

**Figure S1** Mutation spectrum of the 72 osimertinib-treated patients at baseline. The patient number is indicated at the bottom of the oncoprint. Each column represents a patient and each row represents a gene. Numbers on the left represent the percentage of patients with mutations in a specific gene. Top plot represents the overall number of mutations a patient carried. Different colors denote different types of mutations.

**Table S1** Detailed information on the allelic fraction (AF) and maximum allelic fraction (maxAF) of all patient samples at various timepoints

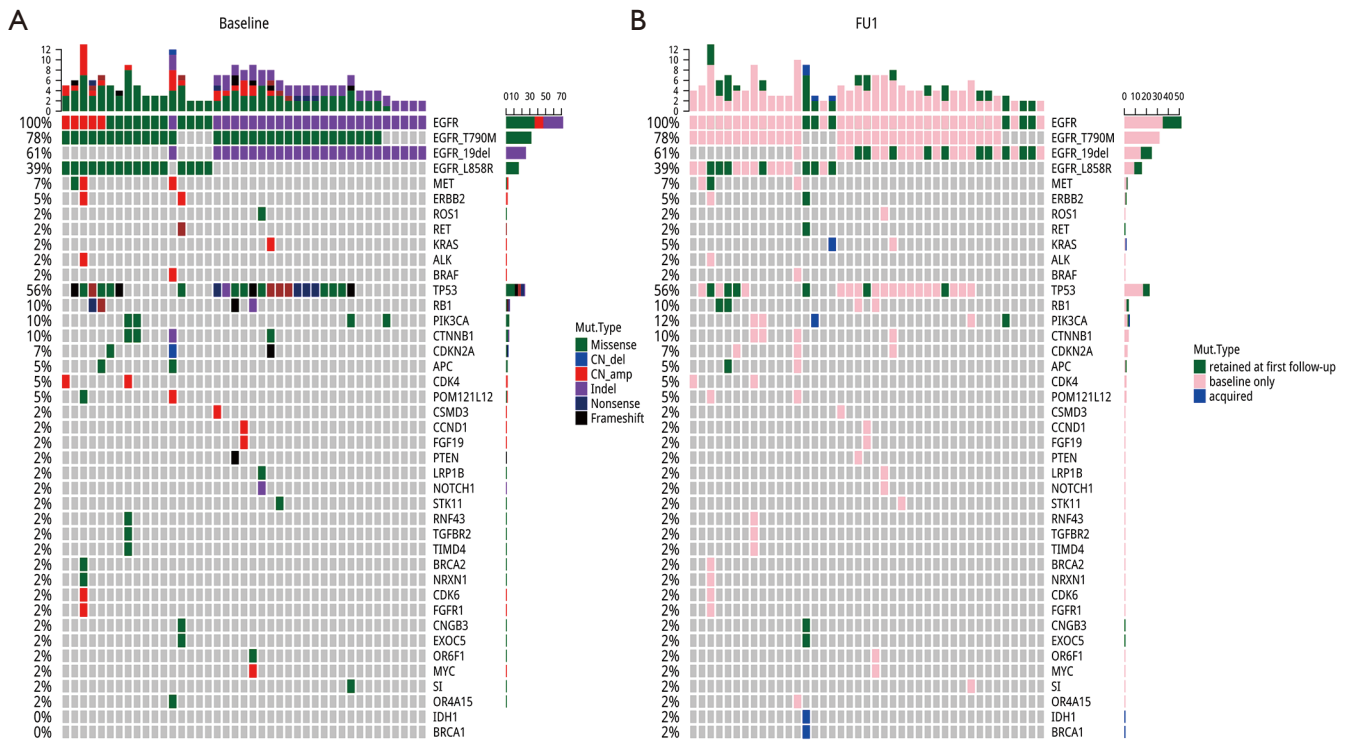
Patient ID	Timepoint	T790M status at baseline	ctDNA clearance status at F1	Gene	Mutation type	Exon number	Variant	AF	maxAF status	Sequencing depth	Chromosome number	Genomic position	dbsnp_ID	COSM_ID	MatchReport	Reference allele (REF)	Variant allele (ALT)	Population Frequency	
P01	baseline	-	-	TP53	missense_variant	7	p.G244S	0.68%	no	22576	17	7577551	NA	COSM10941,COSI	G244	C	T	0	
P01	baseline	present	-	EGFR	missense_variant	20	p.T790M	2.39%	no	29031	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P01	baseline	-	Yes	EGFR	missense_variant	21	p.L858R	3.23%	maxAF	27205	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P01	FU2,FU3	-	-	EGFR	missense_variant	18	p.L718Q	0.90%	no	32010	7	55241705	NA	NA	L718	T	A	0	
P01	FU2,FU3	-	-	EGFR	missense_variant	21	p.L858R	1.47%	maxAF	32035	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P01	FU4	-	-	EGFR	missense_variant	18	p.L718Q	1.05%	no	28333	7	55241705	NA	NA	L718	T	A	0	
P01	FU4	-	-	EGFR	missense_variant	21	p.L858R	1.57%	maxAF	29720	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P02	baseline	-	-	TP53	missense_variant	7	p.M237I	2.30%	no	20647	17	7577570	rs587782664	COSM301404,CO	M237	C	A	0	
P02	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.96%	no	30559	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P02	baseline	-	Yes	EGFR	missense_variant	21	p.L858R	2.80%	maxAF	30575	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P02	FU2	-	-	EGFR	missense_variant	21	p.L858R	0.12%	maxAF	24837	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P02	FU3	-	-	RB1	splice_acceptor_vari	20	c.1961-1G>C	3.54%	no	18631	13	49033823	NA	NA	Exon20_splice_	G	C	0	
P02	FU3	-	-	TP53	missense_variant	7	p.M237I	15.59%	maxAF	19934	17	7577570	rs587782664	COSM301404,CO	M237	C	A	0	
P02	FU3	-	-	POM121L12	missense_variant	1	p.P21H	3.75%	no	33976	7	53103426	NA	NA	P21	C	A	0	
P02	FU3	-	-	EGFR	missense_variant	21	p.L858R	14.52%	no	29857	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P02	FU3	-	-	MET	cn_amp	NA	cn_amp	2.94	no	0.2;4;13;18,7q31.2	7q31.2	NA	NA	CN_gain		29	29 NA	0	
P02	FU4	-	-	RB1	splice_acceptor_vari	20	c.1961-1G>C	6.35%	no	14868	13	49033823	NA	NA	Exon20_splice_	G	C	0	
P02	FU4	-	-	TP53	missense_variant	7	p.M237I	25.81%	maxAF	17421	17	7577570	rs587782664	COSM301404,CO	M237	C	A	0	
P02	FU4	-	-	BRCA1	missense_variant	10	p.E237K	1.16%	no	14264	17	41246839	NA	NA	E237	C	T	0	
P02	FU4	-	-	KIT	stop_gained	11	p.W557X	0.54%	no	16905	4	55593605	NA	COSM1231	LOF	G	A	0	
P02	FU4	-	-	ROS1	missense_variant	36	p.L1937F	0.74%	no	25984	6	117641162	NA	NA	L1937	G	A	0	
P02	FU4	-	-	POM121L12	missense_variant	1	p.P21H	7.75%	no	29700	7	53103426	NA	NA	P21	C	A	0	
P02	FU4	-	-	EGFR	missense_variant	21	p.L858R	19.12%	no	24150	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P03	baseline	-	-	OR2T4	missense_variant	1	p.R171T	1.66%	no	47872	1	248525394	NA	NA	R171	G	C	0	
P03	baseline	-	-	TP53	missense_variant	6	p.L194R	4.93%	no	27897	17	7578268	NA	COSM3403268,C	L194	A	C	4.06E-06	
P03	baseline	-	Yes	EGFR	disruptive_inframe_c	19	p.E746_A750del	24.58%	maxAF	38390	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	GAAGC	0
P03	baseline	present	-	EGFR	missense_variant	20	p.T790M	16.14%	no	52269	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P03	baseline	-	-	EGFR	cn_amp	NA	cn_amp	2.98	no	0.327;16;16;7p11.2	7p11.2	NA	NA	CN_gain		16	16 NA	0	
P03	FU3	-	-	OR2T4	missense_variant	1	p.R171T	1.64%	no	39909	1	248525394	NA	NA	R171	G	C	0	
P03	FU3	-	-	TP53	missense_variant	6	p.L194R	4.90%	no	26758	17	7578268	NA	COSM3403268,C	L194	A	C	4.06E-06	
P03	FU3	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	6.78%	maxAF	25515	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	GAAGC	0
P03	FU3	-	-	EGFR	missense_variant	20	p.T790M	0.29%	no	35120	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05	
P03	FU3	-	-	EGFR	cn_amp	NA	cn_amp	2.38	no	0.431;2;42;7p11.2	7p11.2	NA	NA	CN_gain		16	17 NA	0	
P03	FU3	-	-	MET	cn_amp	NA	cn_amp	3.11	no	0.296;7;10;7q31.2	7q31.2	NA	NA	CN_gain		29	29 NA	0	
P04	baseline	-	-	TP53	missense_variant	7	p.L257P	18.02%	maxAF	23264	17	7577511	NA	COSM1386606,C	L257	A	G	0	
P04	baseline	-	-	CDH18	missense_variant	15	p.S734F	4.84%	no	60100	5	19473507	NA	NA	S734	G	A	0	
P04	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	15.12%	no	30008	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	GAAGC	0
P04	baseline	present	-	EGFR	missense_variant	20	p.T790M	7.11%	no	43111	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P04	baseline	-	-	EGFR	cn_amp	NA	cn_amp	2.52	no	0.151;2;15;7p11.2	7p11.2	NA	NA	CN_gain		16	15 NA	0	
P04	FU4	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.04%	maxAF	27602	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	GAAGC	0
P05	baseline	-	-	TP53	missense_variant	7	p.C242Y	1.00%	no	18017	17	7577556	rs121912655	COSM2744612,C	C242	C	T	0	
P05	baseline	present	Yes	EGFR	missense_variant	20	p.T790M	6.05%	maxAF	24327	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P05	baseline	-	-	EGFR	missense_variant	21	p.L858R	5.17%	no	26087	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P05	FU3	-	-	EGFR	missense_variant	20	p.T790M	0.31%	no	27326	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P05	FU3	-	-	EGFR	missense_variant	21	p.L858R	0.69%	maxAF	21879	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P05	FU5	-	-	EGFR	missense_variant	21	p.L858R	0.14%	maxAF	26420	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P06	baseline	-	-	CTNBN1	missense_variant	3	p.S37F	1.40%	no	35311	3	41266113	rs121913403	COSM5662	S37	C	T	0	
P06	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.80%	no	33652	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P06	baseline	-	-	EGFR	missense_variant	21	p.L858R	2.74%	maxAF	32212	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P06	baseline	-	-	MET	missense_variant	6	p.D597H	1.74%	no	34483	7	116395496	rs769073123	NA	D597	G	C	0	
P06	baseline	-	-	TP53	stop_gained	10	p.R342X	5.72%	no	17666	17	7574003	rs730882029	COSM99721,COSI	LOF	G	A	0	
P08	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	10.57%	maxAF	22956	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	GAAGC	0
P08	baseline	present	-	EGFR	missense_variant	20	p.T790M	4.99%	no	32748	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P08	baseline	-	-	EGFR	cn_amp	NA	cn_amp	2.33	no	0.217;3;11;7p11.2	7p11.2	NA	NA	CN_gain		16	14 NA	0	
P09	baseline	-	-	APC	missense_variant	16	p.N827Y	1.61%	no	21207	5	112173770	NA	NA	N827	A	T	0	
P09	baseline	-	-	ERBB2	cn_amp	NA	cn_amp	2.38	no	0.424;2;40;17q12	17q12	NA	NA	CN_gain		18	17 NA	0	
P09	baseline	-	-	RB1	frameshift_variant	2	p.F57fs	25.24%	no	22146	13	48881444	NA	NA	LOF	GATTTT	G	T	0
P09	baseline	present	-	EGFR	missense_variant	20	p.T790M	21.82%	no	90465	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P09	baseline	-	Yes	EGFR	missense_variant	21	p.L858R	63.94%	maxAF	72434	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P09	baseline	-	-	TP53	missense_variant	8	p.R273L	23.65%	no	24752	17	7577120	rs28934576	COSM3675521,C	R273	C	A	4.07E-06	
P09	baseline	-	-	EGFR	cn_amp	NA	cn_amp	5.28	no	0.234;19;14;7p11.2	7p11.2	NA	NA	CN_gain		16	16 NA	0	
P09	baseline	-	-	CDK6	cn_amp	NA	cn_amp	3.99	no	0.273;4;26;7q21.2	7q21.2	NA	NA	CN_gain		7	7 NA	0	
P09	baseline	-	-	FGFR1	cn_del	NA	cn_del	1.67	no	0.406;2;38;8p11.22	8p11.22	NA	NA	CN_loss		9	7 NA	0	
P09	baseline	-	-	MYC	cn_amp	NA	cn_amp	2.37	no	0.157;1;16;8q24.21	8q24.21	NA	NA	CN_gain		8	6 NA	0	
P09	FU2	-	-	RB1	frameshift_variant	2	p.F57fs	1.41%	no	24385	13	48881444	NA	NA	LOF	GATTTT	G	0	
P09	FU2	-	-	TP53	missense_variant	8	p.R273L	1.99%	no	31591	17	7577120	rs28934576	COSM3675521,C	R273	C	A	4.07E-06	
P09	FU2	-	-	EGFR	missense_variant	21	p.L858R	7.67%	maxAF	34879	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P09	FU3	-	-	RB1	frameshift_variant	2	p.F57fs	4.35%	no	27756	13	48881444	NA	NA	LOF	GATTTT	G	0	
P09	FU3	-	-	TP53	missense_variant	8	p.R273L	6.08%	no	34185	17	7577120	rs28934576	COSM367552					

Patient ID	Timepoint	T790M status at baseline	ctDNA clearance status at F1	Gene	Mutation type	Exon number	Variant	AF	maxAF status	Sequencing depth	Chromosome number	Genomic position	dbsnp_ID	COSM_ID	MatchReport	Reference allele (REF)	Variant allele (ALT)	Population Frequency	
P12	FU1,FU2,FU3	-	-	RB1	splice_donor_variant	13	c.1332+1dup	0.52%	no	24369	13	48951169	NA	NA	Exon13_splice_	A	AG	0	
P12	FU1,FU2,FU3	-	-	TP53	missense_variant	6	p.H214R	0.86%	no	35738	17	757208	NA	COSM3388198.C1	H214	T	C	0	
P12	FU1,FU2,FU3	-	-	APC	missense_variant	21	p.N1533S	0.63%	no	19222	5	112175889	NA	NA	N1533	A	G	0	
P12	FU1,FU2,FU3	-	No	EGFR	missense_variant	16	p.L858R	2.74%	maxAF	36293	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P12	FU4	-	-	RB1	splice_donor_variant	13	c.1332+1dup	3.24%	no	28451	13	48951169	NA	NA	Exon13_splice_	A	AG	0	
P12	FU4	-	-	TP53	missense_variant	6	p.H214R	4.97%	no	33603	17	757208	NA	COSM3388198.C1	H214	T	C	0	
P12	FU4	-	-	APC	missense_variant	21	p.N1533S	3.05%	no	19588	5	112175889	NA	NA	N1533	A	G	0	
P12	FU4	-	-	EGFR	missense_variant	16	p.L858R	9.55%	maxAF	40041	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P12	FU5	-	-	MET	cn_amp	NA	NA	2.56	no	0.369,15,10	7q31.2	7q31.2	NA	NA	cn_gain	A	29	29 NA	
P12	FU5	-	-	RB1	splice_donor_variant	13	c.1332+1dup	11.11%	no	22012	13	48951169	NA	NA	Exon13_splice_	A	AG	0	
P12	FU5	-	-	TP53	missense_variant	6	p.H214R	20.02%	no	27661	17	757208	NA	COSM3388198.C1	H214	T	C	0	
P12	FU5	-	-	APC	missense_variant	21	p.N1533S	11.27%	no	15977	5	112175889	NA	NA	N1533	A	G	0	
P12	FU5	-	-	EGFR	missense_variant	16	p.L858R	25.73%	maxAF	35610	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P12	FU5	-	-	EGFR	cn_amp	NA	NA	2.37	no	0.371,9,26,;7p11.2	7p11.2	7p11.2	NA	NA	cn_gain	A	16	15 NA	
P12	baseline	-	-	PIK3CA	missense_variant	10	p.E542K	0.30%	maxAF	11681	3	178936082	rs121913273	COSM760,COSM1	E542	G	A	0	
P14	baseline	absent	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.25%	no	22128	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0	
P14	FU1,FU2,FU3	-	No	PIK3CA	missense_variant	10	p.E542K	0.12%	maxAF	11720	3	178936082	rs121913273	COSM760,COSM1	E542	G	A	0	
P14	FU1,FU2,FU3	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.07%	no	24936	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0	
P14	FU4	-	-	TP53	missense_variant	8	p.E286K	0.65%	no	30634	17	7577082	rs786201059	COSM99924,COSI	E286	C	T	0	
P14	FU4	-	-	PIK3CA	missense_variant	10	p.E542K	1.24%	maxAF	10319	3	178936082	rs121913273	COSM760,COSM1	E542	G	A	0	
P14	FU4	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.24%	no	20313	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0	
P14	FU5	-	-	TP53	missense_variant	8	p.E286K	4.10%	no	33303	17	7577082	rs786201059	COSM99924,COSI	E286	C	T	0	
P14	FU5	-	-	TP53	missense_variant	8	p.R273C	0.15%	no	24216	17	7577121	rs121913343	COSM1645518.C1	R273	G	A	5.81E-05	
P14	FU5	-	-	PIK3CA	missense_variant	10	p.E542K	5.93%	maxAF	12277	3	178936082	rs121913273	COSM760,COSM1	E542	G	A	0	
P14	FU5	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	1.07%	no	20405	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0	
P15	baseline	-	-	TP53	stop_gained	8	p.R306X	2.48%	no	35095	17	7577022	rs121913344	COSM1640820.C1	LOF	G	A	0	
P15	baseline	-	-	EGFR	conservative_infram	19	p.E746_A750del	11.00%	maxAF	28628	7	55242465	rs727504233	COSM6225	Exon19_infram	GGAATTAAGAG	A	0	
P15	baseline	present	-	EGFR	missense_variant	20	p.T790M	4.23%	no	38279	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P15	baseline	-	-	EGFR	cn_amp	NA	NA	2.42	no	0.353,11,11	7p11.2	7p11.2	NA	NA	cn_gain	A	16	15 NA	
P15	baseline	-	-	CSMD3	cn_amp	NA	NA	2.51	no	NA,0,NA	8q23.3	8q23.3	NA	NA	cn_gain	5	5 NA		
P16	baseline	-	-	CNDN1	cn_amp	NA	NA	2.36	no	0.434,4,42,;11q13.3	11q13.3	11q13.3	NA	NA	cn_gain	6	3 NA		
P16	baseline	-	-	FGFR1	cn_amp	NA	NA	2.39	no	0.421,2,42,;11q13.3	11q13.3	11q13.3	NA	NA	cn_gain	5	4 NA		
P16	baseline	-	-	TP53	missense_variant	7	p.R249S	13.38%	no	18106	17	7577534	NA	COSM1679495.C1	R249	C	G	0	
P16	baseline	-	-	EGFR	disruptive_inframe_c	19	p.L747_A750delir	43.02%	maxAF	38315	7	55242465	rs121913436	NA	Exon19_infram	GGAATTAAGAG	A	GGAAC	0
P16	baseline	present	-	EGFR	missense_variant	20	p.T790M	20.20%	no	54903	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P16	baseline	-	-	EGFR	cn_amp	NA	NA	3.25	no	0.306,17,20	7p11.2	7p11.2	NA	NA	cn_gain	16	16 NA		
P16	FU1	-	-	TP53	missense_variant	7	p.R249S	1.74%	no	21058	17	7577534	NA	COSM1679495.C1	R249	C	G	0	
P16	FU1	-	No	EGFR	disruptive_inframe_c	19	p.L747_A750delir	7.06%	maxAF	24323	7	55242465	rs121913436	NA	Exon19_infram	GGAATTAAGAG	A	GGAAC	0
P16	FU2,FU3	-	-	TP53	missense_variant	7	p.R249S	9.87%	no	18809	17	7577534	NA	COSM1679495.C1	R249	C	G	0	
P16	FU2,FU3	-	-	BRAF	missense_variant	15	p.V600E	1.82%	no	23717	7	140453136	rs113488022	COSM476	V600	A	T	4.07E-06	
P16	FU2,FU3	-	-	EGFR	disruptive_inframe_c	19	p.L747_A750delir	22.18%	maxAF	25558	7	55242465	rs121913436	NA	Exon19_infram	GGAATTAAGAG	A	GGAAC	0
P16	FU2,FU3	-	-	EGFR	cn_amp	NA	NA	2.51	no	0.361,14,22	7p11.2	7p11.2	NA	NA	cn_gain	16	5 NA		
P16	FU2,FU3	-	-	BRAF	cn_amp	NA	NA	2.71	no	NA,0,NA	7q34	7q34	NA	NA	cn_gain	5	5 NA		
P16	FU4	-	-	TP53	missense_variant	7	p.R249S	17.48%	no	19724	17	7577534	NA	COSM1679495.C1	R249	C	G	4.07E-06	
P16	FU4	-	-	BRAF	missense_variant	15	p.V600E	0.34%	no	29687	7	140453136	rs113488022	COSM476	V600	A	T	4.07E-06	
P16	FU4	-	-	EGFR	disruptive_inframe_c	19	p.L747_A750delir	30.59%	maxAF	26853	7	55242465	rs121913436	NA	Exon19_infram	GGAATTAAGAG	A	GGAAC	0
P16	FU4	-	-	EGFR	cn_amp	NA	NA	2.64	no	0.357,15,31	7p11.2	7p11.2	NA	NA	cn_gain	16	5 NA		
P16	FU4	-	-	BRAF	cn_amp	NA	NA	3.34	no	NA,0,NA	7q34	7q34	NA	NA	cn_gain	5	5 NA		
P17	baseline	-	-	EGFR	conservative_infram	19	p.E746_A750del	0.15%	maxAF	30589	7	55242465	rs727504233	COSM6225	Exon19_infram	GGAATTAAGAG	A	0	
P18	baseline	present	-	EGFR	missense_variant	20	p.T790M	0.20%	no	29204	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05	
P18	baseline	-	-	EGFR	missense_variant	21	p.L858R	0.44%	maxAF	30412	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P19	baseline	-	No	EGFR	disruptive_inframe_c	19	p.L747_T751del	0.07%	maxAF	27378	7	55242467	rs121913442	COSM23571	Exon19_infram	AATTAAGAGAA	A	0	
P19	FU1,FU2	-	-	EGFR	disruptive_inframe_c	19	p.L747_T751del	0.02%	maxAF	30136	7	55242467	rs121913442	COSM23571	Exon19_infram	AATTAAGAGAA	A	0	
P20	baseline	-	-	PIK3CA	missense_variant	21	p.H1047L	1.10%	no	16705	3	178952085	rs121913279	COSM94987	H1047	A	T	0	
P20	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.21%	no	5706	7	55249071	rs121434569	COSM6240	T790	C	T	0	
P20	baseline	-	-	EGFR	missense_variant	21	p.L858R	3.88%	maxAF	12315	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P20	baseline	-	-	CTNBN1	missense_variant	3	p.A13S	0.97%	no	12770	3	41266040	NA	NA	A13	G	T	0	
P20	FU1,FU2	-	No	EGFR	missense_variant	21	p.L858R	0.19%	maxAF	13890	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P20	FU4	-	-	EGFR	missense_variant	21	p.L858R	0.28%	maxAF	39605	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P22	baseline	absent	-	EGFR	missense_variant	21	p.L858R	36.07%	maxAF	17421	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P22	baseline	-	-	TP53	missense_variant	8	p.R273L	13.86%	no	12594	17	7577120	NA	COSM3675521	R273	C	A	0	
P22	baseline	-	-	BRCA1	splice_region_varian	11	NA	1.75%	no	11446	17	41242938	NA	NA	Exon11_splice_	GCACA	GCA	0	
P22	baseline	-	-	FGFR1	fusion	intergenic_in	LINC00662-FGFR1	3.06%	no	15851	19:2773210	19:27732102_8:	NA	NA	Intron3_fusion	11;13;33;34	2,7;2;12	NA	
P23	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.29%	no	6434	7	55249071	rs121434569	COSM6240	T790	C	T	0	
P23	baseline	-	-	EGFR	missense_variant	21	p.L858R	2.95%	maxAF	15314	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P24	baseline	absent	-	EGFR	missense_variant	21	p.L858R	0.36%	maxAF	14968	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P24	FU1,FU2	-	acquired at FU	PIK3CA	missense_variant	10	p.E545K	0.24%	no	6713	3	178936091	rs104886003	COSM763	E545	G	A	0	
P24	FU1,FU2	-	No	EGFR	missense_variant	21	p.L858R	0.25%	maxAF	10673	7	55259515	rs121434568	COSM6224	L858	T	G	0	
P24	FU3	-	-	TP53	missense_variant														

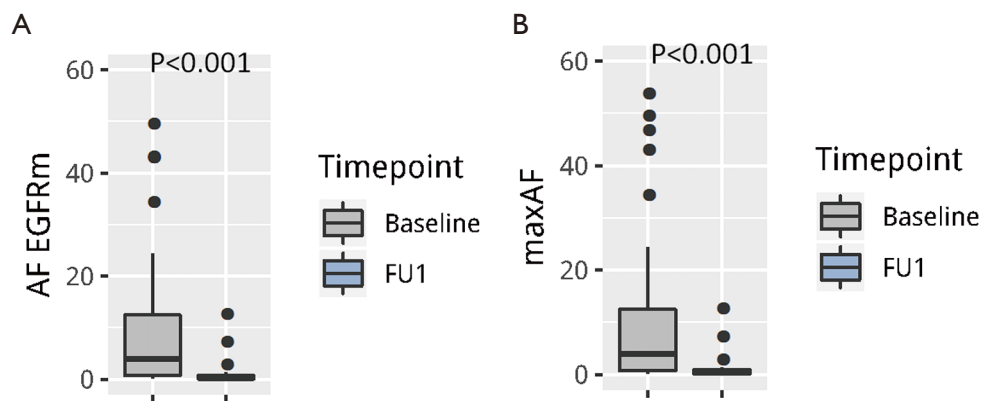
Patient ID	Timepoint	T790M status at baseline	ctDNA clearance status at F1	Gene	Mutation type	Exon number	Variant	AF	maxAF status	Sequencing depth	Chromosome number	Genomic position	dbSNP_ID	COSM_ID	MatchReport	Reference allele (REF)	Variant allele (ALT)	Population Frequency
P26	FU4	-	-	EGFR	conservative_infram	19	p.E746_A750del	5.74%	no	11686	7	55242465	NA	COSM6225	Exon19_infram	GGAAATTAAGAG AAGCA	G	0
P26	FU4	-	-	RB1	missense_variant	6	p.V190M	24.25%	no	8411	13	48923120	NA	NA	V190	G	A	0
P26	FU4	-	-	TP53	missense_variant	6	p.Y220C	24.74%	maxAF	13081	17	7578190	NA	COSM99720	Y220	T	C	0
P26	FU4	-	-	PTEN	frameshift_variant	8	p.T319fs	14.55%	no	10165	10	89720798	rs146650273	COSM4898	LOF	GTACT	G	0
P26	FU4	-	-	RB1	frameshift_variant	6	p.V193fs	23.65%	no	8848	13	48923124	NA	NA	LOF	TA	T	0
P26	FU4	-	-	MYC	cn_amp	NA	cn_amp	2.73	no	NA	8q24.21	8q24.21	NA	NA	CN_gain		23	20 NA
P27	baseline	absent	-	EGFR	missense_variant	21	p.L858R	0.69%	maxAF	13674	7	55259515	rs121434568	COSM6224	L858	T	G	0
P28	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	1.13%	maxAF	17487	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA GAAGC	A	0
P28	baseline	present	-	EGFR	missense_variant	20	p.T790M	0.18%	no	7743	7	55249071	rs121434569	COSM6240	T790	C	T	0
P28	baseline	-	-	TP53	missense_variant	7	p.R248Q	0.31%	no	12989	17	7577538	rs11540652	COSM99602	R248	C	T	2.00E-04
P29	baseline	present	-	EGFR	missense_variant	20	p.T790M	0.34%	no	7727	7	55249071	rs121434569	COSM6240	T790	C	T	0
P29	baseline	-	-	EGFR	missense_variant	21	p.L858R	1.48%	maxAF	15237	7	55259515	rs121434568	COSM6224	L858	T	G	0
P29	baseline	-	-	TP53	missense_variant	8	p.R273H	0.32%	no	15475	17	7577120	rs28934576	COSM99729	R273	C	T	2.00E-04
P29	baseline	-	-	CDKN2A	missense_variant	2	p.H83Y	0.52%	no	8660	9	21971111	rs121913385	COSM99724	H83	G	A	0
P29	FU1,FU2	-	No	TP53	missense_variant	8	p.R273H	0.32%	maxAF	13935	17	7577120	rs28934576	COSM99729	R273	C	T	2.00E-04
P29	FU3	-	-	TP53	missense_variant	8	p.R273H	0.46%	maxAF	32289	17	7577120	rs28934576	COSM10660, COSI	R273	C	T	2.00E-04
P29	FU3	-	-	EGFR	missense_variant	21	p.L858R	0.20%	no	35364	7	55259515	rs121434568	COSM6224	L858	T	G	0
P29	FU4	-	-	TP53	missense_variant	8	p.R273H	0.37%	no	21072	17	7577120	rs28934576	COSM10660, COSI	R273	C	T	2.00E-04
P29	FU4	-	-	TP53	missense_variant	7	p.L257V	2.72%	no	16503	17	7577512	NA	COSM3742462, C1257	G	C	0	
P29	FU4	-	-	EGFR	missense_variant	21	p.L858R	6.39%	maxAF	27370	7	55259515	rs121434568	COSM6224	L858	T	G	0
P29	FU4	-	-	CDKN2A	missense_variant	2	p.H83Y	1.60%	no	10872	9	21971111	rs121913385	COSM1650884, C1	H83	G	A	0
P30	baseline	-	-	EGFR	disruptive_inframe_c	19	p.L747_T751del	10.02%	no	15221	7	55242467	rs121913442	COSM392194	Exon19_infram	AATTAAGAGAA GCAAC	A	0
P30	baseline	present	-	EGFR	missense_variant	20	p.T790M	4.10%	no	7740	7	55249071	rs121434569	COSM6240	T790	C	T	0
P30	baseline	-	-	TP53	missense_variant	8	p.R273H	10.35%	maxAF	14014	17	7577120	rs28934576	COSM99729	R273	C	T	2.00E-04
P30	baseline	-	-	LRP1B	missense_variant	22	p.L1156P	5.83%	no	19490	2	141665499	NA	NA	L1156	A	G	0
P30	baseline	-	-	ROS1	missense_variant	34	p.I1866S	6.16%	no	12441	6	117645539	NA	NA	I1866	A	C	0
P30	baseline	-	-	NOTCH1	conservative_infram	34	p.P2415del	2.13%	no	12114	9	139390944	NA	NA	Exon34_infram	TGTGGTG	TGTTG	0
P31	baseline	-	Yes	EGFR	disruptive_inframe_c	19	p.E746_A750del	2.62%	maxAF	20199	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA GAAGC	A	0
P31	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.70%	no	9085	7	55249071	rs121434569	COSM6240	T790	C	T	0
P31	baseline	-	-	TP53	splice_donor_variant	9	c.993>2T>C	1.74%	no	25362	17	7576851	NA	COSM45552	Exon9_splice_si	A	C	0
P31	baseline	-	-	STK11	missense_variant	4	p.Q159H	0.79%	no	13392	19	1220384	NA	NA	Q159	G	C	0
P31	FU3	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.22%	maxAF	20663	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA GAAGC	A	0
P31	FU3	-	-	EGFR	missense_variant	20	p.T790M	0.18%	no	27568	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05
P31	FU4	-	-	TP53	splice_donor_variant	9	c.993>2T>C	0.57%	maxAF	8666	17	7576851	NA	COSM4170831, C1	Exon9_splice_si	A	G	0
P31	FU4	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.28%	no	11782	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA GAAGC	A	0
P32	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	3.96%	no	12505	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA GAAGC	A	0
P32	baseline	present	-	EGFR	missense_variant	20	p.T790M	2.86%	no	6714	7	55249071	rs121434569	COSM6240	T790	C	T	0
P32	baseline	-	-	TP53	splice_region_varian	10	p.I332S	4.18%	no	6835	17	7574032	NA	NA	Exon10_splice_	A	C	0
P32	baseline	-	-	CTNBN1	missense_variant	3	p.S33F	4.36%	maxAF	15476	3	41266101	rs121913400	COSM5669	S33	C	C	0
P32	baseline	-	-	CDKN2A	frameshift_variant	1	p.Y44fs	3.04%	no	10878	9	21974694	NA	COSM4448825	LOF	CG	C	0
P32	baseline	-	-	KRAS	cn_amp	NA	cn_amp	2.46	no	NA	12p12.1	12p12.1	NA	NA	CN_gain		5	5 NA
P32	FU1,FU2	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.22%	maxAF	17713	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA GAAGC	A	0
P32	FU3	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.16%	maxAF	26196	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA GAAGC	A	0
P32	FU4	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.23%	maxAF	11276	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA GAAGC	A	0
P33	baseline	present	-	EGFR	missense_variant	20	p.T790M	11.65%	no	11174	7	55249071	rs121434569	COSM6240	T790	C	T	0
P33	baseline	-	-	EGFR	missense_variant	21	p.L858R	43.02%	no	17728	7	55259515	rs121434568	COSM6224	L858	T	G	0
P33	baseline	-	-	RB1	stop_gained	13	p.K420X	46.74%	maxAF	13958	13	48951096	NA	NA	LOF	A	T	0
P33	baseline	-	-	TP53	splice_region_varian	8	NA	11.46%	no	14890	17	7576943	NA	NA	Exon8_splice_si	GAGGATAACT GCACCCCTTG	G	0
P33	baseline	-	-	EGFR	cn_amp	NA	cn_amp	2.32	no	NA	7p11.2	7p11.2	NA	NA	CN_gain		20	15 NA
P33	FU1,FU2	-	No	RB1	stop_gained	13	p.K420X	0.98%	maxAF	17364	13	48951096	NA	NA	LOF	A	T	0
P33	FU1,FU2	-	-	EGFR	missense_variant	21	p.L858R	0.70%	no	30904	7	55259515	rs121434568	COSM6224	L858	T	G	0
P33	FU3	-	-	KRTAP5-5	missense_variant	1	p.S151C	0.66%	no	14552	11	1651522	NA	NA	S151	C	G	0
P33	FU3	-	-	ERBB2	cn_amp	NA	cn_amp	2.34	no	NA;0;NA	17q12	17q12	NA	NA	CN_gain		18	17 NA
P33	FU3	-	-	ALK	fusion	Intron13_int	EML4-ALK	0.08%	no	44040	2:42523448	2:42523448_2;2	NA	NA	fusion	1;0;1;2	1;0;0;1	NA
P33	FU3	-	-	RB1	stop_gained	13	p.K420X	35.42%	maxAF	19473	13	48951096	NA	NA	LOF	A	T	0
P33	FU3	-	-	EGFR	missense_variant	20	p.T790M	5.20%	no	37292	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05
P33	FU3	-	-	EGFR	missense_variant	20	p.C797S	0.21%	no	37960	7	55249092	NA	COSM5945664	C797(in-cis_T79	C	C	0
P33	FU3	-	-	EGFR	missense_variant	21	p.L858R	25.15%	no	35795	7	55259515	rs121434568	COSM6224	L858	T	G	0
P33	FU4	-	-	PTEN	cn_del	NA	cn_del	1.49	no	0.179;3;17;1	10q23.31	10q23.31	NA	NA	CN_loss		9	7 NA
P33	FU4	-	-	KRTAP5-5	missense_variant	1	p.S151C	0.52%	no	18127	11	1651522	NA	NA	S151	C	G	0
P33	FU4	-	-	ERBB2	cn_amp	NA	cn_amp	2.59	no	NA;0;NA	17q12	17q12	NA	NA	CN_gain		18	18 NA
P33	FU4	-	-	ALK	fusion	Intron13_int	EML4-ALK	0.06%	no	37326	2:42523448	2:42523448_2;2	NA	NA	fusion	1;0;0;0	1;0;0;0	NA
P33	FU4	-	-	RB1	stop_gained	13	p.K420X	78.89%	maxAF	20194	13	48951096	NA	NA	LOF	A	T	2.00E-05
P33	FU4	-	-	EGFR	missense_variant	20	p.T790M	15.74%	no	45299	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05
P33	FU4	-	-	EGFR	missense_variant	20	p.C797S	0.75%	no	45674	7	55249092	NA	COSM5945664	C797(in-cis_T79	G	C	0
P33	FU4	-	-	EGFR	missense_variant	21	p.L858R	56.41%	no	38569	7	55259515	rs121434568	COSM6224	L858	T	G	0
P33	FU4	-	-	EGFR	cn_amp	NA	cn_amp	2.29	no	0.298;6;16;1	7p11.2	7p11.2	NA	NA	CN_gain		16	12 NA
P33	FU4	-	-	FGFR1	cn_del	NA	cn_del	1.48	no	0.217;2;21;1	8p11.22	8p11.22	NA	NA	CN_loss		9	9 NA
P34	baseline	absent	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.40%	maxAF	13519	7	55242464	rs121913421	COSM62				

Patient ID	Timepoint	T790M status at baseline	ctDNA clearance status at F1	Gene	Mutation type	Exon number	Variant	AF	maxAF status	Sequencing depth	Chromosome number	Genomic position	dbsnp_ID	COSM_ID	MatchReport	Reference allele (REF)	Variant allele (ALT)	Population Frequency
P39	FU4	-	-	EGFR	missense_variant	20	p.T790M	10.39%	no	26757	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05
P39	FU4	-	-	EGFR	missense_variant	20	p.C797S	6.65%	no	24779	7	55249091	NA	NA	C797(in-cis_T79	T	A	0
P39	FU4	-	-	TP53	splice_region_varian	9	c.920-12_920-3del	5.08%	no	23543	17	7576928	NA	NA	Exon9_splice_si	TAGGAAAGAGG	T	0
P39	FU4	-	-	EGFR	cn_amp	NA	cn_amp	2.73	no	0.344;16;10	7p11.2	7p11.2	NA	NA	CN_gain	16	15 NA	0
P40	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	1.01%	maxAF	31228	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0
P40	baseline	present	-	EGFR	missense_variant	20	p.T790M	0.50%	no	11202	7	55249071	rs121434569	COSM6240	T790	C	T	0
P40	FU1,FU2	-	No	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.05%	maxAF	28535	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0
P40	FU4	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.06%	maxAF	30317	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0
P41	baseline	-	-	EGFR	disruptive_inframe_c	19	p.L747_T751del	4.76%	no	17426	7	55242467	rs121913442	COSM392194	Exon19_infram	AGGAATTAAGA	A	0
P41	baseline	present	-	EGFR	missense_variant	20	p.T790M	4.98%	maxAF	18389	7	55249071	rs121434569	COSM6240	T790	C	T	0
P41	baseline	-	-	TP53	stop_gained	9	p.Q317X	1.32%	no	25495	17	7576897	NA	COSM3388166	LOF	G	A	0
P41	FU1	-	No	EGFR	disruptive_inframe_c	19	p.L747_T751del	0.07%	maxAF	20859	7	55242467	rs121913442	COSM23571	Exon19_infram	AATTAAGAGAA	A	0
P41	FU2	-	-	EGFR	disruptive_inframe_c	19	p.L747_T751del	0.03%	maxAF	27737	7	55242467	rs121913442	COSM23571	Exon19_infram	AATTAAGAGAA	A	0
P41	FU3	-	-	EGFR	disruptive_inframe_c	19	p.L747_T751del	0.17%	maxAF	26464	7	55242467	rs121913442	COSM23571	Exon19_infram	AATTAAGAGAA	A	0
P41	FU4	-	-	EGFR	disruptive_inframe_c	19	p.L747_T751del	0.19%	maxAF	28249	7	55242467	rs121913442	COSM23571	Exon19_infram	AATTAAGAGAA	A	0
P42	baseline	absent	-	EGFR	missense_variant	21	p.L858R	0.27%	maxAF	31595	7	55259515	rs121434568	COSM6224	L858	T	G	0
P42	FU1,FU2	-	acquired at FU	KRAS	missense_variant	2	p.G12V	0.16%	no	13678	12	25398284	rs121913529	COSM520,COSM1	G12	C	A	0
P42	FU1,FU2	-	No	EGFR	missense_variant	21	p.L858R	0.34%	maxAF	33353	7	55259515	rs121434568	COSM6224	L858	T	G	0
P42	FU3	-	-	MTOR	splice_region_varian	43	c.6033+5G>T	1.04%	no	33128	1	11188056	NA	NA	Exon43_splice_c	C	A	0
P42	FU3	-	-	KRAS	missense_variant	2	p.G12V	2.01%	no	14955	12	25398284	rs121913529	COSM520,COSM1	G12	C	A	0
P42	FU3	-	-	TP53	stop_gained	6	p.R196X	1.19%	no	32596	17	7578263	rs397516435	COSM99668,COSI	LOF	G	A	8.24E-06
P42	FU3	-	-	KEAP1	missense_variant	2	p.I128F	2.57%	maxAF	26417	19	10610328	NA	NA	I128	T	A	0
P42	FU3	-	-	EGFR	missense_variant	21	p.L858R	1.73%	no	34884	7	55259515	rs121434568	COSM6224	L858	T	G	0
P42	FU3	-	-	CDKN2A	stop_gained	2	p.E69X	0.94%	no	16935	9	21971153	rs121913383	COSM3092316,CI	LOF	C	A	0
P42	FU4	-	-	MTOR	splice_region_varian	43	c.6033+5G>T	0.64%	no	12342	1	11188056	NA	NA	Exon43_splice_c	C	A	0
P42	FU4	-	-	KRAS	missense_variant	2	p.G12V	2.04%	no	10276	12	25398284	rs121913529	COSM520,COSM1	G12	C	A	0
P42	FU4	-	-	TP53	stop_gained	6	p.R196X	2.66%	no	12296	17	7578263	rs397516435	COSM99668,COSI	LOF	G	A	4.06E-06
P42	FU4	-	-	KEAP1	missense_variant	2	p.I128F	3.76%	maxAF	9869	19	10610328	NA	NA	I128	T	A	0
P42	FU4	-	-	EGFR	missense_variant	21	p.L858R	3.19%	no	11955	7	55259515	rs121434568	COSM6224	L858	T	G	0
P42	FU4	-	-	CDKN2A	stop_gained	2	p.E69X	2.19%	no	5032	9	21971153	rs121913383	COSM3092316,CI	LOF	C	A	0
P43	baseline	-	-	BRCA2	missense_variant	10	p.A565S	5.85%	no	18903	13	32907308	NA	NA	A565	G	T	0
P43	baseline	-	-	TP53	missense_variant	8	p.C275Y	17.57%	no	29226	17	7577114	rs863224451	COSM165084,CO	C275	C	T	0
P43	baseline	-	-	ERBB2	cn_amp	NA	cn_amp	2.54	no	0.396;2;40;17	17q12	17q12	NA	NA	CN_gain	18	18 NA	0
P43	baseline	-	-	NRXN1	missense_variant	19	p.V1204L	4.51%	no	42952	2	50463983	NA	COSM5494954,CI	V1204	C	A	4.07E-06
P43	baseline	-	-	ALK	cn_amp	NA	cn_amp	2.32	no	NA;0;NA	2p23.1	2p23.1	NA	NA	CN_gain	10	9 NA	0
P43	baseline	-	-	POM121L12	missense_variant	1	p.S149I	7.12%	no	46162	7	53103810	NA	NA	S149	G	T	0
P43	baseline	present	-	EGFR	missense_variant	20	p.T790M	6.46%	no	55544	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05
P43	baseline	-	-	EGFR	missense_variant	21	p.L858R	24.42%	maxAF	48548	7	55259515	rs121434568	COSM6224	L858	T	G	0
P43	baseline	-	-	EGFR	cn_amp	NA	cn_amp	3.09	no	0.345;4;24;7	7p11.2	7p11.2	NA	NA	CN_gain	16	16 NA	0
P43	baseline	-	-	CDK6	cn_amp	NA	cn_amp	2.82	no	0.426;2;43;7	7q21.2	7q21.2	NA	NA	CN_gain	7	7 NA	0
P43	baseline	-	-	MET	cn_amp	NA	cn_amp	2.28	no	0.298;5;15;7	7q31.2	7q31.2	NA	NA	CN_gain	29	21 NA	0
P43	baseline	-	-	FGFR1	cn_amp	NA	cn_amp	2.34	no	0.337;10;30	8p11.22	8p11.22	NA	NA	CN_gain	9	6 NA	0
P43	FU1,FU2	-	No	TP53	missense_variant	8	p.C275Y	0.59%	no	25616	17	7577114	rs863224451	COSM165084,CO	C275	C	T	0
P43	FU1,FU2	-	-	EGFR	missense_variant	21	p.L858R	1.44%	maxAF	28268	7	55259515	rs121434568	COSM6224	L858	T	G	0
P43	FU1,FU2	-	-	MET	cn_amp	NA	cn_amp	2.28	no	0.296;5;12;7	7q31.2	7q31.2	NA	NA	CN_gain	29	20 NA	0
P44	baseline	present	-	EGFR	missense_variant	20	p.T790M	0.12%	no	12728	7	55249071	rs121434569	COSM6240	T790	C	T	0
P44	baseline	-	-	EGFR	missense_variant	21	p.L858R	0.50%	no	13903	7	55259515	rs121434568	COSM6224	L858	T	G	0
P44	baseline	-	-	TP53	missense_variant	5	p.V143M	1.53%	maxAF	13101	17	7578503	NA	COSM43878	V143	C	T	0
P44	baseline	-	-	RB1	frameshift_variant	19	p.A628fs	0.55%	no	18116	13	49030405	NA	NA	LOF	A	AT	0
P45	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.25%	no	25269	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0
P45	baseline	present	-	EGFR	missense_variant	20	p.T790M	0.29%	maxAF	32967	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05
P45	FU1,FU2,FU3	-	No	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.02%	maxAF	23275	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0
P45	FU4	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.08%	maxAF	13032	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0
P46	baseline	-	-	PIK3CA	missense_variant	10	p.E545K	0.16%	no	7504	3	178936091	rs104886003	COSM763	E545	G	A	0
P46	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	0.46%	maxAF	12418	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0
P46	baseline	present	-	EGFR	missense_variant	20	p.T790M	0.26%	no	8715	7	55249071	rs121434569	COSM6240	T790	C	T	0
P47	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.00%	no	7703	7	55249071	rs121434569	COSM6240	T790	C	T	0
P47	baseline	-	-	EGFR	missense_variant	21	p.L858R	1.90%	maxAF	14320	7	55259515	rs121434568	COSM6224	L858	T	G	0
P47	baseline	-	-	TP53	missense_variant	8	p.R273H	0.26%	no	12866	17	7577120	rs28934576	COSM99729	R273	C	A	2.00E-04
P47	baseline	-	-	BRINP3	missense_variant	8	p.T504M	0.59%	no	17077	1	190067938	NA	NA	T504	G	A	0
P47	baseline	-	-	PTEN	stop_gained	2	p.Y189X	1.42%	no	9538	10	89624274	NA	COSM28916	LOF	T	A	0
P47	baseline	-	-	TP53	missense_variant	5	p.S127F	0.63%	no	12966	17	7578550	NA	COSM44226	S127	G	A	0
P47	baseline	-	-	HGF	missense_variant	4	p.H158Q	0.84%	no	17790	7	81386513	NA	NA	H158	G	T	0
P48	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	1.12%	maxAF	14071	7	55242464	rs121913421	COSM6223	Exon19_infram	AGGAATTAAGA	A	0
P48	baseline	present	-	EGFR	missense_variant	20	p.T790M	0.49%	no	7612	7	55249071	rs121434569	COSM6240	T790	C	T	0
P49	baseline	-	-	BRCA2	missense_variant	18	p.A2730V	1.00%	no	33435	13	32937528	rs80359067	NA	A2730	C	T	4.08E-06
P49	baseline	-	-	EGFR	conservative_infram	19	p.E746_A750del	2.08%	maxAF	23797	7	55242465	rs727504233	COSM6225	Exon19_infram	AGGAATTAAGA	G	0
P49	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.47%	no	29401	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05
P50	baseline	present	-	EGFR	missense_variant	20	p.T											

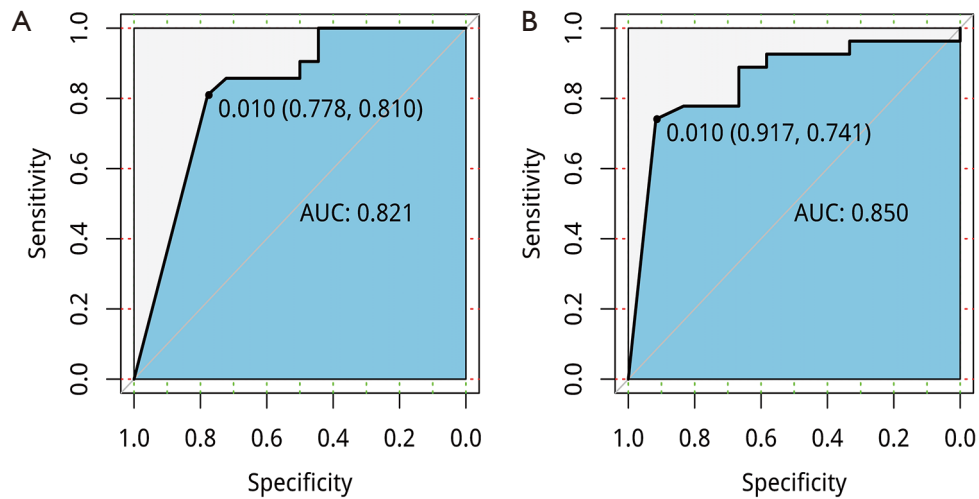
Patient ID	Timepoint	T790M status at baseline	ctDNA clearance status at F1	Gene	Mutation type	Exon number	Variant	AF	maxAF status	Sequencing depth	Chromosome number	Genomic position	dbsnp_ID	COSM_ID	MatchReport	Reference allele (REF)	Variant allele (ALT)	Population Frequency
P58	baseline	-	-	EGFR	disruptive_inframe_c	19	p.L747_P753del	7.28%	maxAF	19771	7	55242469	rs121913438	COSM133197	Exon19_inframe	TTAAGAGAAGC	T	0
P58	baseline	present	-	EGFR	missense_variant	20	p.T790M	2.48%	no	7392	7	55249071	rs121434569	COSM6240	T790	C	T	0
P58	baseline	-	-	TP53	frameshift_variant	3	p.V31fs	4.32%	no	9812	17	7579702	NA	NA	LOF	GAA	G	0
P59	baseline	-	-	EGFR	conservative_infram	19	p.E746_A750del	12.20%	maxAF	20047	7	55242465	NA	COSM6225	Exon19_inframe	GGAAATTAAGAG	G	0
P59	baseline	present	-	EGFR	missense_variant	20	p.T790M	4.20%	no	6635	7	55249071	rs121434569	COSM6240	T790	C	T	0
P59	baseline	-	-	SI	missense_variant	10	p.S358R	3.01%	no	10928	3	16477764	NA	NA	S358	T	G	0
P59	baseline	-	-	PIK3CA	missense_variant	21	p.N1044K	3.14%	no	21443	3	178952077	NA	COSM27504	N1044	T	G	0
P59	baseline	-	-	TP53	frameshift_variant	3	p.N29fs	6.78%	no	8022	17	7579707	NA	NA	LOF	TTG	T	0
P60	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	21.82%	maxAF	19558	7	55242464	rs121913421	COSM6223	Exon19_inframe	AGGAATTAAGA	A	0
P60	baseline	present	-	EGFR	missense_variant	20	p.T790M	16.17%	no	9240	7	55249071	rs121434569	COSM6240	T790	C	T	0
P60	baseline	-	-	TP53	stop_gained	5	p.W146X	13.26%	no	14747	17	7578492	NA	COSM3079703	LOF	C	T	0
P61	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.98%	no	16128	7	55249071	rs121434569	COSM6240	T790	C	T	0
P61	baseline	-	-	EGFR	missense_variant	21	p.L858R	4.63%	maxAF	19096	7	55259515	rs121434568	COSM6224	L858	T	G	0
P61	baseline	-	-	TP53	frameshift_variant	7	p.C242fs	1.95%	no	16504	17	7577554	NA	NA	LOF	TGCG	T	0
P62	baseline	-	-	TP53	missense_variant	8	p.R283H	9.12%	no	36017	17	7577090	rs371409680	COSM11483	R283	C	T	1.00E-04
P62	baseline	-	-	TP53	missense_variant	6	p.Y205C	21.28%	maxAF	31168	17	7578235	NA	COSM99630,COSI	Y205	T	C	0
P62	baseline	-	-	BRAF	missense_variant	15	p.V600E	0.37%	no	21502	7	140453136	rs113488022	COSM476	V600	A	T	1.65E-05
P62	baseline	present	-	EGFR	missense_variant	20	p.T790M	11.31%	no	37018	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05
P62	baseline	-	-	EGFR	missense_variant	21	p.L858R	19.88%	no	35470	7	55259515	rs121434568	COSM6224	L858	T	G	0
P62	baseline	-	-	EGFR	cn_amp	NA	cn_amp	2.35	no	0.252;6;11;1	7p11.2	7p11.2	NA	NA	CN_gain		16	13 NA
P62	baseline	-	-	FGFR1	cn_del	NA	cn_del	1.62	no	NA;0;NA	8p11.22	8p11.22	NA	NA	CN_loss		9	9 NA
P62	baseline	-	-	MYC	cn_del	NA	cn_del	1.75	no	0.327;3;16;6	8q24.21	8q24.21	NA	NA	CN_loss		8	4 NA
P62	FU1	-	No	TP53	missense_variant	6	p.Y205C	0.81%	maxAF	31644	17	7578235	NA	COSM99630,COSI	Y205	T	C	0
P62	FU1	-	-	EGFR	missense_variant	21	p.L858R	0.56%	no	35192	7	55259515	rs121434568	COSM6224	L858	T	G	0
P62	FU1	-	-	BRAF	missense_variant	15	p.V600E	0.23%	no	22132	7	140453136	rs113488022	COSM476	V600	A	T	1.65E-05
P62	FU3	-	-	TP53	missense_variant	8	p.R283H	0.81%	no	34608	17	7577090	rs371409680	COSM11483	R283	C	T	1.00E-04
P62	FU3	-	-	TP53	missense_variant	6	p.Y205C	1.35%	no	26919	17	7578235	NA	COSM99630,COSI	Y205	T	C	0
P62	FU3	-	-	EGFR	missense_variant	21	p.L858R	1.45%	maxAF	25442	7	55259515	rs121434568	COSM6224	L858	T	G	0
P62	FU4	-	-	TP53	missense_variant	8	p.R283H	0.90%	no	29528	17	7577090	rs371409680	COSM11483	R283	C	T	1.00E-04
P62	FU4	-	-	TP53	missense_variant	6	p.Y205C	2.41%	no	23928	17	7578235	NA	COSM99630,COSI	Y205	T	C	0
P62	FU4	-	-	EGFR	missense_variant	21	p.L858R	2.57%	maxAF	23446	7	55259515	rs121434568	COSM6224	L858	T	G	0
P63	baseline	-	-	TP53	splice_region_variant	6	p.E224-	32.39%	no	32890	17	7578177	rs1267605076	COSM707897,CO	Exon6_splice_si	C	T	0
P63	baseline	-	-	TP53	missense_variant	5	p.C176V	1.86%	no	34789	17	7578403	rs786202962	COSM1649384,CI	C176	C	T	0
P63	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	43.42%	maxAF	36238	7	55242464	rs121913421	COSM6223	Exon19_inframe	AGGAATTAAGA	A	0
P63	baseline	present	-	EGFR	missense_variant	20	p.T790M	13.93%	no	65684	7	55249071	rs121434569	COSM6240	T790	C	T	4.12E-05
P63	baseline	-	-	EGFR	cn_amp	NA	cn_amp	2.8	no	0.282;10;14	7p11.2	7p11.2	NA	NA	CN_gain		16	16 NA
P64	baseline	-	-	APC	missense_variant	16	p.K2052T	18.62%	no	22469	5	112177446	NA	NA	K2052	A	C	0
P64	baseline	present	-	EGFR	missense_variant	20	p.T790M	12.88%	no	14305	7	55249071	rs121434569	COSM6240	T790	C	T	0
P64	baseline	-	-	OR4A15	missense_variant	1	p.K53N	1.05%	no	26354	11	55135518	NA	NA	K53	G	T	0
P64	baseline	-	-	CTNNB1	inframe_deletion	3	p.S23_S33del	8.58%	no	15587	3	41266068	NA	NA	Exon3_inframe	TTAGTCACTGG	T	0
P64	baseline	-	-	EGFR	inframe_deletion	19	p.E746_A750del	34.29%	maxAF	23159	7	55242465	NA	COSM6225	Exon19_inframe	GGAAATTAAGAG	G	0
P64	baseline	-	-	BRAF	cn_amp	NA	cn_amp	2.62	no	NA	7q34	7q34	NA	NA	CN_gain		6	6 NA
P64	baseline	-	-	CDKN2A	cn_del	NA	cn_del	1.23	no	NA	9p21.3	9p21.3	NA	NA	CN_loss		12	11 NA
P64	baseline	-	-	EGFR	cn_amp	NA	cn_amp	2.49	no	NA	7p11.2	7p11.2	NA	NA	CN_gain		20	18 NA
P64	baseline	-	-	MET	cn_amp	NA	cn_amp	2.58	no	NA	7q31.2	7q31.2	NA	NA	CN_gain		45	43 NA
P64	baseline	-	-	POM121L12	cn_amp	NA	cn_amp	2.77	no	NA	7p12.1	7p12.1	NA	NA	CN_gain		8	8 NA
P64	FU4	-	-	EGFR	missense_variant	20	p.C797S	4.20%	no	30193	7	55249092	NA	COSM5945664	C797(in-cis_T79	G	C	0
P64	FU4	-	-	EGFR	conservative_infram	19	p.E746_A750del	9.93%	maxAF	31103	7	55242465	rs727504233	COSM6225	Exon19_inframe	GGAAATTAAGAG	G	0
P64	FU4	-	-	APC	missense_variant	16	p.K2052T	5.44%	no	28328	5	112177446	NA	NA	K2052	A	C	0
P64	FU4	-	-	CTNNB1	conservative_infram	3	p.S23_S33del	1.39%	no	36303	3	41266068	NA	NA	Exon3_inframe	TTAGTCACTGG	T	0
P64	FU4	-	-	EGFR	missense_variant	20	p.T790M	5.05%	no	31174	7	55249071	rs121434569	COSM6240	T790	C	T	2.84E-05
P65	baseline	present	-	EGFR	missense_variant	20	p.T790M	20.08%	no	22144	7	55249071	rs121434569	COSM6240	T790	C	T	0
P65	baseline	-	-	EGFR	missense_variant	21	p.L858R	58.42%	maxAF	32248	7	55259515	rs121434568	COSM6224	L858	T	G	0
P65	baseline	-	-	EGFR	cn_amp	NA	cn_amp	4.04	no	NA	7p11.2	7p11.2	NA	NA	CN_gain		20	20 NA
P67	baseline	-	-	EGFR	disruptive_inframe_c	19	p.E746_A750del	5.27%	maxAF	27832	7	55242464	rs121913421	COSM6223	Exon19_inframe	AGGAATTAAGA	A	0
P67	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.63%	no	11804	7	55249071	rs121434569	COSM6240	T790	C	T	0
P67	baseline	-	-	TP53	missense_variant	8	p.R273C	0.25%	no	20616	17	7577121	rs121913343	COSM99933	R273	G	A	0
P68	baseline	-	-	EGFR	conservative_infram	19	p.E746_A750del	3.49%	no	19630	7	55242465	NA	COSM6225	Exon19_inframe	GGAAATTAAGAG	A	0
P68	baseline	present	-	EGFR	missense_variant	20	p.T790M	6.45%	maxAF	7243	7	55249071	rs121434569	COSM6240	T790	C	T	0
P68	baseline	-	-	TP53	missense_variant	5	p.A159P	6.41%	no	17917	17	7578455	NA	COSM562628	A159	C	G	0
P68	baseline	-	-	CTNNB1	missense_variant	3	p.S37C	5.74%	no	19590	3	41266113	rs121913403	COSM5679	S37	C	G	0
P68	baseline	-	-	CSMD1	stop_gained	25	p.R1288X	4.43%	no	19524	8	3165305	NA	COSM4782185	LOF	G	A	0
P69	baseline	-	-	TP53	frameshift_variant	4	p.G112fs	5.93%	no	10003	17	7579351	NA	NA	LOF	GC	G	0
P69	baseline	-	-	MET	missense_variant	19	p.Y1235C	1.89%	no	15795	7	116423429	NA	NA	Y1235	A	G	0
P69	baseline	present	-	EGFR	missense_variant	20	p.T790M	28.10%	no	52170	7	55249071	rs121434569	COSM6340	T790	C	T	4.12E-05
P69	baseline	-	-	EGFR	missense_variant	21	p.L858R	49.55%	maxAF	41700	7	55259515	rs121434568	COSM6224	L858	T	G	0
P69	baseline	-	-	EGFR	cn_amp	NA	cn_amp	4.23	no	0.266;10;23	7p11.2	7p11.2	NA	NA	CN_gain		16	16 NA
P81	baseline	-	-	TP53	missense_variant	6	p.I195T	0.54%	no	35857	17	7578265	rs760043106	COSM116923,CO	I195	A	G	0
P81	baseline	-	-	EGFR	conservative_infram	19	p.E746_A750del	2.66%	maxAF	30410	7	55242465	rs727504233	COSM6225	Exon19_inframe	GGAAATTAAGAG	G	0
P81	baseline	present	-	EGFR	missense_variant	20	p.T790M	1.47%	no	37957	7	55249071	rs121434569	COSM6240	T790	C	T	



**Figure S2** Mutation spectrum of the 32 T790M-positive patients at baseline (A) and at follow-up after 50 days of initiating osimertinib therapy (FU1) (B). Each column represents a patient and each row represents a gene. Numbers on the left represent the percentage of patients with mutations in a specific gene. Top plot represents the overall number of mutations a patient carried. Different colors denote different types of mutations.

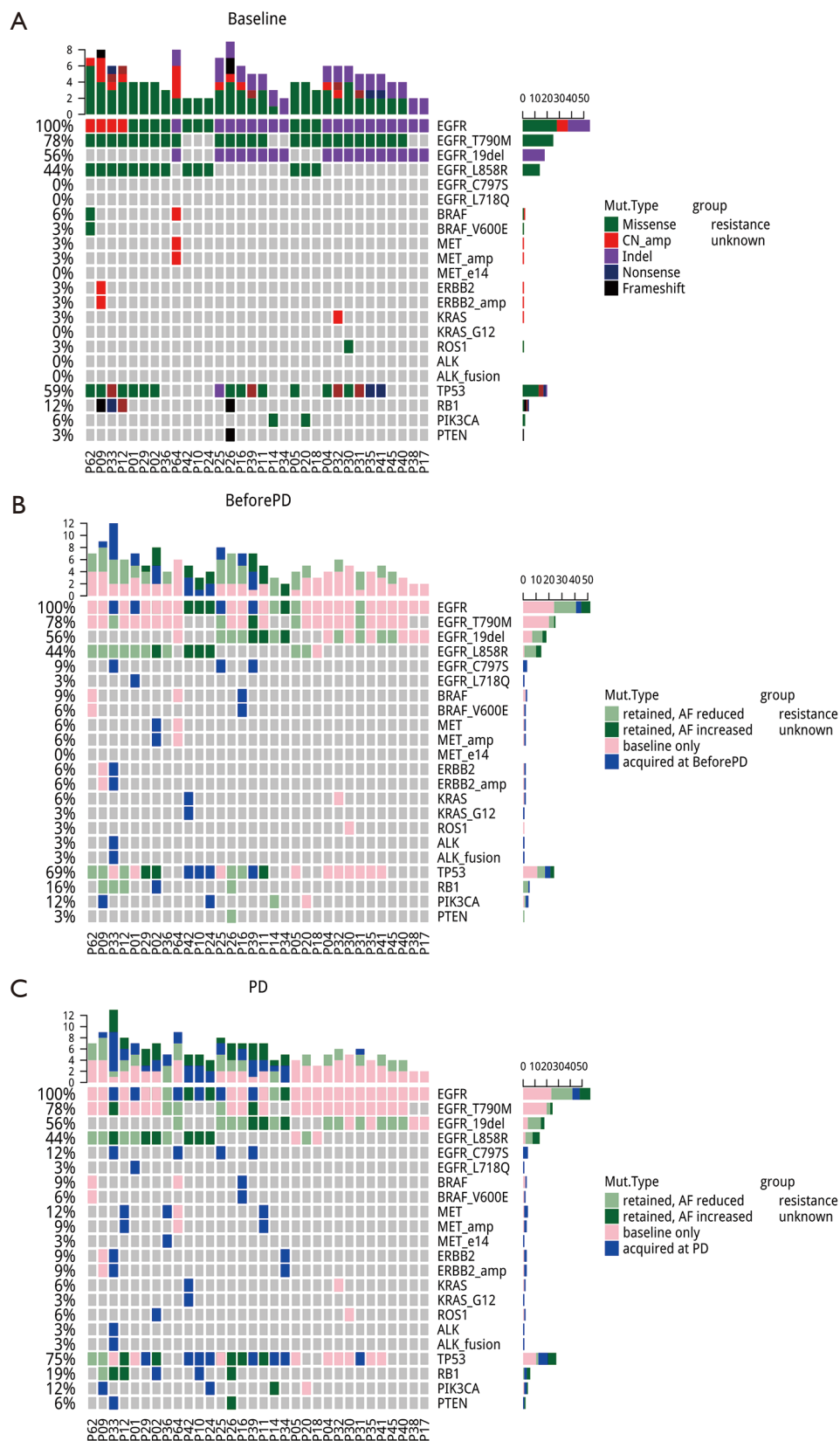


**Figure S3** The significant reduction in the allelic fraction (AF) of *EGFR* sensitizing mutation (A) and maximum allelic fraction (maxAF) (B) were observed in 38 patients at first follow-up within 50 days of osimertinib therapy (FU1) as compared to baseline.

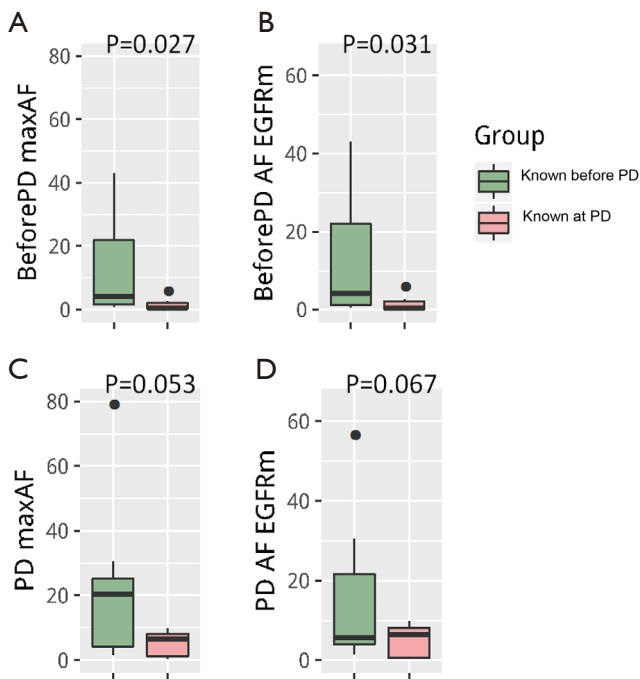


**Figure S4** Receiver operating characteristic curves illustrating the area under the curve (AUC), which indicates that the cut-off of allelic fraction 0.01% as ctDNA clearance was an independent predictor of progression-free survival (A) and overall survival (B).





**Figure S5** Mutation spectrum of the 32 T790M-positive patients at baseline (A) before radiological progression (B) and at confirmation of radiological progression (C). Each column represents a patient and each row represents a gene. Numbers on the left represent the percentage of patients with mutations in a specific gene. Top plot represents the overall number of mutations a patient carried. (A) Different colors denote different types of mutations. (B,C) Light green denotes the mutations detected at both samples at baseline and at confirmation of progression (retained) but with reduced allelic fraction (AF); dark green denotes the mutations retained but with increased AF; pink denotes the mutations detected only at baseline and were lost of progression; blue denotes the mutations that were acquired, which is defined as the mutations that are not present in baseline samples and were only detected before progression (before PD) or at progression (at PD). PD, progressive disease.



**Figure S6** Patients with known osimertinib resistance mechanisms (green bar) detected at one time point prior to radiological progression (before PD) had significant elevation of maximum allelic fraction (maxAF) (A,C) and AF of *EGFR* sensitizing mutations (AF EGFRm, B,D) at one time point prior to radiological PD (before PD, A,B) and upon confirmation of clinical PD (C,D) as compared to patients with acquired mutations detected at PD (pink bar). AF, allele fraction; PD, progressive disease.