

Supplemental Table S1. Patients information with lung cancers

Patient	Age	Sex	Cancer	Stage	Treatment History	ERBB2 alterations (sample type, time point, AF%)	ERBB2 Exonic change	Concurrent Driver Mutations
1	54	F	NSCLC	IV	Chemotherapy; Icotinib (11 months; PD); Osimertinib (10 months; PD)	c.1899-166_1946+44del (FFPE, post-Osimertinib, 3.56%)	Full exon 16 deletion	EGFR exon19 deletion
3	55	M	Lung	NA	Surgery+Chemotherapy; Whole-brain radiotherapy; γ-knife treatment	c.1898+2T>G (FFPE, primary, 3.98%)	Intron 15 splice site point mutation	NA
4	50	M	NSCLC	IV	Surgery+Chemotherapy+Radiotherapy; Gefitinib (20 months; PD); Afatinib (7 months; PD); Osimertinib (1 months; PD)	c.1898+541_1946+1063del (Tissue, post-Afatinib, 52.5%)	Full exon 16 deletion (RNA seq verified)	EGFR exon19 deletion
5	51	M	NSCLC	IV	Chemotherapy; Afatinib (11 months; PD); Chemotherapy+Trastuzumab (5 months; PD); Afatinib+Trastuzumab (4 months; PD); Osimertinib (5 months); Osimertinib+Trastuzumab (4 months; PD); Chemotherapy	c.1845_1947-1216delinsTTACAGGTGT (Plasma, post-Afatinib, 3.07%) c.1845_1947-1216delinsTTACAGGTGT (Plasma, post-Afatinib, 14.67%) c.1845_1947-1216delinsTTACAGGTGT / c.1899-1G>T (Plasma, post-Osimertinib, 30.34% / 4.76%)	Full exon 16 deletion Full exon 16 deletion Full exon 16 deletion / Intron 15 splice site point mutation	EGFR exon19 deletion
8	52	F	NSCLC	IV	Gefitinib (5 months; PD); Osimertinib (4 months; PD); Gefitinib+Osimertinib	c.1899-658_1947-264delinsG / c.1926_1946+15delCCCCGCCGAGCAGAGAG CCAGGTTGGCCTGGACCCC (Plasma, post-Osimertinib, 5.00% / 1.36%)	Full exon 16 deletion	EGFR L858R
10	67	M	NSCLC	NA	Chemotherapy (2 months; PD); Radiotherapy (3 months; PD)	c.1899-2A>T (FFPE, post-radiotherapy, 16.45%) c.1899-2A>T (Plasma, post-radiotherapy, 0.18%)	Intron 15 splice site point mutation Intron 15 splice site point mutation	NA
11	50	F	NSCLC	IV	Gefitinib (4 months; PD); Afatinib (1 months; PD); Anlotinib (3 months; PD)	c.1899-1G>C (Plasma, post-Anlotinib, 53.05%)	Intron 15 splice site point mutation	EGFR L858R

12	51	F	NSCLC	NA	Chemotherapy; Gefitinib; Erlotinib; Icotinib; Afatinib; Osimertinib; anti-PD-1	c.1946_1946+1509del (Plasma, post-TKIs, 13.51%)	Intron 16 splice site deletion	EGFR L858R
14	70	F	NSCLC	IV	Chemotherapy (15 months; PD); Gefitinib (14 months; PD); Osimertinib	c.1898+195_1947-677delinsTTAC (FFPE, post-Gefitinib, 55.00%)	Full exon 16 deletion	EGFR exon19 deletion
15	43	F	NSCLC	IV	Chemotherapy (1 cycle; PD); Gefitinib+Osimertinib (2 months; PD); Radiotherapy (4 months; SD); Bevacizumab (2 months; PD); Chemotherapy (2 months; PD); Bevacizumab (1 month; PD); Bevacizumab+Docetaxel	c.1899-144_1918del (Plasma, post-Bevacizumab+Docetaxel, 1.38%)	Partial exon 16 deletion	EGFR exon19 deletion
16	65	F	NSCLC	NA	Icotinib (10 months; PD); Chemotherapy+Osimertinib (3 months; PD); Anlotinib (4 months; PD)	c.1898+86_1946+50del (Plasma, post-Osimertinib, 1.51%)	Full exon 16 deletion	EGFR exon19 deletion
					c.1898+86_1946+50del (Plasma, post-Anlotinib, 1.23%)	Full exon 16 deletion		
17	28	F	Lung	NA	NA	c.1898+99_1946+718del (FFPE, primary, 74.00%)	Full exon 16 deletion	NA
						c.1898+99_1946+718del (Plasma, primary, 86.00%)	Full exon 16 deletion	

Notes: F, female; M, male; NA, not applicable; NSCLC, non-small cell lung cancer; PD, progressed disease; SD, stable disease; AF, allele frequency

Supplemental Table S2. Patients information with non-lung cancers

Patient	Age	Sex	Cancer	Stage	Treatment History	ERBB2 alterations (sample type, time point, AF%)	ERBB2 Exonic change
2	62	M	Gallbladder	IV	Surgery; Chemotherapy	c.1898+430_1946+142del (Plasma, primary, 8.48%)	Full exon 16 deletion
6	49	F	Rectal	NA	Surgery+Chemotherapy+Radiotherapy; Irinotecan+Raltitrexed+Cetuximab (4 months; PD); Surgery*; Bevacizumab (5 cycles; PD); Trastuzumab (2 cycles; PD)	c.1898+210_1947-449del (FFPE, primary, 10.71%)	Full exon 16 deletion (RNA seq verified)
						c.1898+210_1947-449del (FFPE, post-surgery*, 28.30%)	Full exon 16 deletion
						c.1898+210_1947-449del (Plasma, post-trastuzumab, 51.98%)	Full exon 16 deletion
7	62	M	Rectal	NA	Surgery+Chemotherapy; Cetuximab (8 months; PD); Surgery*; Trastuzumab+Lapatinib (1 month; PR)	c.1898+162_1946+1681delinsT (FFPE, primary, 66.97%)	Full exon 16 deletion
						c.1898+162_1946+1681delinsT (FFPE, post-surgery*, 52.00%)	Full exon 16 deletion
9	49	F	Ovarian	IV	NA	c.1945_1946+35delAGGTTGGCCTGGACCCAG GATGTACCCTTCATTGCC (FFPE, primary, 37.14%)	Intron 16 splice site deletion (full exon 16 deletion verified by RNA seq)
						c.1945_1946+35delAGGTTGGCCTGGACCCAG GATGTACCCTTCATTGCC (Plasma, primary, 2.84%)	Intron 16 splice site deletion
13	80	M	Gastric	NA	NA	c.1899-106_1946+317del (Plasma, primary, 5.81%)	Full exon 16 deletion
						c.1899-106_1946+317del (Tissue, primary, 3.03%)	Full exon 16 deletion
18	62	F	Gastric	NA	NA	c.1898+79_1946+1247del (FFPE, primary, 47.00%)	Full exon 16 deletion

Notes: F, female; M, male; NA, not applicable; PD, progressed disease; PR, partial response; AF, allele frequency