

ROS1 Cohort

Supplementary Table 3

Pt ID	line of TKI therapy	Prior Chemotherapy	Days until systemic progression or intolerance	prior tx	On- Target resistance mechanisms		Off- Target resistance mechanisms	
					KDM	ROS1 CNG	Alternate oncogenic mutation	CNV
1	2	no	51	criz/cer	neg	NA	CTNNB1 S45F	ERBB2/SRC/NOTCH
2	2	yes	57	criz/brig	neg	NA	neg	neg
6	2	yes	30	criz//cer	neg	NA	neg	neg
3	1	yes	156	none	neg	neg	neg	neg
4	1	yes	106	none	neg	NA	neg	NA
5	1	no	450	none	neg	neg	KIT D816G	NA
7	1	no	533	none	L1951R (9%); L2026M (19%)	NA	neg	neg
8	1	no	187	none	neg	NA	neg	neg
9	1	no	151	none	neg	NA	neg	KDR/PDGFRA
10	1	no	264	none	neg	NA	neg	neg
11	1	no	74	none	neg	NA	neg	neg
12	1	yes	1461	none	neg	NA	MET A347T; GNA11 D301A	neg

ALK Crizotinib Cohort

Pt ID	line of TKI therapy	Prior Chemotherapy	Days until systemic progression or intolerance	prior target tx	On- Target resistance mechanisms		Off- Target resistance mechanisms	
					KDM	ALK CNG	Alternate oncogenic mutation	CNV
4*	1	yes	126	none	L1196M	neg	neg	NA
5*	1	yes	793	none	L1196M	neg	neg	NA
6*	1	yes	394	none	G1269A	neg	neg	NA
7*	1	yes	197	none	G1269A	positive	neg	neg
9*	1	yes	168	none	neg	neg	EGFR L858R	NA
10*	1	yes	28	none	neg	neg	KRAS G12C	DDR2/KRAS
11*	1	yes	215	none	neg	neg	KRAS G12V	NA
12*	3	yes	42	criz/cer	neg	neg	lost ALK	neg
13*	1	yes	32	none	neg	neg	NA	NA
14*	1	yes	273	none	neg	neg	neg	NA
16*	1	yes	852	none	neg	neg	neg	neg
17_1*	1	yes	396	none	F1174C	neg	neg	NA
17_3	3	yes	121	criz/cer	F1174C	neg	neg	ARAF
18*	1	yes	218	none	neg	neg	KRAS G13D	NA
19	1	no	277	none	neg	NA	neg	NA
20	1	yes	886	none	neg	positive	NA	NA
21	1	yes	153	none	neg	NA	neg	EGFR
23	1	yes	394	none	Test fail	NA	neg	NA
24_1	1	yes	182	none	neg	neg	neg	neg
26	1	yes	94	none	neg	neg	neg	MAP2K1/ARAF
27	1	no	76	none	neg	neg	IDH1	EGFR/CDH1/ AXL/ARAF
28	1	no	139	none	neg	NA	NF1	neg
29_1	1	yes	629	none	E12010K	neg	neg	neg
31	1	yes	636	none	neg	positive	EGFR e19d	NA
32	1	yes	73	none	neg	neg	neg	neg
37	1	yes	455	none	neg	neg	neg	FOXL2/HRAS/ AKT1/TP53/ ERBB2/STK11/ GNA11/AXL/ SRC
39	1	yes	133	none	L1196M	NA	neg	neg
40	1	no	83	none	neg	NA	neg	GNAS
41	1	yes	1035	none	neg	NA	Neg	DDR2
46	1	no	191	none	neg	NA	RIT1 K139	neg

Ceritinib Cohort

Supplementary Table 3 cont.

Pt ID	Line of Therapy	Prior Chemotherapy	Days until Systemic Progression or Intolerance	prior target tx	On- Target resistance mechanisms		Off- Target resistance mechanisms	
					KDM	ALK CNG	Alternate oncogenic mutation	CNV
8*	2	yes	213	criz	neg	positive	<i>NOTCH1</i> D1533A	neg
15*	2	yes	76	criz	D1203N	neg	neg	NA
17_2	2	yes	326	criz	F1174C	neg	neg	neg
24_2	2	yes	166	criz	neg	positive	neg	NA
25	2	yes	110	criz	G1202R (25%); G1202X (19%)	NA	neg	<i>RIT1/NTRK1/H</i> <i>RAS/AKT1</i>
38	3	no	672	criz/brig	F1174L	NA	neg	NA

Alectinib Cohort

Pt ID	Line of Therapy	Prior Chemotherapy	Days until Systemic Progression or Intolerance	prior target tx	On- Target resistance mechanisms		Off- Target resistance mechanisms	
					KDM	ALK CNG	Alternate oncogenic mutation	CNV
22_2	6	yes	41	criz/alec/ criz/lor/ criz/	neg	NA	<i>RALGAPA1- NRG1</i>	neg
33	2	no	401	criz	G1202S	NA	neg	<i>CTNNB1/KIT/ KDR/ARAF</i>
43	2	yes	226	criz	G1202R	NA	neg	<i>CDH1</i>
44_1	2	no	466	criz	neg	NA	neg	neg

Brigatinib Cohort

Pt ID	Line of Therapy	Prior Chemotherapy	Days until Systemic Progression or Intolerance	prior target tx	On- Target resistance mechanisms		Off- Target resistance mechanisms	
					KDM	ALK CNG	Alternate oncogenic mutation	CNV
29_2	2	yes	329	criz	S1206C (24%); E1210K (26%)	neg	neg	NA
30	2	yes	128	criz	F1174L	neg	neg	neg
35	2	no	612	criz	neg	test fail	neg	<i>APC/FGFR1/ AXL</i>
36	2	no	350	criz	neg	NA	neg	<i>ARAF</i>
42	2	yes	539	criz	neg	NA	<i>NOTCH1</i> D1538A	neg
44_2	3	no	390	criz/alec	NA	NA	<i>CCDC6-RET</i>	NA
47	2	yes	1546	criz	F1174L (20%); L1198V (10%)	NA	neg	<i>NTRK1/ MSH6/APC/ FGFR1/ NOTCH1/ PTEN/ MAP2K1</i>

Lorlatinib Cohort

Pt ID	Line of Therapy	Prior Chemotherapy	Days until Systemic Progression or Intolerance	prior target tx	On- Target resistance mechanisms		Off- Target resistance mechanisms	
					KDM	ALK CNG	Alternate oncogenic mutation	CNV
22_1	4	no	22	criz/alec/criz	neg	positive	neg	NA
45	4	no	146	criz/brig/alec	D1203A	NA	neg	neg

Abbreviations: Pt – patient; criz- crizotinib, cer – ceritinib, brig – brigatininb, alec – alectinib, neg – not found, KDM – kinase domain mutation, AM – alternative mutation, CNG – copy number gain
Key: direct sequencing- green, NGS – blue, SNaPshot-yellow, Direct sequencing and NGS-purple, NGS and snapshot –orange. * Indicates patients whose data has been presented previously.