Supplemental Table 1. List of gene panel analyzed by FoundationOne™ next-generation sequencing–based assay

ABL1	C11orf30 (EMSY)	DDR2	FGFR4	IL7R	MET	PIK3CA	SDHD	TSHR
ABL2	CARD11	DICER1	FH	INHBA	MITF	PIK3CB	SETD2	U2AF1
ACVR1B	CBFB	DNMT3A	FLCN	INPP4B	MLH1	PIK3CG	SF3B1	VEGFA
AKT1	CBL	DOT1L	FLT1	IRF2	MPL	PIK3R1	SLIT2	VHL
AKT2	CCND1	EGFR	FLT1	IRF4	MRE11A	PIK3R2	SMAD2	WISP3
AKT3	CCND2	EP300	FLT4	IRS2	MSH2	PLCG2	SMAD3	WT1
ALK	CCND3	EPHA3	FOXL2	JAK1	MSH6	PMS2	SMAD4	XPO1
AMER1	CCNE1	EPHA5	FOXP1	JAK2	MTOR	POLD1	SMARCA4	ZBTB2
APC	CD274	EPHA7	FRS2	JAK3	MUTYH	POLE	SMARCB1	ZNF217
AR	CD79A	EPHB1	FUBP1	JUN	MYC	PPP2R1A	SMO	ZNF703
ARAF	CD79B	ERBB2	GABRA6	KAT6A (MYST3)	MYCL (MYCL1)	PRDM1	SNCAIP	
ARFRP1	CDC73	ERBB3	GATA1	KDM5A	MYCN	PREX2	SOCS1	
ARID1A	CDH1	ERBB4	GATA2	KDM5C	MYD88	PRKAR1A	SOX10	
ARID1B	CDK12	ERG	GATA3	KDM6A	NF1	PRKCI	SOX2	
ARID2	CDK4	ERRFI1	GATA4	KDR	NF2	PRKDC	SOX9	
ASXL1	CDK6	ESR1	GATA6	KEAP1	NFE2L2	PRSS8	SPEN	
ATM	CDK8	EZH2	GID4	KEL	NFKBIA	PTCH1	SPOP	
ATR	CDKN1A	FAM46C	GLI1	KIT	NKX2-1	PTEN	SPTA1	
ATRX	CDKN1B	FANCA	GNA11	KLHL6	NOTCH1	PTPN11	SRC	
AURKA	CDKN2A	FANCC	GNA13	KMT2A (MLL)	NOTCH2	QKI	STAG2	
AURKB	CDKN2B	FANCD2	GNAQ	KMT2C (MLL3)	NOTCH3	RAC1	STAT3	
AXIN1	CDKN2C	FANCE	GNAS	KMT2D (MLL2)	NPM1	RAD50	STAT4	
AXL	CEBPA	FANCF	GPR124	KRAS	NRAS	RAD51	STK11	

BAP1	CHD2	FANCG	GRIN2A	LMO1	NSD1	RAF1	SUFU	
BARD1	CHD4	FANCL	GRM3	LRP1B	NTRK1	RANBP2	SYK	
BCL2	CHEK1	FAS	GSK3B	LYN	NTRK2	RARA	TAF1	
BCL2L1	CHEK2	FAT1	H3F3A	LZTR1	NTRK3	RB1	TBX3	
BCL2L2	CIC	FBXW7	HGF	MAGI2	NUP93	RBM10	TERC	
BCOR	CREBBP	FGF10	HNF1A	MAP2K1	PAK3	RET	TERT(promoter)	
BCORL1	CRKL	FGF14	HRAS	MAP2K2	PALB2	RICTOR	TET2	
BLM	CRLF2	FGF19	HSD3B1	MAP2K4	PARK2	RNF43	TGFBR2	
BRAF	CSF1R	FGF23	HSP90AA1	MAP3K1	PAX5	ROS1	TNFAIP3	
BRCA1	CTCF	FGF3	IDH1	MCL1	PBRM1	RPTOR	TNFRSF14	
BRCA2	CTNNA1	FGF4	IDH2	MDM2	PDCD1LG2	RUNX1	TOP1	
BRD4	CTNNB1	FGF6	IGF1R	MDM4	PDGFRA	RUNX1T1	TOP2A	
BRIP1	CUL3	FGFR1	IGF2	MED12	PDGFRB	SDHA	TP53	
BTG1	CYLD	FGFR2	IKBKE	MEF2B	PDK1	SDHB	TSC1	
BTK	DAXX	FGFR3	IKZF1	MEN1	PIK3C2B	SDHC	TSC2	

Supplemental Table 2: Distribution of MAPK pathway alterations identified in all patients and by treatment arm

Distribution of MAPK Pathway Alterations	Overall (n=215)	Binimetinib (n=144)	PCC (n=71)
BRAF V600E	9 (4·2%)	8 (5·6%)	1 (1·4%)
KRAS G12A	2 (0·9%)	1 (0·7%)	1 (1·4%)
KRAS G12C	5 (2·3%)	4 (2·8%)	1 (1·4%)
KRAS G12D	20 (9·3%)	14 (9·7%)	6 (8·5%)
KRAS G12V	35 (16%)	20 (13.9%)	15 (21%)
KRAS G13D	2 (0·9%)	2 (1·4%)	0 (0%)
KRAS Q61H	2 (0·9%)	1 (0·7%)	1 (1·4%)
KRAS Q61K	3 (1·4%)	3 (2·1%)	0 (0%)
KRAS Q61L	1 (0·5%)	1 (0·7%)	0 (0%)
NRAS amplification	1 (0·5%)	1 (0·7%)	0 (0%)
NRAS G12V	1 (0·5%)	0 (0%)	1 (1·4%)
NRAS Q61K	2 (0·9%)	2 (1·4%)	0 (0%)
NRAS Q61R	17 (7·9%)	9 (6.3%)	8 (11%)
NF1 D1122fs*20	1 (0·5%)	1 (0·7%)	0 (0%)
NF1 duplication	1 (0·5%)	0 (0%)	1 (1·4%)
NF1 E2368*	1 (0·5%)	1 (0·7%)	0 (0%)
NF1 I679fs*21	1 (0·5%)	1 (0·7%)	0 (0%)
NF1 L2604V	1 (0·5%)	0 (0%)	1 (1·4%)
NF1 loss	1 (0·5%)	0 (0%)	1 (1·4%)
NF1 P2509S	1 (0·5%)	1 (0·7%)	0 (0%)
NF1 P563T	1 (0·5%)	0 (0%)	1 (1·4%)
NF1 R440*	1 (0·5%)	1 (0·7%)	0 (0%)
NF1 R873C	1 (0·5%)	1 (0·7%)	0 (0%)
NF1 S2186*	1 (0·5%)	1 (0·7%)	0 (0%)
NF1 splice site 1687_1721+8del43	1 (0·5%)	0 (0%)	1 (1·4%)
NF1 splice site 6819+1G>A	1 (0·5%)	1 (0·7%)	0 (0%)
NF1 T676P	1 (0·5%)	1 (0·7%)	0 (0%)
RAF1 loss	1 (0·5%)	1 (0·7%)	0 (0%)
RAF1 R191I	1 (0·5%)	0 (0%)	1 (1·4%)
RAF1 Y340C	1 (0·5%)	1 (0·7%)	0 (0%)

PCC, physician’s choice of chemotherapy

Supplemental Table 3a and 3b: Multivariate genomic models for PFS and best overall response outcomes.

Supplemental Table 3a: Multivariable Cox regression on PFS

Characteristic	HR[1]	95% CI[1]	*P*
KRAS	0·53	0·32, 0·89	**0·016**
ARID1B	0·48	0·24, 0·95	**0·034**

[1]HR, hazard ratio; CI, confidence interval

Supplemental Table 3b: Multivariable logistic regression for Overall Response

Characteristic	OR[1]	95% CI[1]	*P*
KRAS	4·47	1·94, 10·7	**<0·001**
NRAS	4·65	1·18, 18·0	**0·024**

[1]OR, odds ratio; CI, confidence interval

Supplemental Table 4: Comparison of best response for patients treated with binimetinib and with *KRAS* G12V vs other *KRAS* variants.

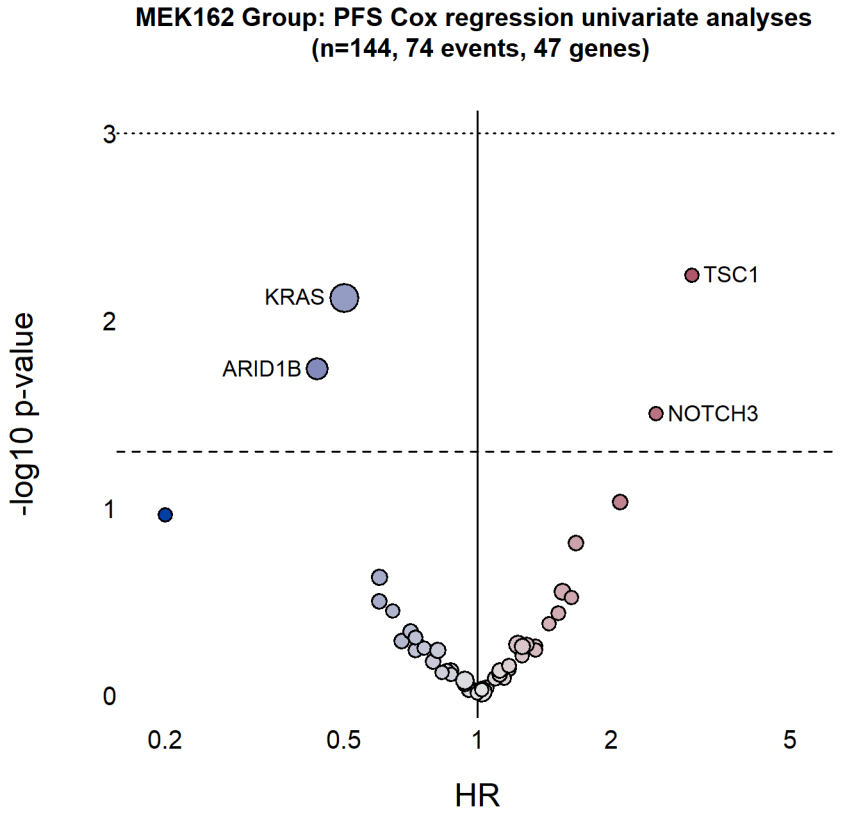
	***KRAS* G12V Mutation (n=19)**	**Other *KRAS* Mutation (n=26)**	***P* value**
Best Response by RECIST 1.1	n (%)	n (%)	0·3
Complete Response	1 (5·3%)	3 (12%)	
Partial Response	9 (47%)	7 (27%)	
Stable Disease	8 (42%)	16 (62%)	
Progressive Disease	1 (5·3%)	0 (0%)	

RECIST, Response Evaluation Criteria in Solid Tumors

P value calculated with the Fisher exact test.

Supplemental Figure 1a and 1b: Volcano plots PFS (1a) and best overall response (1b). Lower dotted line is *P*<0·05 threshold and higher dotted line is FDR< 0·05 threshold for multiple testing adjustment. (responder= best response of complete response or partial response; non-responder = best response of stable disease or progressive disease)

Supplemental Figure 1a:



Supplemental Figure 1b: