G>T ; p.Met237Ile	Exon 7	Missense	0,75	Negative
P132	c.445_446insT ; p.Ser149fs	Exon 5	Frameshift	0,43	Positive
P133	c.610G>T ; p.Glu204*	Exon 6	Nonsense	0,93	NR
P134	c.974_984del ; p.Gly325fs	Exon 9	Frameshift	0,42	NR
P135	c.659A>G ; p.Tyr220Cys	Exon 6	Missense	0,76	NR
P136	c.1025G>A ; p.Arg342Gln	Exon 10	Missense	0,35	NR
P137	c.524 G>A ; p.Arg175His	Exon 5	Missense	0,42	NR
P138	c.392A>T ; p.Asn131Ile	Exon 5	Missense	0,46	NR
P139	c.439_449del ; p.p.Val147fs	Exon 5	Frameshift	0,52	NR
P140	c.645T>G ; p.Ser215Arg	Exon 6	Missense	0,70	Negative
P141	c.743 G>A ; p.Arg248Gln	Exon 7	Missense	0,80	Positive
P142	c.398T>G ; p.Met133Arg	Exon 5	Missense	0,35	Positive
P143	c.766_767insA ; p.Thr256_Leu257fs	Exon 7	Frameshift	0,54	Positive

P144	c.537T>A ; p.His179Gln	Exon 5	Missense	0,75	NR
P145	c.955_956del ; p.Lys319fs	Exon 9	Frameshift	0,40	Positive
P146	c.517G>T ; p.Val173Leu	Exon 5	Missense	0,43	Negative
P147	c.376-2A>G	Intron 4	Splicing	0,70	Positive
P148	c.706T>C ; p.Tyr236His	Exon 7	Missense	0,35	Positive
P149	c.818G>T ; p.Arg273Leu	Exon 8	Missense	0,72	NR
P150	c.824G>A ; p.Cys275Tyr	Exon 8	Missense	0,74	Positive
P151	c.824G>A ; p.Cys275Tyr	Exon 8	Missense	0,22	Positive
P152	c.396G>T ; p.Lys132Asn	Exon 5	Missense	0,64	Positive
P153	c.338T>C ; p.Phe113Ser	Exon 4	Missense	0,89	Positive
P154	c.713G>T ; p.Cys238Phe	Exon 7	Missense	0,33	NR
P155	c.1010G>T ; p.Arg337Leu	Exon 10	Missense	0,52	NR
P156	c.1024C>T ; p.Arg342*	Exon 10	Nonsense	0,19	Positive
P157	c.273G>A ; p.Trp91*	Exon 4	Nonsense	0,28	Positive
P158	c.734G>A ; p.Gly245Asp	Exon 7	Missense	0,39	NR
P159	c.659A>G ; p.Tyr220Cys	Exon 6	Missense	0,72	NR
P160	c.824G>A ; p.Cys275Tyr	Exon 8	Missense	0,62	Positive
P161	c.743 G>A ; p.Arg248Gln	Exon 7	Missense	0,53	Positive
P162	c.818 G>T ; p.Arg273Leu	Exon 8	Missense	0,48	NR
P163	c.376-2A>G	Intron 4	Splicing	0,90	Positive
P164	c.818 G>A ; p.Arg273His	Exon 8	Missense	0,56	NR
P165	c.637C>T ; p.Arg213*	Exon 6	Nonsense	0,71	NR
P166	c.209_231del ; p.Ala70fs	Exon 4	Frameshift	0,56	NR
P167	c.818G>T ; p.Arg273Leu	Exon 8	Missense	0,23	NR
P168	c.658T>C ; p.Tyr220His	Exon 6	Missense	0,60	NR

A/



B/



Supplementary Figure S1. A/ Progression free survival (PFS) curve oh the cohort. B/Overall survival (OS) curve of the cohort.