

Supplementary Table S1. Patient characteristics.

Median age		60 (range: 30-77)
Sex	Female	18 (72%)
	Male	7 (28%)
Race	White	14 (56%)
	Asian	5 (20%)
	African American	5 (20%)
	Multirace	1 (4%)
Histology	Adenocarcinoma	25 (100%)
<i>EGFR</i> mutations	Exon 19 deletion	10 (40%)
	L858R	4 (16%)
	Exon 19 deletion/T790M	8 (32%)
	Exon L8585R/T790M	2 (8%)
	Exon 20 insertion/V769L	1 (4%)
Cohort	1	15 (60%)
	2	7 (28%)
	3	3 (12%)

Supplementary Table S2. List of *EGFR* mutations detected by ddPCR.

Amino Acid Change	Nucleotide Mutation	Chromosomal Location (hg19)	Amplicon Length (bp)	COSMIC ID	Mutation Description
p.E746_A750delELREA	c.2235_2249del15	chr7:55242404-55242540	78	COSM6223	Deletion - In frame
p.E746_A750delELREA	c.2236_2250del15	chr7:55242405-55242541	91	COSM6225	Deletion - In frame
p.E746_S752>V	c.2237_2256>TC	chr7:55242406-55242547	99	COSM18426	Complex - deletion inframe
p.L747_A750>P	c.2239_2248TTAA GAGAAG>C	chr7:55242408-55242539	84	COSM12382	Complex - deletion inframe
p.V769L	c.2305G>C	chr7:55248946-55249068	59	NA	Substitution - Missense
p.T790M	c.2369C>T	chr7:55249010-55249132	80	COSM6240	Substitution - Missense
p.L858R	c.2573T>G	chr7:55259454-55259576	73	COSM6224	Substitution - Missense

Supplementary Table S3. 36 genes included in InvisionFirst™-Lung

AKT1	● ALK	BRAF	CCND1	● CDKN2A	CTNNB1
● EGFR	● ERBB2	ESR1	● FGFR1	FGFR2	FGFR3
GATA3	GNA11	GNAQ	GNAS	HRAS	IDH1
IDH2	KIT	KRAS	MAP2K1	● MET	MYC
NFE2L2	NRAS	NTRK1	NTRK3	PDGFRA	PIK3CA
PPP2R1A	● PTEN	● ROS1	● STK11	● TP53	U2AF1

SNVs + Indels - Hotspot Regions

● Fusions + SNVs + Indels

● CNVs + SNVs + Indels

● CNVs only

● SNVs + Indels - Exon Coverage
70% for PTEN, 88-100% for TP53,
STK11 and CDKN2A

Supplementary Table S4. Probe sequences: Capture probe and detector probe oligonucleotide sequences for three TKI-sensitive mutations. The detector probes are biotinylated at the 3' end.

	Capture Probe Sequences	Detector Probe Sequences
Exon 19 deletion	5' – TGTTGCTTCCTTG – 3'	5' – ATAGCGACGGGAATTTTAACTTTCTCACCT – 3'
p.L858R	5' – GTTTGACCCGCCCA – 3'	5' – AAAATCTGTGATCTTGACATGCTGCGGTGTTTTGTGCAG – 3'
p.T790M	5' – GAGCGGCATGATGA – 3'	5' – GCTGCACGGTGGAGGTGAGGCAGATGCCCAGC – 3'

Supplementary Table S5. Number and sites of lesions measured by volumetric measurements.

LAT	CT Scan (time point)	Total Lesion	Pulmonary	Liver	Node	Other
001	8	26	1	25	0	0
002	9	2	1	0	1	0
003	11	3	1	2	0	0
004	14	1	1	0	0	0
005	4	5	2	0	1	2
006	10	10	5	0	4	1
007	17	1	1	0	0	0
008	13	3	1	1	1	0
009	12	3	1	0	0	2
010	13	4	1	1	2	0
011	12	6	3	2	0	1
013	4	3	1	2	0	0
014	13	3	2	1	0	0
015	5	2	2	0	0	0
016	19	4	1	1	0	2
017	5	6	1	0	1	4
019	9	1	1	0	0	0
020	6	2	2	0	0	0
021	12	6	1	0	2	3
022	14	3	3	0	0	0
023	13	2	1	0	1	0
024	11	2	2	0	0	0
025	12	5	2	0	3	0
026	13	3	1	0	1	1
028	6	6	2	0	1	3
Average	10.6	4.48	1.6	1.4	0.72	0.76
Min	4	1	1	0	0	0
Max	19	26	5	25	4	4
total	265	112	40	35	18	19
Median	12	3	1	0	0	0

Supplementary Table S6. Spearman correlation between allele frequencies of sensitizing *EGFR* mutations by ddPCR and NGS, current values (nA) of eLB, and calculated tumor volume.

	ddPCR	NGS	eLB	Calculated tumor volume
ddPCR	1	0.93*	0.24*	0.35*
NGS	0.93*	1	0.24**	0.46*
eLB	0.24*	0.24**	1	0.28*
Total tumor volume	0.35*	0.46*	0.28*	1

* P value <0.001 (test of $r=0$)

** P value <0.05