

Patient		Physician
Name : xxxxxxxxxxxx		Name : xx xxxxxxxxxxxx
Gender : M	Date of Birth : DD/MMM/YYYY	Institute : xxxxxxxxxxxx

Diagnosis : Pancreas Adenocarcinoma			
Sample Type : Plasma	Sample Collection Date : DD/MMM/YYYY	Sample ID : PB_CG_SP_XXXX-XX_X	
Test : PositiveSelect Plus	Technology : Illumina NGS	Coverage :1000x	Report Date : DD/MMM/YYYY

### Patient Tumor Type Specific Genes

Gene	Genetic Alteration	Result
CDKN2A	c.131dupA	Positive
KRAS	p.G12D	Positive
SMAD4	No alteration detected	Negative
TP53 [P53]	No alteration detected	Negative

### Implications To Immunotherapy

Microsatellite status	MSI-Stable
<b>Tumor Mutation Burden</b>	<b>TMB-High</b>
<small>Note: TMB-Low :- &lt;19 mutations/MB, TMB-High - &gt;20 mutations/MB; MS-Stable &lt;2% unstable sites, MS-Unstable &gt;2% unstable sites</small>	

Note: Genomic alterations in genes related to cancer type (Pancreatic Cancer) as listed in mycancergenome.org and NCCN guidelines are reported here. Genomic alterations with therapeutic implications are reported in the next page.

**Genomic Alterations With Therapeutic Implications**

Guideline approved treatment(s) (in patient tumor type)	Off label therapy/ Clinical Trials	Biomarker	Result	Targeted Pathways	Recommendation
-	MEK Inhibitors [Trametinib Selumetinib]  [Pembrolizumab with Trametinib and Dabrafenib]	KRAS	Positive	KRAS/BRAF/MEK signaling pathway	✓
-	PI3K inhibitors [Buparlisib]	KRAS	Positive	KRAS/PI3K/AKT signaling pathway	✓
-	CDK4 Inhibitors [Palbociclib and Nab- Paclitaxel] [Palbociclib with Cisplatin/Carboplatin]	CDKN2A	Positive	Cell Cycle signaling pathway	✓
-	Pembrolizumab	Microsatellite Unstable  High Tumor mutation burden	Positive	PDL-1 signaling pathway	✓
5-Fluorouracil	-	MTHFR - AC	Positive	Drug metabolism	✓
Docetaxel	-	CYP1B1 - GG	Positive	Drug metabolism	✗

- ✓ - Better Response, Better Prognosis
- ✗ - Poor Response, Poor Prognosis, Resistance

Note: Though all the genes mentioned in the appendix have been analyzed, only those which have clinically actionable information have been highlighted in this report.

Note: This report is meant to be used only by the clinicians. Therapeutic indications mentioned here in are to be practised as per clinicians discretion depending on the pathophysiological status of the patient and prior clinical history.

**Positive Biosciences Ltd.**

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## References

Kweekel, D. M., et al. "GSTP1 Ile105Val polymorphism correlates with progression free survival in MCRC patients treated with or without irinotecan: a study of the Dutch Colorectal Cancer Group." *British journal of cancer* 99.8 (2008): 1316-1321.

Phase I/NCT02501902 - An Open-label Phase Ib Study Of Palbociclib (Oral Cdk 4/6 Inhibitor) Plus Abraxane (Registered) (Nab-paclitaxel) In Patients With Metastatic Pancreatic Ductal Adenocarcinoma.

Phase I/NCT02897375 - A Phase 1 Study of Palbociclib in Combination With Cisplatin or Carboplatin in Advanced Solid Malignancies.

Phase I/II NCT02130466 - A Phase I/II Study to Assess the Safety and Efficacy of MK-3475 in Combination With Trametinib and Dabrafenib in Subjects With Advanced Melanoma.

Planchard D, Besse B, Groen HJ, et al. Dabrafenib plus trametinib in patients with previously treated BRAF(V600E)-mutant metastatic non-small cell lung cancer: an open-label, multicentre phase 2 trial. *Lancet Oncol* 2016;17:984-993.

Sherr, Charles J., David Beach, and Geoffrey I. Shapiro. "Targeting CDK4 and CDK6: from discovery to therapy." *Cancer discovery* 6.4 (2016): 353-367.

Troiani, T., et al. "Intrinsic resistance to selumetinib, a selective inhibitor of MEK1/2, by cAMP-dependent protein kinase A activation in human lung and colorectal cancer cells." *British journal of cancer* 106.10 (2012): 1648-1659.

Wu, Xifeng, et al. "Genetic variations in radiation and chemotherapy drug action pathways predict clinical outcomes in esophageal cancer." *Journal of Clinical Oncology* 24.23 (2006): 3789-3798.

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## ABOUT PositiveSelect

PositiveSelect is a range of comprehensive genomics test offering definitive clinical as well as prognostic markers from deep analysis of Next Generation Sequencing (NGS) data delivering clinically relevant actionable recommendations. This complete genomics test begins with sample collection, through DNA isolation followed by sequencing and data processing finally towards analysis and expert personalized recommendations. Following are some highlights of the PositiveSelect test significance.

**Test Significance :** PositiveSelect Plus covers identification of all four types of genomic alterations viz. Single Nucleotide Variations (SNV), Copy Number Variations (CNV), Indels and Structural Variations (SV) apart from Tumor Mutation Burden (TMB) and Micro-satellite Instability (MSI). This test also reports on possibility towards usage of off-label drugs and immunotherapeutics apart from the guideline recommendations and pertinent clinical trials. The test does not report on large SV and we do not include reporting on Variants of Unknown Significance (VUS). However the same can be provided on request if detected.

Analyzed by:

Verified by:

Scientific Officer

Sr. Scientific Officer

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Gene List

Single Nucleotide Variations

ABCB1	BCL2	CDKN1A	DNMT3B	FGF3	IDH2	MAP2K2	MYD88	PDGFRA	RAD51B	SF3B1	TNFRSF14
ABCC1	BCL2L1	CDKN1B	DOT1L	FGF4	IFNGR1	MAP2K4	MYOD1	PDGFRB	RAD51C	SH2D1A	TOP1
ABCC2	BCL2L11	CDKN2A	E2F3	FGFR1	IGF1	MAP3K1	NBN	PDPK1	RAD51D	SLC22A1	TP53
ABCC4	BCL6	CDKN2B	EGFL7	FGFR2	IGF1R	MAP3K13	NCOR1	PGR	RAD52	SMAD2	TP63
ABCG2	BCOR	CDKN2C	EGFR	FGFR3	IGF2	MAPK1	NF1	PIK3C2G	RAD54L	SMAD3	TRAF7
ABL1	BCR	CHEK1	EML4	FGFR4	IKBKE	MAX	NF2	PIK3C3	RAF1	SMAD4	TSC1
AKT1	BLM	CHEK2	EP300	FH	IKZF1	MCL1	NFE2L2	PIK3CA	RARA	SMARCA4	TSC2
AKT2	BRAF	CREBBP	EPCAM	FLCN	IL10	MDC1	NKX2-1	PIK3CB	RASA1	SMARCB1	TSHR
AKT3	BRCA1	CRKL	EPHA3	FLT1	IL7R	MDM2	NKX3-1	PIK3CD	RB1	SMO	TSPY4
ALK	BRCA2	CRLF2	EPHA5	FLT3	INSR	MDM4	NOTCH1	PIK3CG	RECQL4	SOCS1	TTTY23
ALOX12B	BRD4	CSF1R	EPHB1	FLT4	IRF4	MED12	NOTCH2	PIK3R1	REL	SOX17	TYMS
AMELY	BRIP1	CTCF	ERBB2	FOXA1	IRS1	MEF2B	NOTCH3	PIK3R2	RET	SOX2	U2AF1
APC	BTK	CTLA4	ERBB3	FOXL2	IRS2	MEN1	NOTCH4	PIK3R3	RFWD2	SOX9	USP9Y
AR	CARD11	CTNNB1	ERBB4	FOXP1	JAK1	MET	NPM1	PIM1	RHOA	SPOP	VHL
ARAF	CASP8	CUL3	ERCC2	FUBP1	JAK2	MITF	NR12	PLK2	RICTOR	SRC	WT1
ARID1A	CBFB	CYP19A1	ERCC3	GATA1	JAK3	MLH1	NRAS	PMAIP1	RIT1	SRY	XIAP
ASXL1	CBL	CYP1A1	ERCC4	GATA2	JUN	MLL	NSD1	PMS1	RNF43	STAG2	XPO1
ASXL2	CCND1	CYP1A2	ERCC5	GATA3	KDM5A	MLL2	NTRK1	PMS2	ROS1	STK11	YAP1
ATM	CCND2	CYP1B1	ERG	GNA11	KDM5C	MLL3	NTRK2	PNRC1	RPS4Y2	STK40	YES1
ATR	CCND3	CYP2A4	ESR1	GNAQ	KDM5D	MPL	NTRK3	POLE	RPS6KA4	SUFU	ZFY
ATRX	CCNE1	CYP2A6	ETV1	GNAS	KDM6A	MSH2	NUTM1	PPP2R1A	RPS6KB2	SYK	
AURKA	CD274	CYP2B6	ETV6	GSK3B	KDR	MSH6	PAK1	PRDM1	RPTOR	TBX3	
AURKB	CD276	CYP2E1	EWSR1	GSTA1	KEAP1	MTHFD1	PAK7	PRKAR1A	RUNX1	TERT	
AXIN1	CD79B	DAXX	EZH2	GSTP1	KIT	MTHFD1L	PALB2	PRKY	RYBP	TET1	
AXIN2	CDC73	DAZ1	FAM123B	HGF	KLF4	MTHFR	PARK2	PTCH1	SDHA	TET2	
AXL	CDH1	DDR2	FANCA	HIF1A	KRAS	MTOR	PARP1	PTEN	SDHAF2	TGFBR1	
B2M	CDK12	DICER1	FANCC	HIST1H3B	LATS1	MUTYH	PAX5	PTPN11	SDHB	TGFBR2	
BAP1	CDK4	DIS3	FAT1	HNF1A	LATS2	MYC	PAX8	RAC1	SDHC	TMEM127	
BARD1	CDK6	DNMT1	FBXW7	HRAS	LMO1	MYCL1	PBRM1	RAD50	SDHD	TMPRSS2	
BBC3	CDK8	DNMT3A	FGF19	IDH1	MAP2K1	MYCN	PDCD1	RAD51	SETD2	TNFAIP3	

Rearrangements

Amplifications

Insertions/Deletions (Indels)

ALK	AR	BRAF	ATM	GATA3	SMAD4
FGFR2	CCNE1	CDK4	APC	KIT	STK11
FGFR3	CCND1	CDK6	ARID1A	MET	TP53
RET	CCND2	EGFR	BRCA1	MLH1	TSC1
ROS1	ERBB2	FGFR1	BRCA2	MTOR	VHL
NTRK1	FGFR2	KIT	CDH1	NF1	
	KRAS	MET	CDKN2A	PDGFRA	
	PIK3CA	PDGFRA	EGFR	PTEN	
	MYC	RAF1	ERBB2	RB1	

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