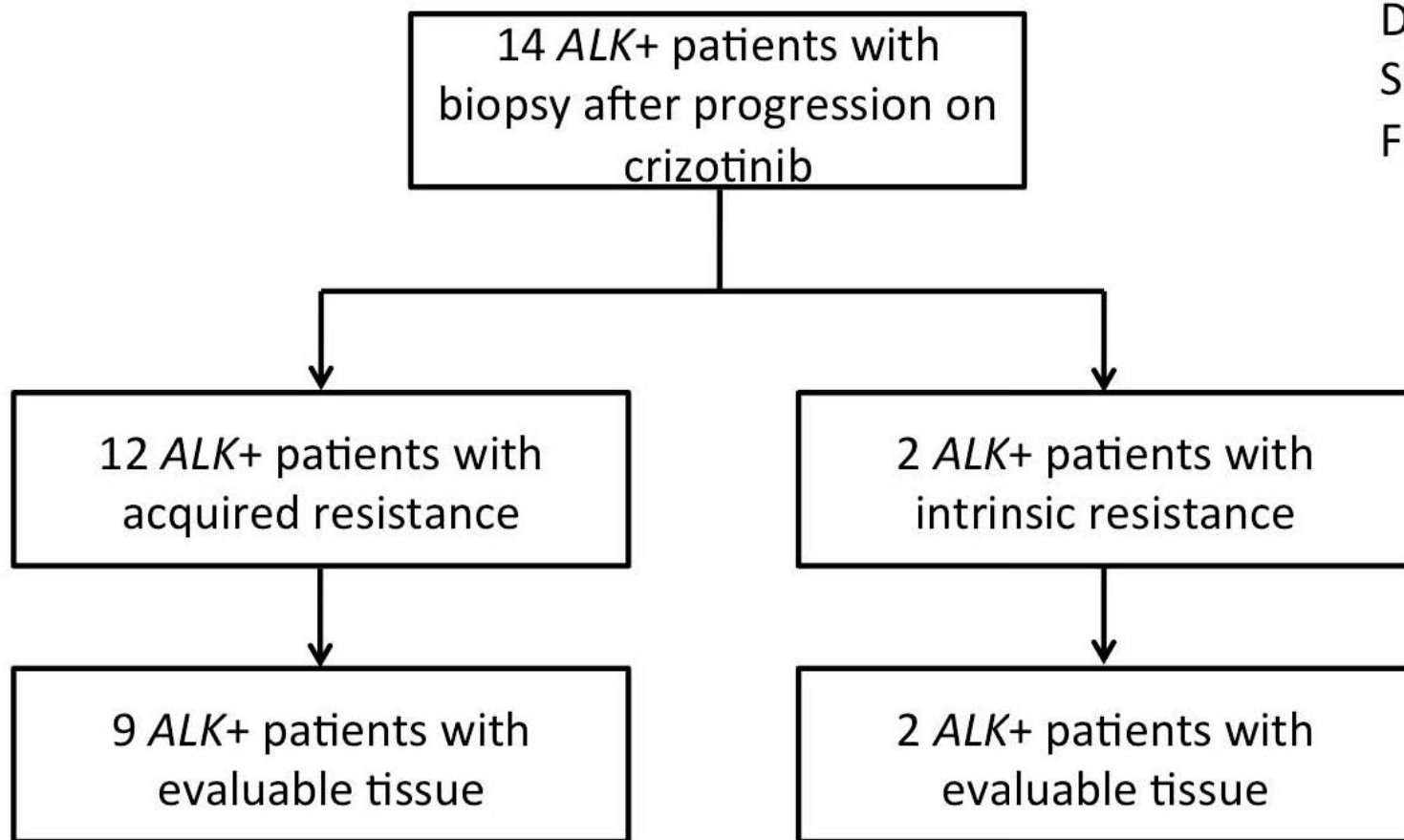
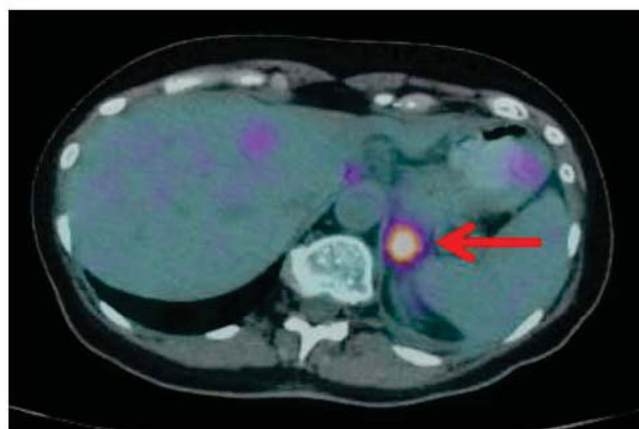


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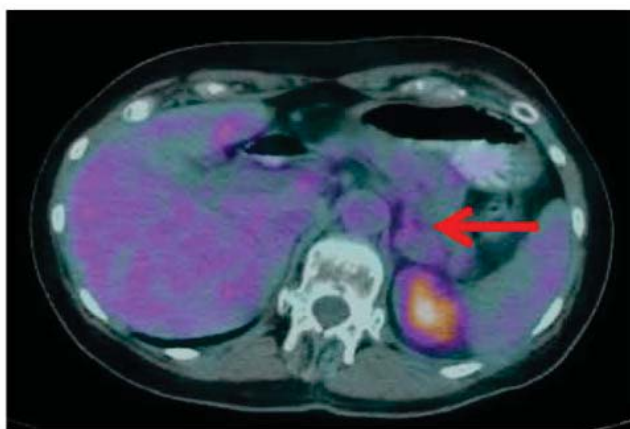


Doebele et al.,
Supplemental
Figure 1

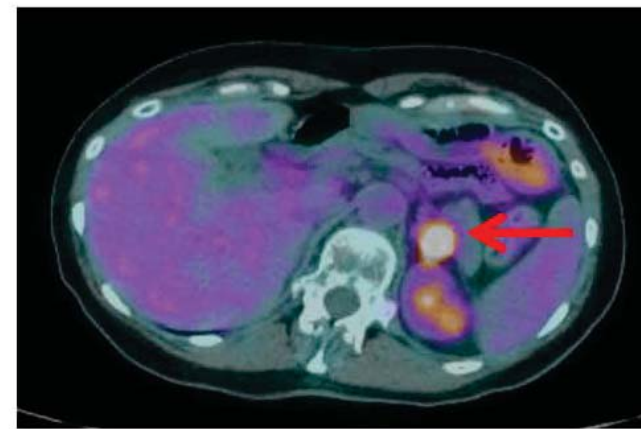
B



Pre-crizotinib



Response to crizotinib
41 days



Progression on crizotinib
197 days

Supplemental Table 1. Clinical and histologic characteristics of ALK positive patients

Patient #	Sex	Age at diagnosis	Pack years	Histology	Pre-crizotinib molecular profile		Time from pre-crizotinib biopsy to initiation (days)	Lines of prior therapy	Best response on crizotinib	Time on crizotinib (days)	Method of re-biopsy post-crizotinib
					EGFR	KRAS					
1	F	53	0	NSCLC with focal spindle cell differentiation	S768I ^a	WT ^a	643	3	SD	269	Bronchoscopy with endobronchial biopsy of LLL tumor
2	F	58	0	Adenocarcinoma	WT ^a	WT ^a	362	1	PR	265	CT-guided percutaneous right adrenal biopsy
3	F	58	0	Adenocarcinoma	WT ^a	WT ^a	425	2	PR	633	Bronchoscopy with transbronchial biopsy of LLL tumor
4	M	52	0	Large cell carcinoma	WT ^b	WT ^b	1121	3	PR	124	US-guided percutaneous liver biopsy
5	F	49	0	Adenocarcinoma	WT ^a	WT ^a	369	3	PR	825	CT-guided percutaneous RLL lung mass biopsy
6	M	21	0	Adenocarcinoma	WT ^c	ND	421	1	SD	377	US-guided percutaneous anterior mediastinal mass biopsy
7	F	62	0	Adenocarcinoma	WT ^a	WT ^a	474	1	PR	197	laparoscopic adrenalectomy
8	M	51	0	Adenocarcinoma	WT ^a	WT ^a	253	2	PR	454	CT-guided percutaneous lung mass biopsy
9a*	F	27	1	Adenocarcinoma	WT ^a	WT ^a	268	3	PR [§]	61	US-guided supraclavicular LN biopsy
9b*										113	US-guided percutaneous liver biopsy
10 [¶]	F	52	30	Adenocarcinoma	ND	G12C ^a	653	2	PD	27	US-guided supraclavicular LN biopsy
11	F	45	0	Adenocarcinoma	WT ^a	WT ^a	208	1	PR	244	US-guided percutaneous liver biopsy
12	M	44	13	Adenocarcinoma	WT ^a	WT ^a	391	2	PR**	170	US-guided infraclavicular lymph node biopsy
13 [¶]	M	64	10	Adenocarcinoma	WT ^a	WT ^a	234	1	PD	32	Bronchoscopy with EBUS subcarinal LN
14	M	70	0	Adenocarcinoma	WT ^a	WT ^a	475	1	PR	293	CT-guided percutaneous lung mass biopsy

*Patient #9 had two biopsies of progressive lesions at different intervals

[¶]Patients with intrinsic resistance

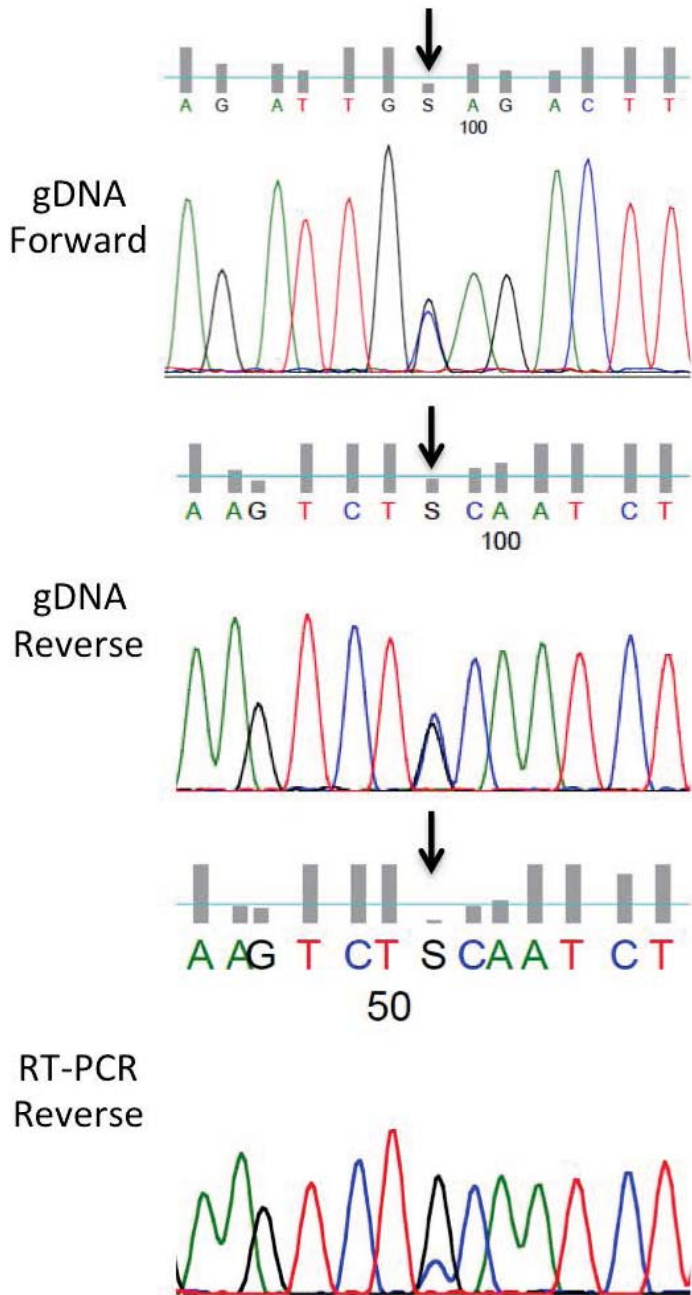
^aDirect sequencing

^bSNaPshot®

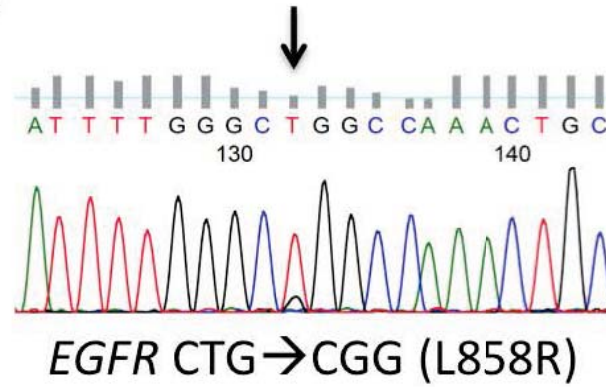
^cPerformed by Genzyme

[§]Unconfirmed PR

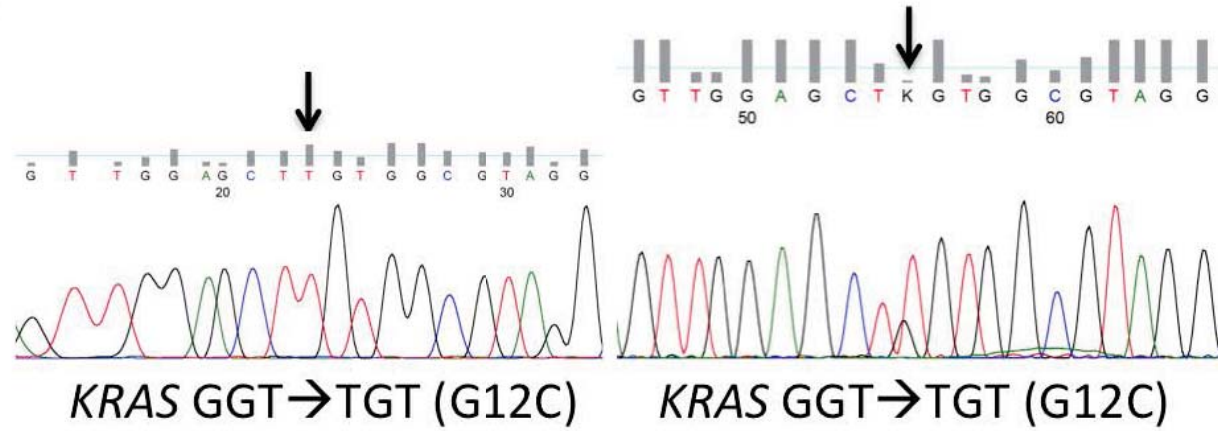
A *ALK* GGA → GCA (G1269A)



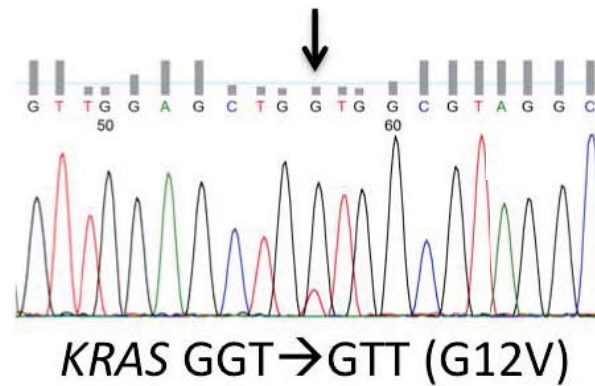
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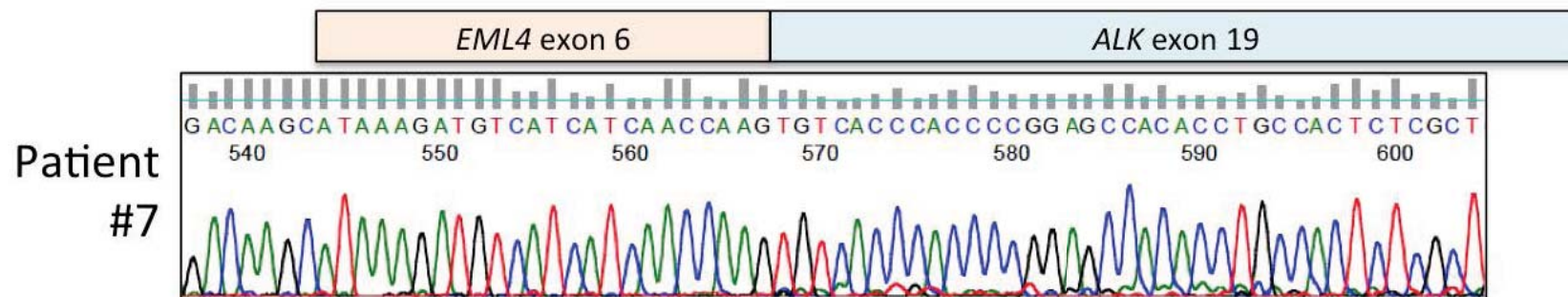
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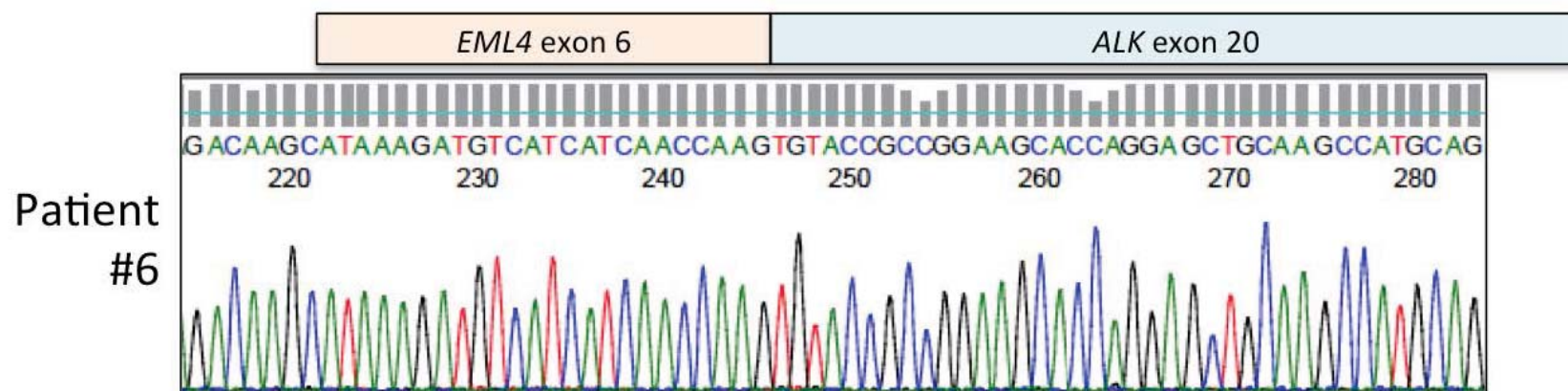
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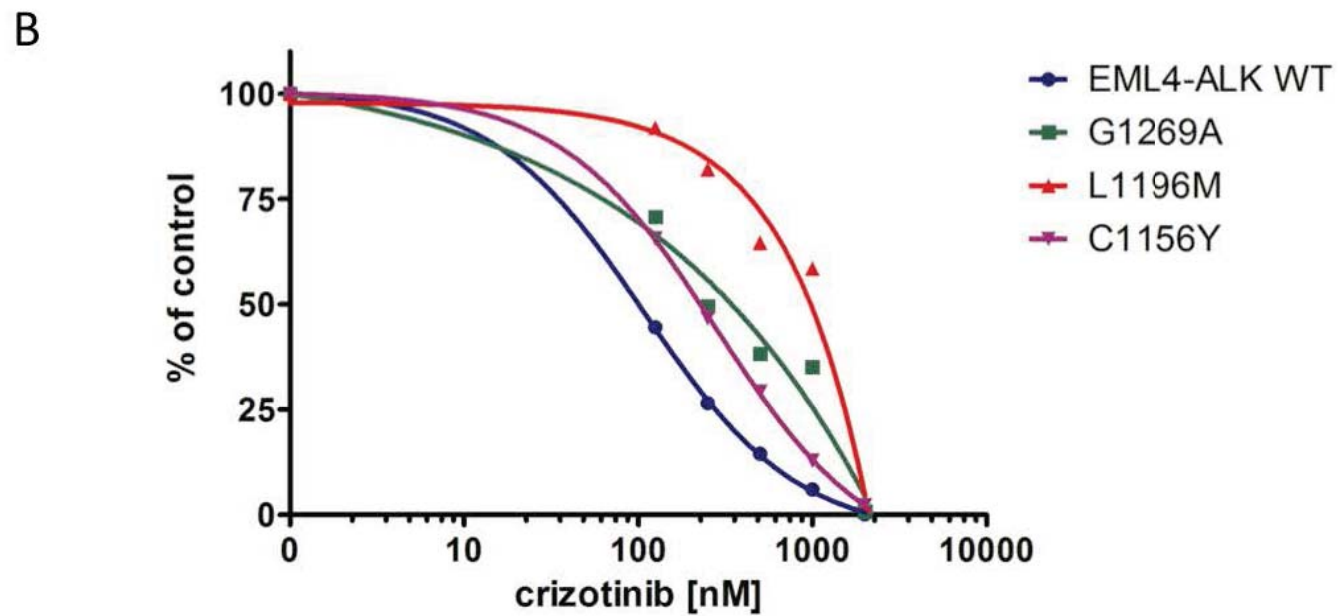
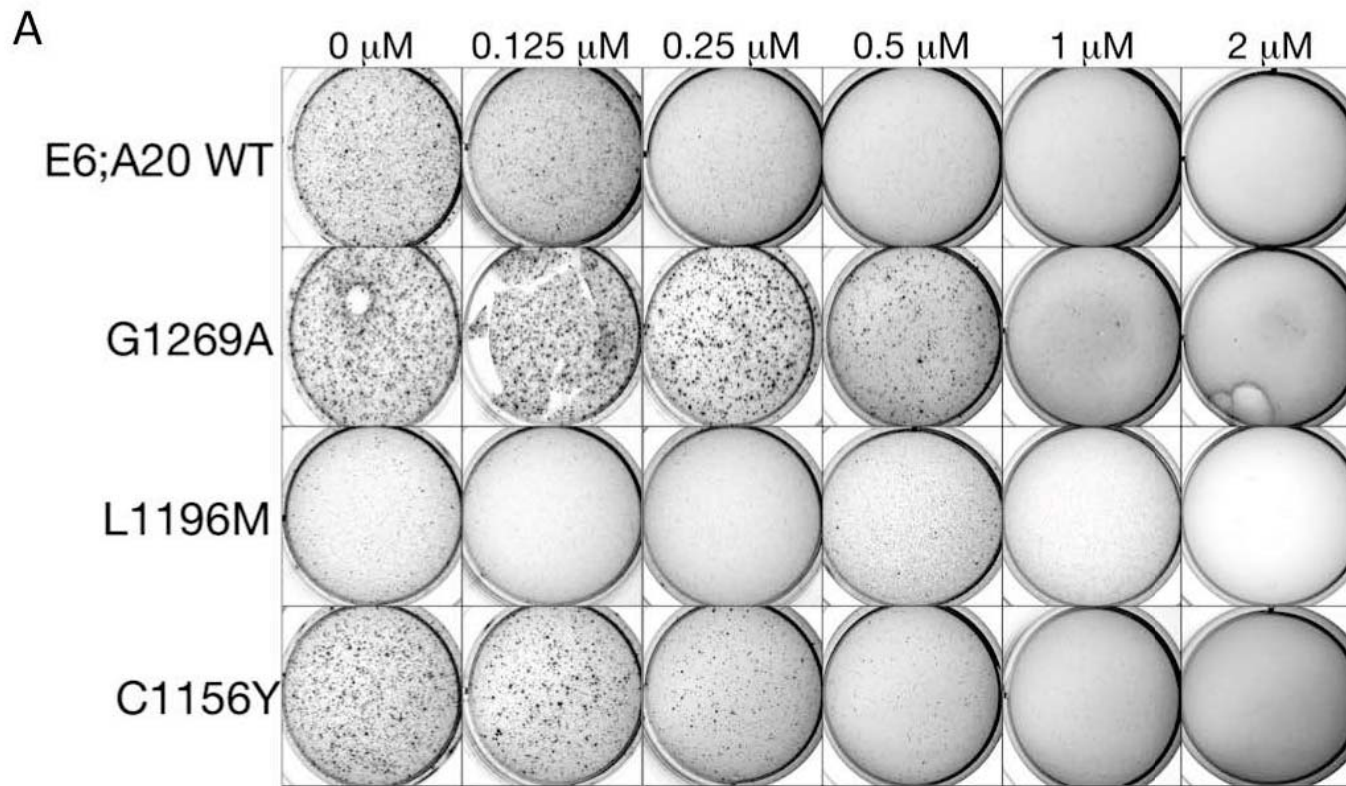


A



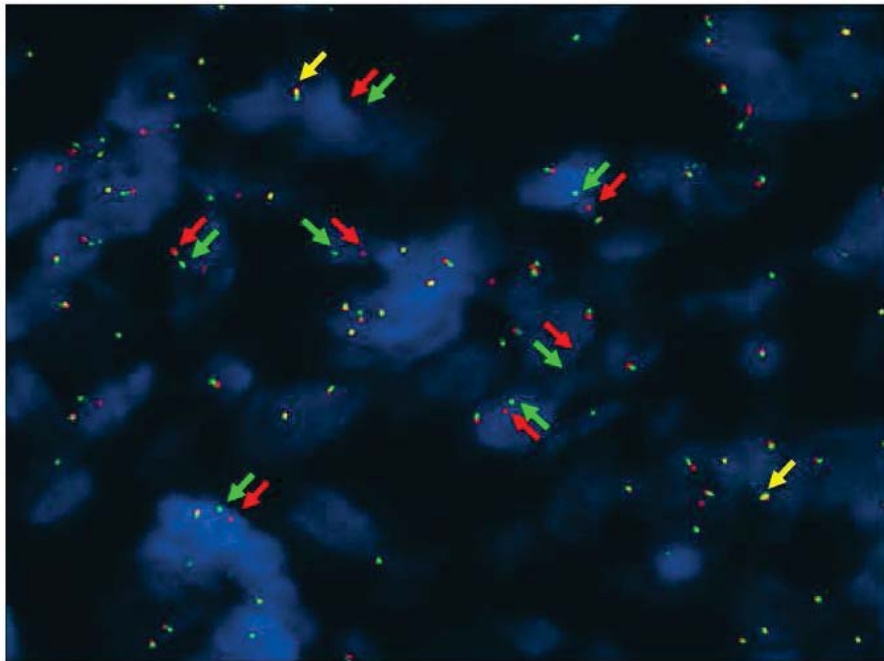
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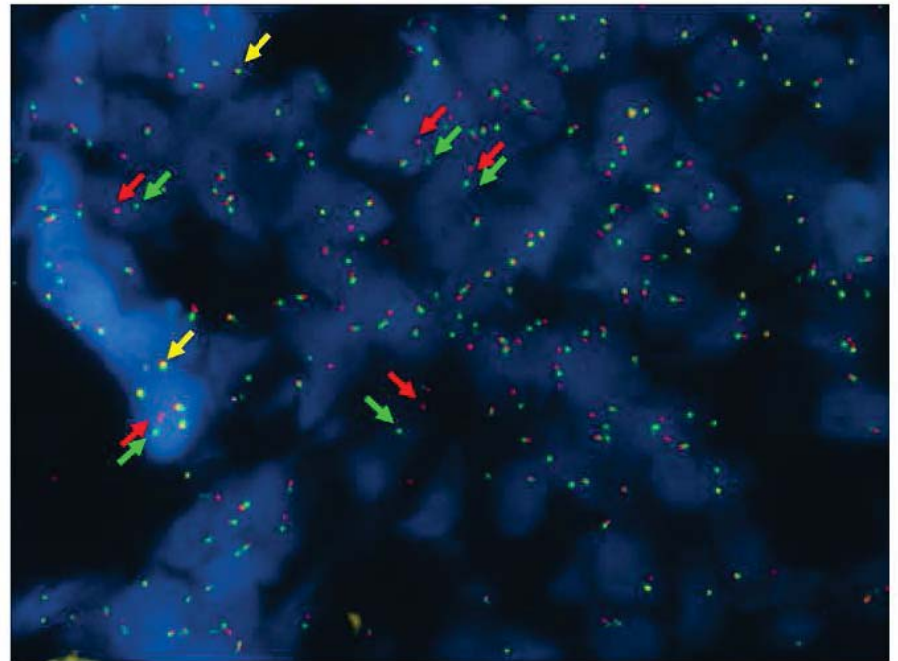
A

Pre-crizotinib



B

Post-crizotinib



Supplemental Table 2. Primer sequences used for PCR of genomic DNA, RT-PCR, and mutagenesis

Amplicon	Forward (5'-->3')	Reverse (5'-->3')
<i>ALK</i> Exon 21	GGACATTCCAGCTACATCAC	CTGTGAGCTGAGAAGTGC
<i>ALK</i> Exon 22	GCAGTTCTCAGCTCACAG	GAATGTTTGGGAGTCTCCT
<i>ALK</i> Exon 21-22 [¥]	TGACTCTGTCTCCTCTTGTC	TTAGAAACCTCTCCAGGTTCC
<i>ALK</i> Exon 23 [¥]	AAGATTTGCCAGACTCAGC	TGTCCTTGGCACAACAAGTGC
<i>ALK</i> Exon 23(L)	TCCACGCACCAGTATCTGAGAAAGAC	ATCTTCTGTCCATTCTCTCCAGCCAGTC
<i>ALK</i> Exon 24 [¥]	AGATTTCCCTCCTCTCACTG	ATGTGAGCCCTTGAGATCTG
<i>ALK</i> Exon 25 [¥]	TAGTGATGGCCGTTGTACAC	CCAGGAGATGATGTAAGGGA
Multiplex <i>EML4-ALK</i> [€]	GTCAGCTCTTGAGTCACGAGTT (<i>EML4</i> exon 2); GTGCAGTGTTTAGCATTCTTGGGG (<i>EML4</i> exon 13)	ATCCAGTTCGTCCTGTTTCAGAGC (<i>ALK</i> exon 22)
<i>EML4</i> (Exon 6)- <i>ALK</i>	CTGCAGACAAGCATAAAGATG	AGCTTGCTCAGCTTGTACTC
<i>ALK</i> G1269A Mutagenesis	GAGTGGCCAAGATTGCAGACTTCGGGATGGC	GCCATCCCGAAGTCTGCAATCTTGGCCACTC

[¥]Chen, Y., J. Takita, et al. (2008). "Oncogenic mutations of *ALK* kinase in neuroblastoma." *Nature* **455**(7215): 971-974

[€]Takeuchi, K., Y. L. Choi, et al. (2008). "Multiplex Reverse Transcription-PCR Screening for *EML4-ALK* Fusion Transcripts." *Clinical Cancer Research* **14**(20): 6618-6624