Supplementary

Table S1 Clinicopathologic characteristics between *KIF5B-RET* cases (N=90) and *CCDC6-RET* cases (N=23)

Variables	*KIF5B-RET*, N=90 [%]	*CCDC6-RET*, N=23 [%]	χ^2	P
Gender			0.054	0.815
Female	61 [68]	15 [65]		
Male	29 [32]	8 [35]		
Smoking			0.425	0.514
Never	79 [88]	19 [83]		
Smoker	11 [12]	4 [17]		
Age (years)			0.175	0.674
≤60	59 [66]	14 [61]		
>60	31 [34]	9 [39]		
Histology			1.907	0.167
ADC	83 [92]	23 [100]		
Non-ADC	7 [8]	0 [0]		
Stage			1.306	0.727
I	28 [31]	6 [26]		
II	4 [4]	2 [9]		
III	14 [16]	5 [22]		
IV	44 [49]	10 [43]		
Distant metastasis (% of stage IV)			2.244	0.134
No	8 [18]	4 [40]		
Yes	36 [82]	6 [60]		
Brain metastasis (% of stage IV)			1.843	0.174
No	25 [57]	8 [80]		
Yes	19 [43]	2 [20]		

RET, rearranged during transfection; ADC, adenocarcinoma.

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Table S2 Concurrent driver gene alteration in *RET*-rearranged NSCLCs

Case No.	Fusion	Concurrent mutations	Gender	Age	Histology	Stage	Treated with other TKI (PFS)
1	*KIF5B-RET* (K15:R12)	*EGFR* p.L858R	Male	41	ADC	III	Icotinib (PFS 23m)
2	*CEP128-RET* (C18:R11)	*EGFR* p.L858R	Female	63	ADC	IV	No
3	*LOC105378330-RET* (Lintergenic:R12)	*EGFR* p.L858R	Male	65	ADC	III	No
4	*NAMPTL-RET* (Nintergenic:R12)	*EGFR* p.19del	Female	49	ADC	III	No
5	*CCDC6-RET* (C1:R12)	*EGFR* p.19del	Female	50	ADC	IV	Gefitinib (PFS 24 m)*
6	*CCDC6-RET* (C1:R12)	*KRAS* p.G12V	Female	50	ADC	III	No
7	*SLC6A11-RET* (S5:R12)	*KRAS* p.G13D	Male	71	ADC	III	No
8	*ADAMTS2-RET* (A10:R3)	*EML4-ALK* (E6:A20)	Male	54	ADC	II	No

*, *CCDC6-RET* was detected as a resistant mechanism to *EGFR*-TKI in Case No 5. *RET*, rearranged during transfection; NSCLC, non-small cell lung cancer; ADC, adenocarcinoma; PFS, progression-free survival.

Table S3 Predictive factors for PFS in late-stage *RET*-rearranged NSCLCs with chemotherapy (N=36)

Variables	Univariable analysis, P	Multivariable analysis	
		Hazard ratio (95% CI)	P
Sex (female *vs.* male)	0.354	–	–
Smoking (never *vs.* ever)	0.828	–	–
Age(years) (≤60 *vs.* >60)	0.173	–	–
Histology (others *vs.* ADC)	0.386	–	–
Stage (III *vs.* IV)	0.429	–	–
Partner (*CCDC6 vs. KIF5B*)	0.014	0.192 (0.044–0.831)	0.027
Breakpoint (non-intron11 *vs.* intron11)	0.356	–	–
Distant Metastasis (no *vs.* yes)	0.083	–	0.724
Brain Metastasis (no *vs.* yes)	0.543	–	

NSCLC, non-small cell lung cancer; *RET*, rearranged during transfection; CI, confidence interval; ADC, adenocarcinoma.

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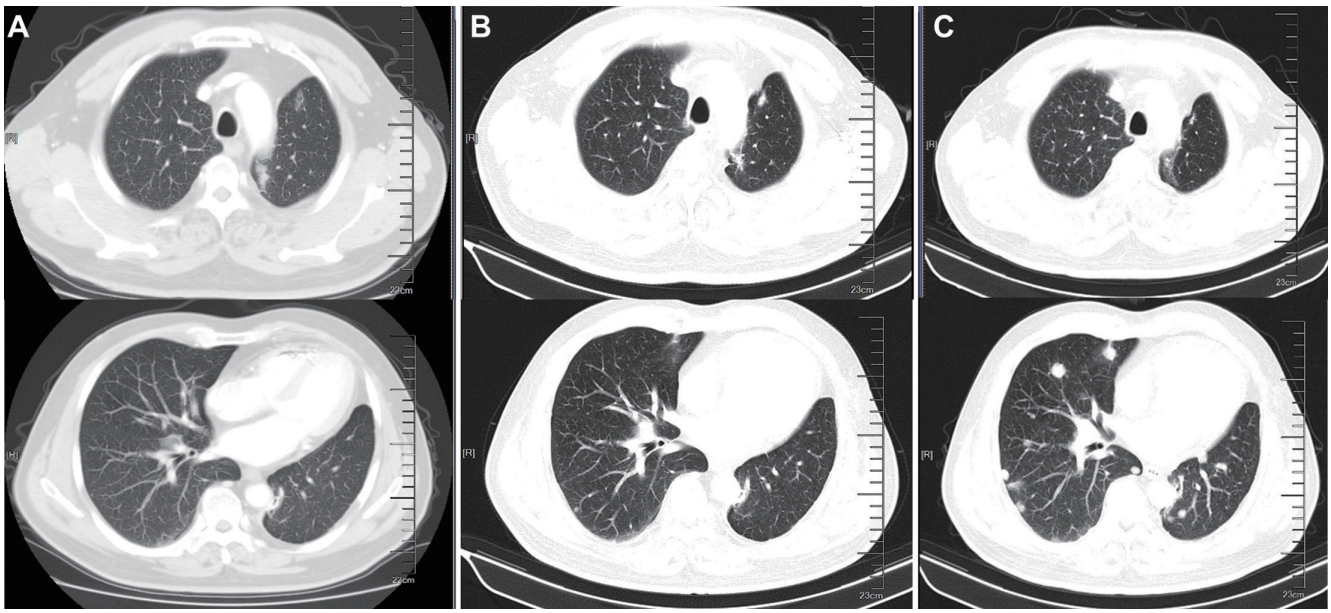

Figure S1 CT scans before and after therapy in a case of *ERC1-RET* fusion. (A) CT scans before Cabozantinib. (B) CT scans after 4 months of treatment with Cabozantinib. (C) CT scans after 10 months of treatment with Cabozantinib. CT, computed tomography.

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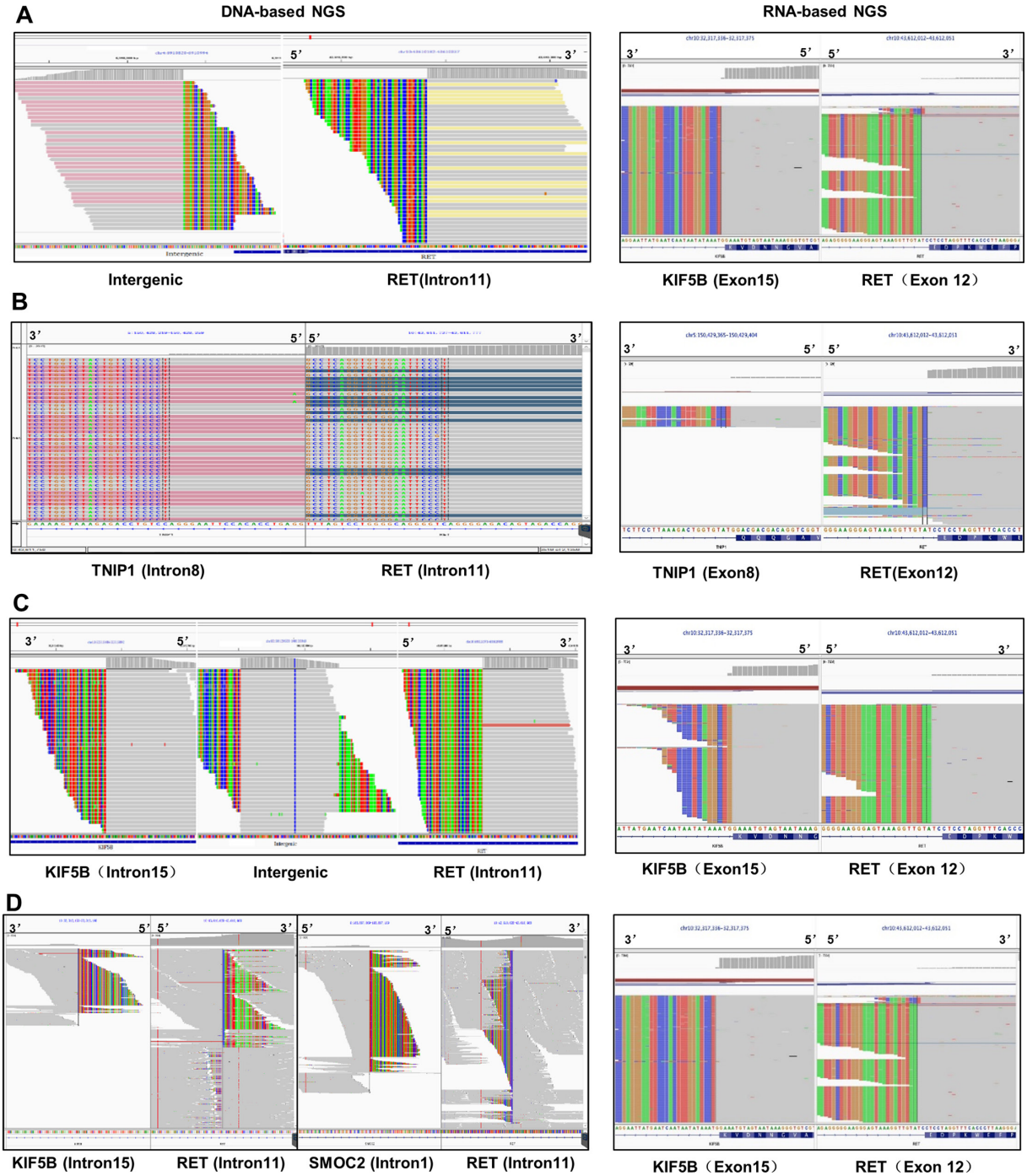

Figure S2 *RET* fusion identified by targeted DNA-NGS and RNA-NGS among 4 representative NSCLC cases. (A) DNA-based NGS revealed that the 3' portion of *RET* was fused to an intergenic region downstream of *TBC1D14*, while targeted RNA-NGS identified the *KIF5B-RET* (K15:R12) fusion transcript. (B) DNA-based NGS revealed *TNIP1-RET* (intron 8: intron 11), while targeted RNA-NGS identified the *TNIP1-RET* fusion transcript. (C) Targeted DNA-NGS revealed that the 3' portion of *RET* was fused to an intergenic region downstream of *LOC105378470* and then connected to the *KIF5B* gene after about 70 bp intervals, while targeted RNA-NGS identified the *KIF5B-RET* (K15:R12) fusion transcript. (D) *RET-KIF5B* (intron 11: intron 15) and *SMOC2-RET* (intron 1: intron 11) were detected simultaneously by targeted DNA-NGS, while canonical *KIF5B-RET* (K15:R12) fusion transcript was identified at the RNA level.

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