

Table S1

Clinical characteristics in cohort 1.

		Total (N=26)
Age (median, range)		64 (41 - 85)
Sex (Female / Male)		19 / 7
Smoking History (never / ex-current)		16 / 10
Stage at diagnosis (III / IV / Post operative recurrence)		1 / 16 / 9
Histology at diagnosis (adeno / other)		26 / 0
Activating mutation (Ex 19 del / L858R)		14 / 12
Treatment history	Treatment lines (1/2/≥3)	8/5/13
	Gefitinib	12
	Erlotinib	15
	Afatinib	11
	Cytotoxic	16
Proportion of test performed	Tumor ddPCR	19
	Plasma ddPCR	15
	Paired (Tumor and plasma) ddPCR	9
	MET FISH	8
	SCLC pathological diagnosis	19
	Tumor NGS	7

Table S2

Clinical characteristics in cohort 2.

	Total (N=18)	cfDNA positive (N=8)	cfDNA negative (N=10)	<i>p</i>
Age (median, range)	67.5 (41 – 80)	71 (41 – 78)	67 (51 - 80)	0.964
Sex (Female / Male)	11 / 7	5 / 3	6 / 4	1
Smoking History (never / ex-current)	11 / 7	5 / 3	6 / 4	1
Stage at diagnosis (IV / Post operative recurrence)	11 / 7	4 / 4	7 / 3	0.63
Histology at diagnosis (adeno / other)	18 / 0	8 / 0	10 / 0	1
Activating mutation (Ex 19 del / L858R)	14 / 4	7 / 1	7 / 3	0.588
Extra thoracic metastasis (yes/no)	9 / 9	6 / 2	3 / 7	0.153
Number of metastatic organ (median, range)	2 (1 – 3)	2.5 (1 - 3)	1 (1 - 3)	0.13
The size of the largest lesion (mm, median, range)	26 (10 – 56)	26 (10 - 56)	28 (10 – 38)	0.732
Response (PR / SD)	11 / 7	5 / 3	6 / 4	1
PFS (median, days)	405.0	390.5	800.0	0.192
TTF (median, days)	520.5	520.5	570.5	0.528
Number of cfDNA collection	16 (4 – 22)	15.5 (4 – 22)	16 (5 - 19)	1

Figure S1

The flow chart representing the availability of each examination.

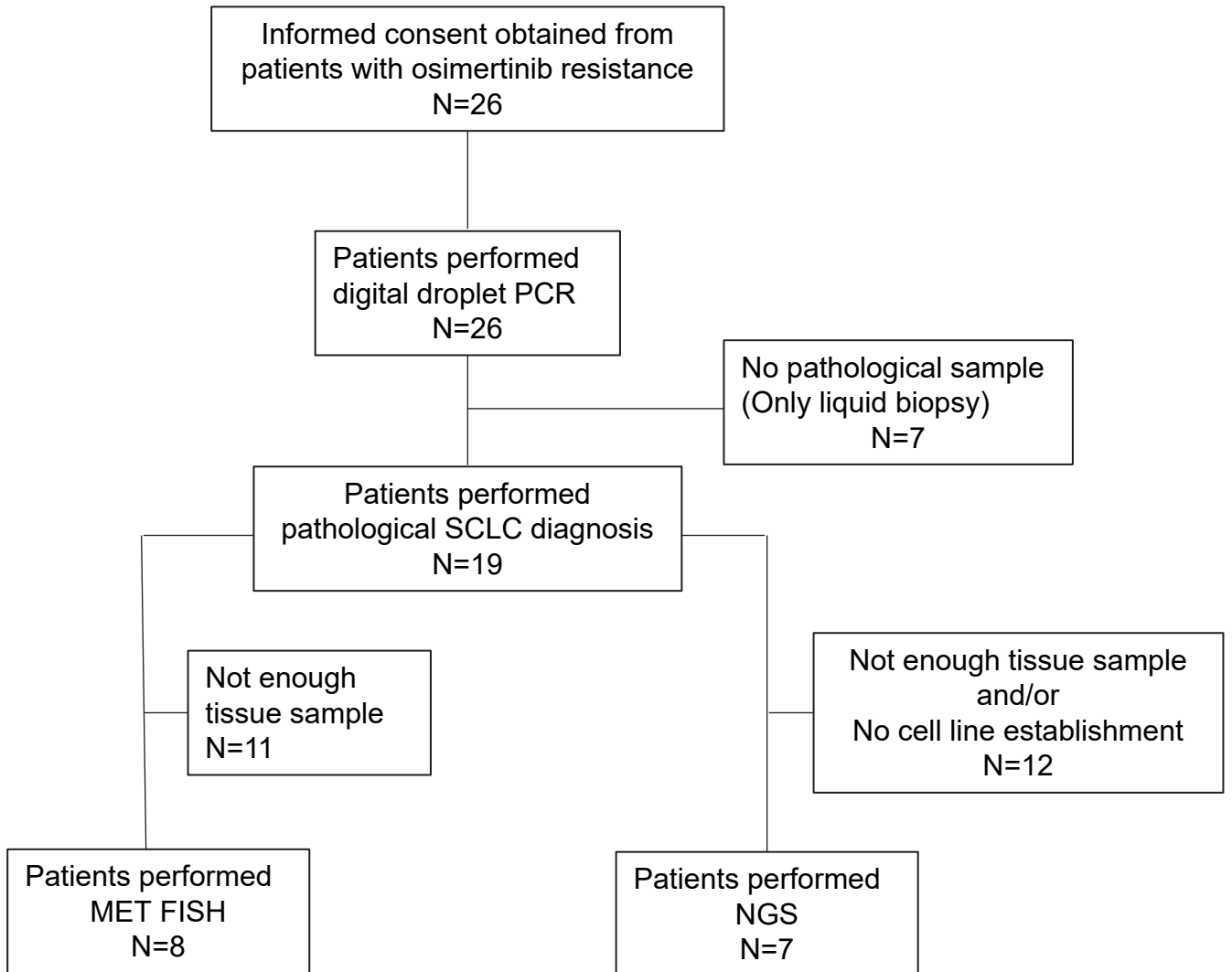


Figure S2 Summary of resistance mechanisms and treatment histories of patients.

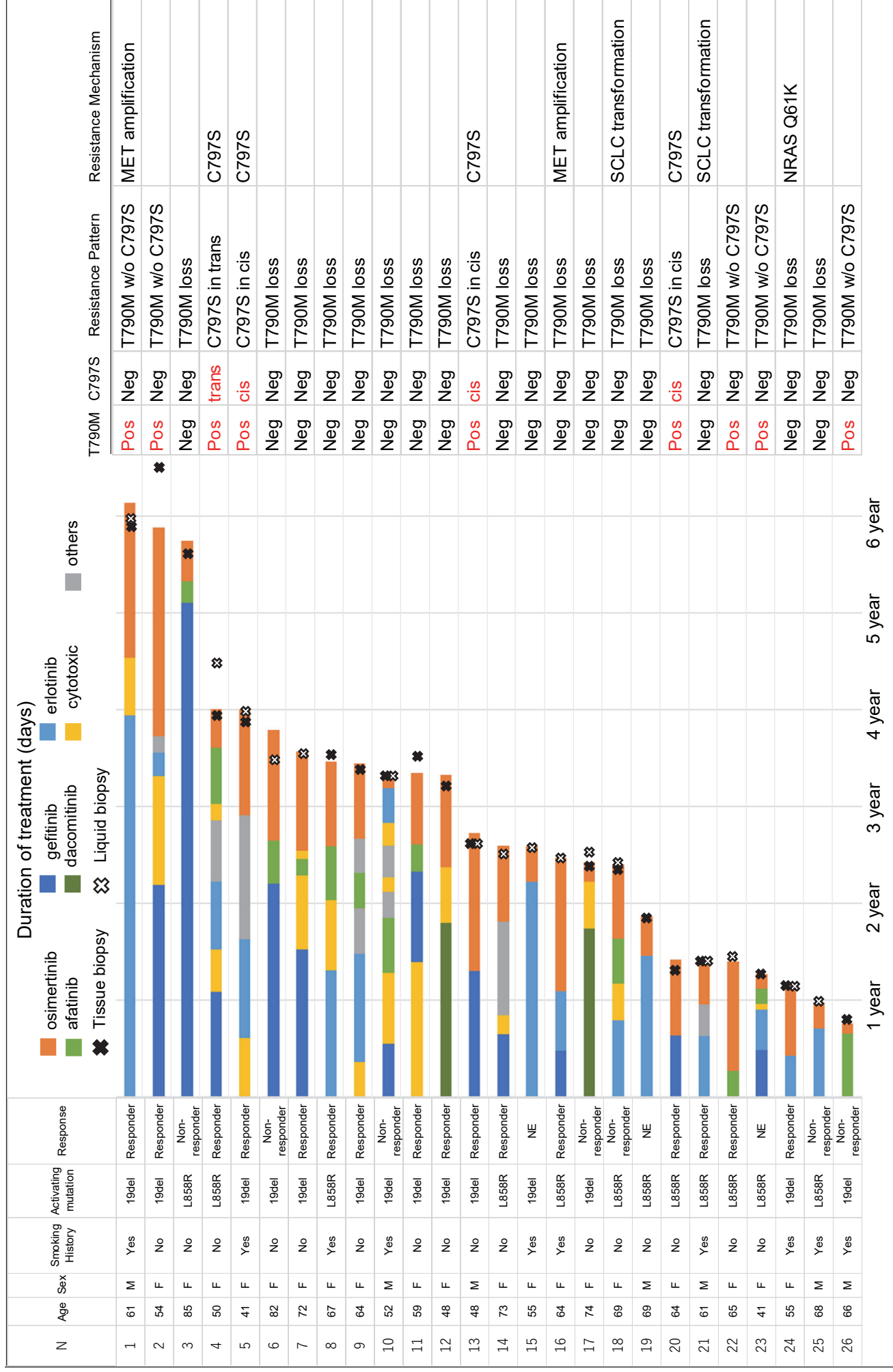


Figure S4

IGV image of EGFR T790M and/or C797S mutation. EGFR exon 20 was PCR amplified from JFCR-129 patients and analyzed by NGS.

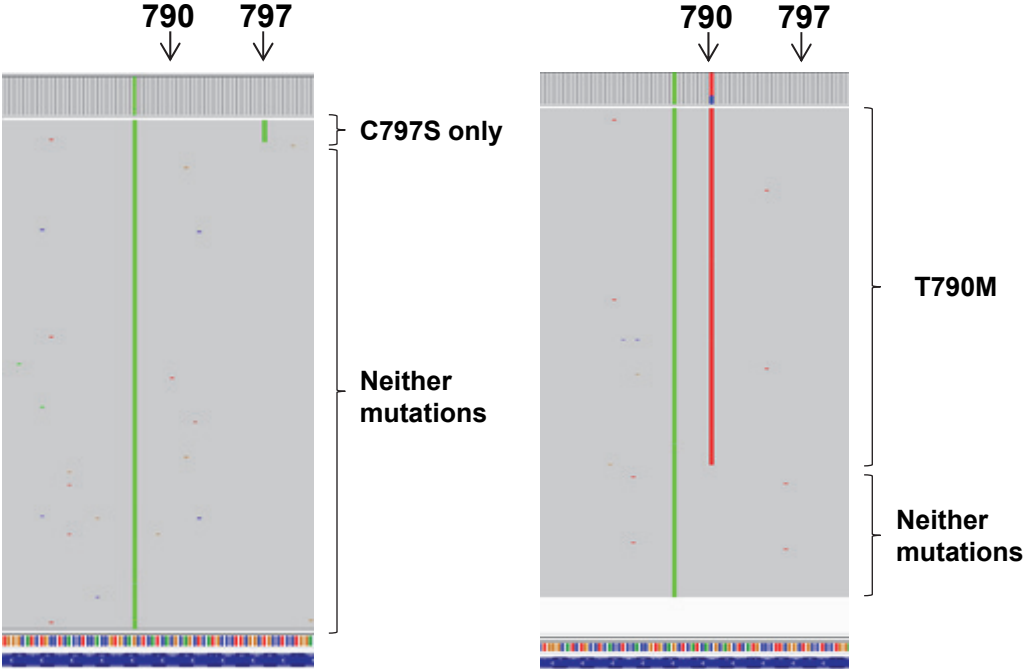
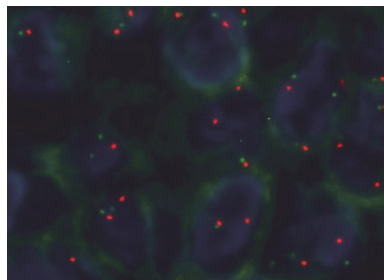


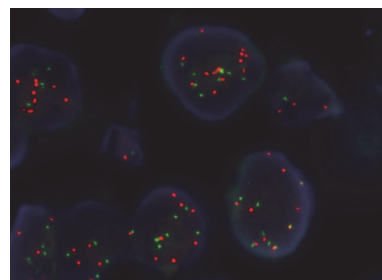
Figure S5

(A) MET amplification with FISH. Green and red signals correspond to CEP7 and MET locus. (B) SCLC transformation was diagnosed with IHC.

(A) MET amplification with FISH

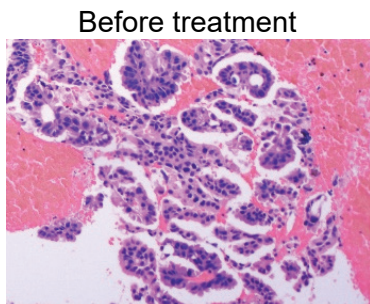


negative

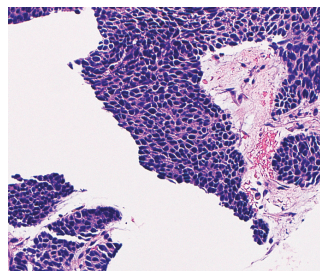


positive

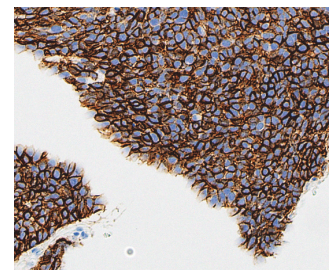
(B) SCLC transformation



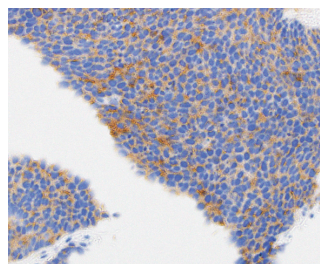
H/E



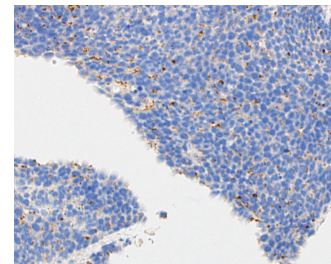
H/E



CD56



Synaptophysin



Chromogranin A