Supplemental Figures and Tables:

Supplemental Table S1

	***MET*ex14 Cohort**	***EGFR*m Cohort**
Total # Samples	332	1653
Total # Patients	289	1489
Date Range	10/2015-3/2018	4/2016-5/2017
Gender (% Patients)		
Female	172 (59.5%)	992 (66.6%)
Male	116 (40.1%)	497 (33.4%)
Not Specified	1 (0.3%)	0 (0%)
Mean Age	73 years	64.4 years
Stage III/IV (% Samples)	289 (100%)	1653 (100%)
Histology (% Patients)		
Lung Adenocarcinoma	163 (56.4%)	532 (35.7%)
NSCLC, not otherwise specified	93 (32.2%)	954 (64.1%)
Lung Squamous Cell Carcinoma	20 (6.9%)	0 (0%)
Other	13 (4.5%)[a]	3 (0.2%)[b]
Treatment History (% Samples)		
Unknown	261 (78.6%)	1653 (100%)
Tyrosine Kinase Inhibitor[c]	26 (7.8%)	
Chemotherapy[d]	22 (6.6%)	
Checkpoint Inhibitor	17 (5.1%)	
Radiation	3 (0.9%)	

[a]Lung cancer NOS (2%), Carcinoid (0.7%), Sarcomatoid (0.7%), Large Cell (0.3%), Carcinosarcoma (0.3%), Small Cell Lung Cancer (0.3%)
[b]Lung cancer, not otherwise specified
[c]Crizotinib (3.3%), Erlotinib (2.7%), Alectinib (0.6%), MET TKI not otherwise specified (0.3%), Crizotinib/trametinib (0.3%), Cabozantinib (0.3%), Afatinib (0.3%)
[d]Including chemotherapy combinations: Pemetrexed/Pembrolizumab (0.3%), docetaxel/nintedanib (0.3%)

Cell-free DNA cohort demographics. Clinical and demographic data for two cohorts of patients with advanced NSCLC, incorporating all patients with either the *MET* exon 14 skipping mutation (*MET*ex14) or an activating epidermal growth factor mutation (*EGFR*m) identified by cfDNA sequencing over the specified time period.

Supplemental Table S2

Patient #	Histology	Sample Prior to Known MET TKI Exposure		Sample After MET TKI Exposure	
		Treatment Status	Genomic Alterations	MET TKI Received	Genomic Alterations % cfDNA/CNG
1	Lung Adeno-carcinoma	Pre-treatment	METex14 (c.3028+3A>G, 7.6%), PTEN E43Q (0.1%), CCNE1 CNG (2.3)	Crizotinib	METex14 (0.9-5.1%), BRAF R199G (0.1-0.2%), CCNE1 CNG (2.2), PIK3CA R38H (0.1%), MET Y1230S (0.3-1.5%), MET F1200I (0.2%), KRAS CNG (2.25-2.28)
2[a]	Lung Adeno-carcinoma	Pre-treatment	METex14 (c.2888-19_2895del27, 8%)[b]	Crizotinib	METex14 (2.2%), KRAS G12D (7.8%)
3	Lung Adeno-carcinoma	Carboplatin/ pemetrexed/ bevacizumab	METex14 (c.3028G>C, 1.2%), BRCA1 R691G (0.1%)	Crizotinib	METex14 (1%), FBXW7 R689Q (0.1%), AR W742C (0.1%), TP53 Y163S (0.1%), KIT CNG (2.2)
4	Lung Adeno-carcinoma	Pre-treatment	METex14 (c.3028G>C, 19.8%), NF1 I1499V (0.3%), BRAF CNG (2.6), NF1 R1534Q (0.1%), EGFR V851A (0.1%), EGFR CNG (2.5), MET CNG (2.6), CDK6 CNG (2.6), MYC CNG (2.4)	Crizotinib[c]	METex14 (2.5%), NF1 I1499V (0.2%), CCND1 CNG (2.5), TP53 N239S (1.8%), TP53 R248W (0.5%), NF1 p.Gln2636fs (1.1%), MET p.Ser244fs (1.2%)
5	Lung Adeno-carcinoma	Pre-treatment	METex14 (c.3028+1delG), MET CNG, CDK6 CNG, ATM splice site, MDM2 CNG, CDKN2A/B loss[b]	Crizotinib	METex14 (53.4%), MET CNG (3.9), CDK6 CNG (3), AR CNG (2.3), PIK3CA CNG (2.3), MET Y1230H (9.1%), MET D1228N (4.3%), EGFR CNG (2.2)
				Glesatinib	METex14 (63.5%), MET CNG (4.9), CDK6 CNG (3.3), PIK3CA CNG (2.4), MET L1195V (0.8%), MET D1228N (13.9%)
6	Lung SCC	Nivolumab	METex14 (c.2888-12_2889delCTCTGTTTTAAGATinsTAAGAG, 4.6%)	Crizotinib	METex14 (7.7%), EGFR CNG (2.7), TP53 p.Arg156del (0.04%)
7	Lung Adeno-carcinoma	Carboplatin/ Paclitaxel	TP53 P27L (0.2%), TP53 c375+1G>C (0.1%)	Crizotinib	METex14 (c.2888-20_2888delTTCTTTCTCTCTGTTTTAAGA, 0.02%)

8	Lung Adeno-carcinoma	Carboplatin/ pemetrexed/ bevacizumab	METex14 (c.3028+2T>C, 0.4%), BRAF S273G (0.5%), MET R1170* (47.7%)	Crizotinib	BRAF S273G (0.3%), TP53 V173M (0.3%)
9	Lung Adeno-carcinoma	Unknown	METex14 (c.3028G>T, 14.5%), MET CNG (2.4), EGFR K80T (0.8%), ERBB2 N68S (0.7%), KRAS G12S (0.1%)	Crizotinib	METex14 (50%), MET CNG (4), EGFR K80T (0.3%), ERBB2 N68S (3.5%), MET L1195V (16.6%), TP53 V216E (0.1%), EGFR CNG (2.4)
10	Lung Adeno-carcinoma	Unknown	METex14 (c.3028+1G>T, 0.5%), BRCA1 I3044V (0.2%), FGFR1 T340M (0.1%)	Crizotinib	BRCA2 I3044V (0.1%), FGFR1 T340M (0.2%)
11	Lung Adeno-carcinoma	Unknown	METex14 (c.3012_3028+3delAG CTACTTTTCCAGAAG GTAinsG, 4.8%), MET CNG (2.2), CDKN2A p.Thr77fs (0.9%)	Crizotinib	TP53 R158H (0.2%), EGFR R836H (0.2%), PDGFRA R558H (0.2%)
12	NSCLC NOS	Pre-treatment	METex14 (c.2888-5_2905delTTAAGATC TGGGCAGTGAATTA, 2%), RECQL4 splice site (2464-1G>C, 46%), SMAD4 Q224X (10%), CDK4 CNG (22.4), KMT2A CNG (7.2), MDM2 CNG (11.5)[b]	Crizotinib	METex14 (0.6%), MET D1228H (0.1%), TP53 F270L (0.1%)

[a]cfDNA analysis via FoundationACT assay.
[b]Sequencing prior to known MET TKI exposure performed on a tumor biopsy sample rather than via plasma cfDNA analysis, utilizing a University of Florida in-house NGS assay (patient 2), Foundation One (patient 5), or Cancer-Select assay (patient 12).
[c]Followed by pemetrexed prior to cfDNA testing.

Genomic alterations in the cfDNA of patients treated with a MET TKI. Genomic alterations identified upon targeted sequencing for cancer-associated genes in cfDNA samples obtained following known MET TKI exposure compared to results of samples obtained prior to known MET TKI exposure. Sequencing performed via the Guardant360 assay, unless otherwise specified. Further details for patient one in Figure 2A and further details for patient two in Figure 2B. Additional details regarding patient five have previously been published (6,8). Abbreviations: NOS, not otherwise specified; CNG, copy number gain

Supplemental Table S3

Treatment Status	**Diagnosis**	**Crizotinib Treatment**			**Crizotinib Held**	**Crizotinib Resumed**			**Crizotinib +Trametinib**
Radiographic Response	**N/A**	**PR**	**PR**	**PR**	**PD**	**PD**	**PD**	**PD**	**Unknown**
Time After Diagnosis (months)	**0**	**1.4**	**2**	**3.7**	**5**	**6.7**	**8.2**	**10**	**10.5**
Gene Variant	**cfDNA frequency (%)/Copy Number Gain**								
***MET*ex14**	7.6	0	0	0	2.1	0.5	0.9	5.1	1.6
***BRAF* R199G**	0	0.2	0	0.2	0	0	0	0.1	0
***PIK3CA* R38H**	0	0	0	0	0	0	0.1	0	0
***PTEN* E43Q**	0.1	0	0	0	0	0	0	0	0
***MET* Y1230S**	0	0	0	0	0	0	0	1.5	0.3
***MET* F1200I**	0	0	0	0	0	0	0	0.2	0.2
***KRAS* copy number gain**	0	0	0	0	0	0	2.28	2.25	0
***CCNE1* copy number gain**	2.3	0	0	0	0	0	0	2.2	0

Serial plasma cfDNA testing (patient one). The results of serial cell-free DNA sequencing utilizing the Guardant360 assay, in a patient with *MET* exon 14 mutated lung adenocarcinoma during response and after acquired resistance to the MET tyrosine kinase inhibitor crizotinib, and following initial treatment with the combination of crizotinib plus trametinib. Samples in the setting of resistance to crizotinib are notable for new *KRAS* copy number gain, as well as new *MET* Y1230S and F1200I mutations. Abbreviations: N/A, not applicable; PD, progressive disease; PR, partial response;

Supplemental Table S4

Gene	Variant	Mutant Allele Frequency/Reads
KRAS	Copy number gain	~22x
MET	c.3028+3A>G (exon 14 skipping)	48%
TP53	c.375_375+2dupGGT	32%
RBM10	p.K700*	36%
ERBB4	c.1490-1G>T	8%
MUTYH	c.788+8G>T	8%
TSHR	p.R450H	8%
PTPRT	p.D113N	8%
ARID2	p.D1703N	6%
ZFHX4	p.A386T, p.Q2415H	8%, 7%
BCORL1	p.G1479R	15%
PARK2	p.D280E	10%
PDGFRB	p.P250H	9%
PRKAR1A	p.S77L	7%
TSHZ3	p.F67V	4%

Tumor next generation sequencing (NGS) results (patient one). Genomic alterations identified by targeted-sequencing for cancer-associated genomic alterations (UCSF500 Assay) within a biopsy specimen from a rib metastasis progressing during treatment with crizotinib, showing 22-fold *KRAS* copy number gain.

Supplemental Table S5

A. Pre-treatment lung biopsy, University of Florida GatorSeq NGS

Gene	cDNA	Alteration	VAF (%)
MET	c.2888-19_2895del27	Exon 14 Skipping	8.0%
BCR	c.2515C>T	p.R839C	46.4% [b]
DNMT3A	c.2645G>A	p.R882H	6.3%[a]
MKL1	c.1942A>G	p.S648G	99.9% [b]
ALK	c.4381A>G	p.I1461V	99.7% [b]
ASXL1	c.2444T>C	p.L815P	99.6% [b]
FLT3	c.680C>T	p.T227M	99.5% [b]
EGFR	c.1562G>A	p.R521K	62.7% [b]
ALK	c.4472A>G	p.K1491R	51.2% [b]
TET2	c.5284A>G	p.I1762V	51.1% [b]
BCR	c.2387A>G	p.N796S	50.5% [b]
PML	c.1933T>C	p.F645L	50.5% [b]
ALK	c.4587C>G	p.D1529E	49.5% [b]
PDGFRA	c.1432T>C	p.S478P	45.9% [b]
TP53	c.215C>G	p.P72R	45.8% [b]

[a]Present in peripheral blood mononuclear cells

[b]Scored as single nucleotide polymorphisms

B. Pre-treatment, plasma cfDNA, Foundation ACT assay

Gene	Alteration	cfDNA Frequency (%)
MET	Exon 14 skipping	2.2%
KRAS	G12D	7.8%
BRAF	S446L	VUS
PDCD1LG2	F3fs*1	VUS

C. Crizotinib progression, liver biopsy, Foundation One assay

Gene	Alteration	VAF(%)/CNG
MET	Exon 14 Skipping	77.9%
KRAS	Amplification	11x
KRAS	G12D	47.4%
HGF	Amplification	11x
MDM2	Amplification	10x
CDKN2A/B	Loss	0x
FRS2	Amplification	10x
ARID1A	Q1334_R1335insQ	VUS
FAT1	T2444I	VUS
MLL2	R3099H	VUS
MLL3	M305L	VUS
FLT1	P1201I	VUS
GLI1	L847R	VUS
GPR124	P168R, P550S	VUS
PLCG2	A420T	VUS
PPP2R1A	P493L	VUS
PRKDC	S1300G	VUS

LRP1B	I844M	VUS
SNCAIP	D36N	VUS

Results of serial sequencing of tumor tissue and plasma cfDNA (patient two). A. Pre-treatment targeted sequencing using the University of Florida GatorSeq NGS assay of a lung tumor lesion which would subsequently respond to crizotinib. **B.** cfDNA sequencing via the Foundation ACT assay prior to mixed response to crizotinib showed a *KRAS* G12D mutation. **C.** Subsequent biopsy of a metastatic liver lesion progressive on crizotinib showed the same *KRAS* G12D mutation as well as 11-fold *KRAS* copy number gain and 11-fold *HGF* copy number gain. Abbreviations: VAF, variant allele fraction; VUS, variant of unknown significance.

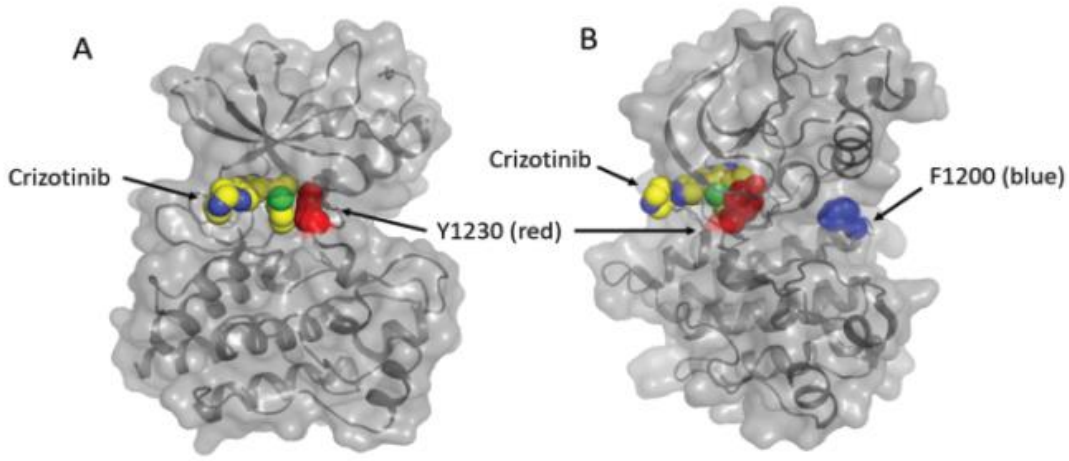
Supplemental Table S6

NGS Panel	Gene List
Guardant360, 70-Gene Assay	AKT1, ALK, APC, AR, ARAF, ARID1A, ATM, BRAF, BRCA1, BRCA2, CCND1, CCND2, CCNE1, CDH1, CDK4, CDK6, CDKN2A, CTNNB1, EGFR, ERBB2, ESR1, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, GATA3, GNA11, GNAQ, GNAS, HNF1A, HRAS, IDH1, IDH2, JAK2, JAK3, KIT, KRAS, MAP2K1, MAP2K2, MET, MLH1, MPL, MYC, NF1, NFE2L2, NOTCH1, NPM1, NRAS, NTRK1, PDGFRA, PIK3CA, PTEN, PTPN11, RAF1, RB1, RET, RHEB, RHOA, RIT1, ROS1, SMAD4, SMO, STK11, TERT, TP53, TSC1, VHL, CDKN2B[a], SRC[a]
Guardant360, 73-Gene Assay	AKT1, ALK, APC, AR, ARAF, ARID1A, ATM, BRAF, BRCA1, BRCA2, CCND1, CCND2, CCNE1, CDH1, CDK4, CDK6, CDKN2A, CTNNB1, DDR2[a], EGFR, ERBB2, ESR1, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, GATA3, GNA11, GNAQ, GNAS, HNF1A, HRAS, IDH1, IDH2, JAK2, JAK3, KIT, KRAS, MAP2K1, MAP2K2, MAPK1[a], MAPK3[a], MET, MLH1, MPL, MTOR[a], MYC, NF1, NFE2L2, NOTCH1, NPM1, NRAS, NTRK1, NTRK3[a], PDGFRA, PIK3CA, PTEN, PTPN11, RAF1, RB1, RET, RHEB, RHOA, RIT1, ROS1, SMAD4, SMO, STK11, TERT, TP53, TSC1, VHL
University of Florida GatorSeq NGS Assay	ABL1, AKT1, ALK, ASXL1, BAALC, BCOR, BCR, BRAF, BRINP3, CBFB, CEBPA, CRLF2, CTNNB1, DDR2, DEK, DNMT3A, EGFR, ERBB2, ERG, ETV6, EZH2, FBXW7, FGFR1, FGFR2, FLT3, GNA11, GNAQ, HOXA9, HRAS, IDH1, IDH2, JAK2, KIT, KMT2A, KRAS, MAP2K1, MECOM, MET, MKL1, MLLT3, MN1, MPL, MYC, MYH11, NF1, NOTCH1, NPM1, NRAS, NUP214, PDGFRA, PHF6, PIK3CA, PML, PTEN, PTPN11, RAD21, RARA, RBM15, RET, RPN1, RUNX1, RUNX1T1, SF3B1, SMAD4, SMC1A, SMC3, SMO, SRSF2, STAG2, TET2, TP53 TSC1, U2AF1, U2AF2, WT1, ZRSR2
UCSF500 NGS Assay	ABL1, ABL2, ACVR1, ACVR1B, AJUBA, AKT1, AKT2, AKT3, ALK, AMER1, APC, APOBEC3G, AR, ARAF, ARFRP1, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASH2L, ASXL1, ASXL2, ATF1, ATM, ATR, ATRX, AURKA, AURKB, AXIN1, AXIN2, AXL, BAP1, BARD1, BCL2, BCL2A1, BCL2L1, BCL2L12, BCL2L2, BCL6, BCOR, BCORL1, BLM, BRAF, BRCA1, BRCA2, BRD4, BRIP1, BTG1, BTK, C11orf30, CALR, CARD11, CBFB, CBL, CBLB, CCND1, CCND2, CCND3, CCNE1, CD274, CD79A, CD79B, CDC42, CDC73, CDH1, CDK12, CDK4, CDK6, CDK8, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CEBPA, CHD1, CHD2, CHD4, CHD5, CHEK1, CHEK2, CIC, CLDN18, CNOT3, COL1A1, COL2A1, CRCT1, CREB1, CREBBP, CRKL, CSF1R, CSF3R, CTCF, CTNNA1, CTNNB1, CUL3, CUX1, CXCR4, CYLD, DCC, DDIT3, DDR2, DDX3X, DDX41, DGKH, DICER1, DIS3, DNAJB1, DNMT3A, DOT1L, DUSP2, DUSP4, DUSP6, DYNC1I1, EBF1, EDNRB, EGFR, EGR1, EIF1AX, ELF3, EP300, EPCAM, EPHA2, EPHA3, EPHA5, EPHA7, EPHB1, EPOR, ERBB2, ERBB3, ERBB4, ERCC1, ERCC2, ERG, ERRFI1, ESPL1, ESR1, ESR2, ETS1, ETV6, EWSR1, EZH1, EZH2, FAM46C, FANCA, FANCC, FANCE, FANCF, FANCG, FANCL, FAT1, FAT3, FBXW7, FGF10, FGF14, FGF19, FGF23, FGF3, FGF4, FGF6, FGFR1, FGFR2, FGFR3, FGFR4, FH, FLCN, FLT1, FLT3, FLT4, FOXA1, FOXL2, FOXO1, FOXP1, FRS2, FUBP1, FUS, FYN, GAB2, GATA1, GATA2, GATA3, GLI1, GLI2, GNA11, GNA13, GNAQ, GNAS, GPC3, GPR124, GRIN2A, GRM3, GSK3B, H3F3A, H3F3B, HDAC4, HDAC9, HEY1, HGF, HIF1A, HIST1H3B, HMGA2, HNF1A, HOXB13, HRAS, HSP90AB1, HSPA2, HSPA5, ID3, IDH1, IDH2, IGF1R, IGF2, IGF2R, IKBKE, IKZF1, IKZF2, IKZF3, IL2RB, IL7R, INHBA, INPP4B, IPMK, IRF4, IRS2, JAK1, JAK2, JAK3, JAZF1, KAT6A, KDM5A, KDM5C, KDM6A, KDR, KEAP1, KIT, KLF4, KLHL6, KMT2A, KMT2B, KMT2D, KNSTRN, KRAS, LEF1, LIFR, LRP1B, LZTR1, MALAT1, MAML2, MAP2K1, MAP2K2, MAP2K4, MAP3K1, MAP3K2, MAP3K5, MAP3K7, MAP3K9, MAPK1, MCL1, MDM2, MDM4, MED12, MEF2B, MEN1, MET, MGA, MGMT, MITF, MLH1, MLH3, MPL, MRE11A, MSH2, MSH3, MSH6, MTOR, MUTYH, MYB, MYBL1, MYC, MYCL, MYCN, MYD88, MYH9, NAV3, NBN, NCKAP5, NCOA2, NCOA3, NCOR1, NF1, NF2, NFE2L2, NFKBIA, NFKBIE, NIPBL, NKX2-1, NOTCH1, NOTCH3, NPM1, NRAS, NSD1, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, NUTM1, OR5L1, PAK1,

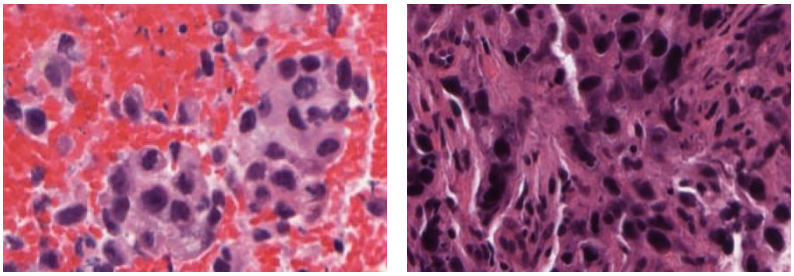
	PAK3, PALB2, PARK2, PAX3, PAX5, PAX7, PAX8, PBRM1, PDCD1LG2, PDGFB, PDGFRA, PDGFRB, PDK1, PHF6, PHOX2B, PIK3CA, PIK3CG, PIK3R1, PIK3R2, PLAG1, PLCB4, PMS1, POLD1, POLE, POLQ, POT1, POU3F2, PPM1D, PPP2R1A, PPP6C, PRDM1, PREX2, PRKACA, PRKAG2, PRKAR1A, PRKCA, PRKCH, PRKDC, PTCH1, PTCH2, PTEN, PTK2B, PTPN1, PTPN11, PTPRB, PTPRD, PTPRK, PTPRT, RAC1, RAD21, RAD50, RAD51, RAD51C, RAD51D, RAF1, RARA, RASA1, RASA2, RB1, RBM10, REL, RELA, RET, RHEB, RHOA, RICTOR, RIT1, RNF43, ROBO1, ROS1, RPL10, RPTOR, RRAGC, RRAS, RRAS2, RSPO2, RSPO3, RUNX1, RUNX1T1, SDHB, SDHD, SETBP1, SETD2, SF3B1, SH2B3, SHH, SIN3A, SLIT2, SLITRK6, SMAD2, SMAD3, SMAD4, SMARCA2, SMARCA4, SMARCB1, SMC1A, SMC3, SMO, SNCAIP, SOCS1, SOS1, SOS2, SOX10, SOX2, SOX9, SPEN, SPOP, SPRED1, SPRY1, SPRY2, SPRY4, SPTA1, SRC, SRSF2, SS18, STAG2, STAT3, STAT4, STAT6, STK11, SUFU, SYK, SYNE1, TADA1, TBX3, TCEB1, TCF7L2, TERT, TET2, TFE3, TFEB, TGFBR2, TLR4, TMPRSS2, TNFAIP3, TNFRSF14, TOP1, TOP2A, TP53, TRAF3, TRAF7, TRIM28, TSC1, TSC2, TSHR, TSHZ2, TSHZ3, TSLP, TTYH1, TYK2, U2AF1, USP7, VEGFA, VHL, WHSC1, WISP3, WRN, WT1, XBP1, XPO1, YAP1, YWHAE, ZBTB20, ZFHX3, ZFHX4, ZMYM3, ZNF217, ZNF703, ZRSR2

[a]Excluded from 68 gene set in common between 70 and 73 gene sets

Genes included in NGS Panels. List of cancer-associated genes included in the 70- and 73-gene versions of the Guardant360 assay, University of Florida GatorSeq NGS assay, and UCSF500 NGS assay.

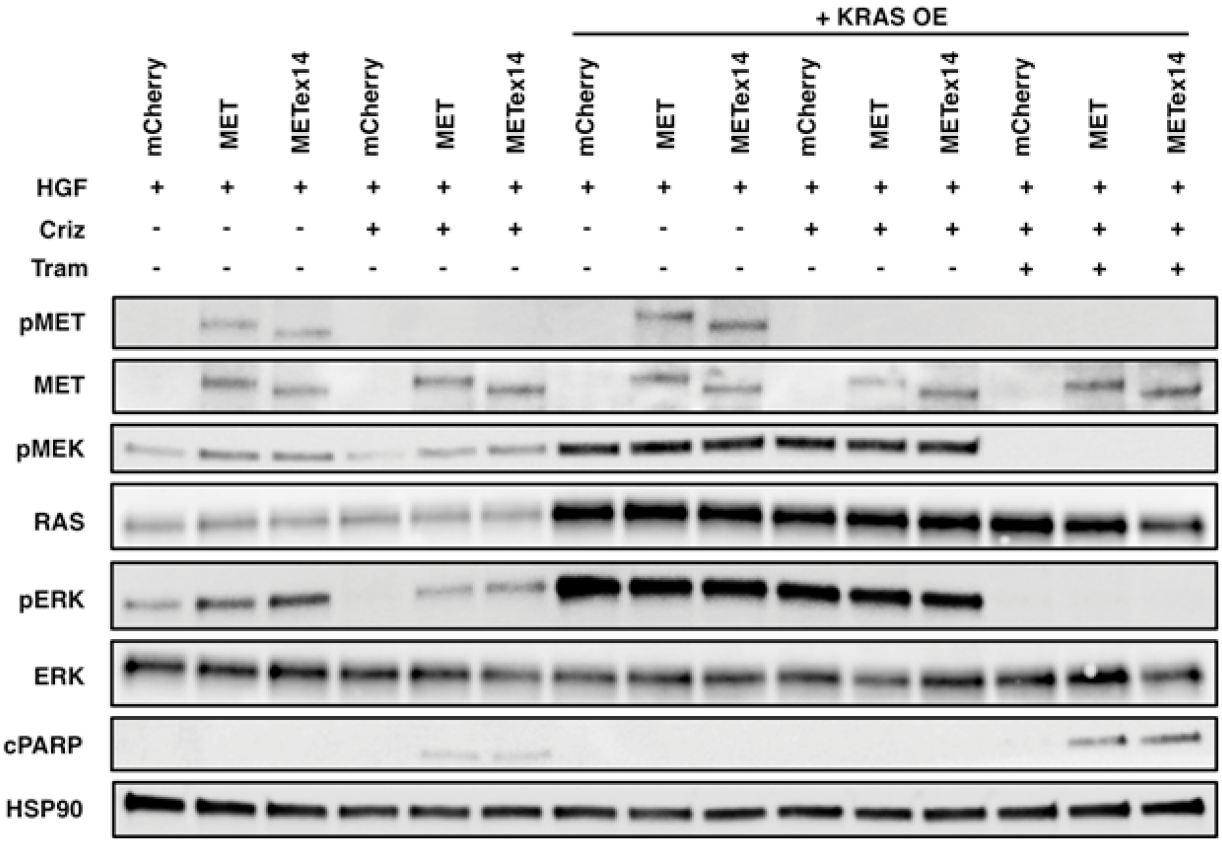


Supplemental Figure S1. MET tyrosine kinase domain modeling location of the F1200 residue. *MET* Y1230 and F1200 residues modeled in their structural context based on PDB 2WGJ. **A.** Crizotinib is shown in yellow, in close approximation to the *MET* Y1230 residue (red), as a frequently reported site of type I MET TKI resistance mutations. **B.** The location of the F1200 mutation at the DFG-out pocket, at a disparate location from the crizotinib binding site, is highlighted in blue.

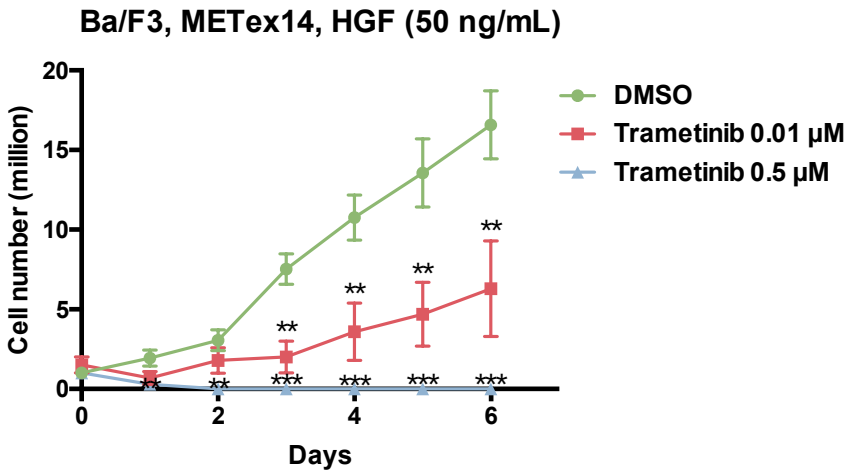


Pre-treatment **Crizotinib Resistance**

Supplemental Figure S2. Serial H&E slides. Tumor biospy samples from a metastatic rib soft tissue lesion obtained prior to treatment and at aquired resistance to crizotinib confirm continued adenocarcinoma histology upon pathology review. Hematoxylin and eosin (H&E) staining on 4 micron FFPE slides, viewed at 20X magnification.



Supplemental Figure S3. Downstream MAPK pathway activation in a Ba/F3 METex14 model is induced by KRAS overexpression and inhibited by addition of trametinib. Ba/F3 cells with stable expression of wild type MET, MET with an exon 14 skipping mutation (METex14), or mCherry control were treated with 50 ng/mL HGF with or without 24 hours treatment with crizotinib at 0.1 □M, trametinib (0.01□M), and/or KRAS overexpression (KRAS OE). Treatment with crizotinib inhibits MET phosphorylation and inhibits downstream Erk phosphorylation, with associated increase in apoptosis as measured by cleaved PARP (cPARP). KRAS overexpression restored downstream Erk phosphorylation and reduced cleaved PARP, despite crizotinib treatment. Addition of trametinib inhibited Erk phosphorylation and increased cleaved PARP, consistent with induction of apoptosis.



Supplemental Figure S4. Relative cell viability of Ba/F3 METex14 cells treated with trametinib monotherapy. Ba/F3 cells overexpressing METex14 were treated with HGF (50 ng/mL) with either DMSO control, trametinib 0.01 µM, or trametinib 0.5 µM. Cell growth is reduced but not eliminated at the 0.01 µM dose of trametinib. ** *p*-value < 0.01, *** *p*-value <0.001 by student's t-test.