PositiveSelect™

Positive Bioscience

Patient		Physician	
Name : xxxxxxxxxx		Name : xx xxxxxxxxx	
Gender : M	Date of Birth : DD/MM/YYYY	Institute : xxxxxxxxx	

Diagnosis : Breast Cancer

Sample Type : Plasma & Blood	Sample Collection Date : DD/MM/YYYY		Sample ID : PB_CG_SL_XXXX-XX_XX
Test : PositiveSelect Match	Technology : Illumina NGS	Coverage : 1000x	Report Date : DD/MM/YYYY

✓ Therapies With Potential Benefit

Drugs	Gene	Result	Targeted Pathways
mTOR inhibitors [Everolimus] N	PTEN Loss	Positive	MTOR signaling pathway
Olaparib	BRCA1 [A433P fs]	Positive	Mismatch Repair
Platinum-based chemotherapy [Paclitaxel and Carboplatin] N	BRCA1 [A433P fs]	Positive	Mismatch Repair

✗ Therapies With Potential Lack Of Benefit

Drugs	Gene	Result	Targeted Pathways
Tamoxifen, Letrozole N	ESR1 [D538G]	Positive	Estrogen signaling pathway
Trastuzumab N	PTEN Loss	Positive	Receptor tyrosine kinase

N- NCCN approved drugs

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.

Positive Biosciences Ltd.
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preTADME [Toxicity, Absorption, Distribution, Metabolism and Excretion]

Drugs	Gene-Genotype	Inference
Platinum-based chemotherapy [Paclitaxel and Carboplatin]	ABCB1 - AA	Higher risk of toxicity
Capecitabine	DPYD- CC	Decreased likelihood of developing grade 3 hand-foot syndrome

Mutation Status [NCCN Recommended Genes]

Gene	Genetic Alteration	Result
BRCA1	A433P fs	Positive
BRCA2	No alteration detected	Negative
ERBB2	Amplification	Positive
ESR1	D538G	Positive
TP53	No alteration detected	Negative

Mutation Signature

Gene	Genetic Alteration	Germline	True Somatic
BRCA1	A433P fs	✓	
ESR1	D538G		✓
ABCB1	C3435T	✓	
DPYD	D974V	✓	

Note: All the genomic alterations relevant to the cancer type and the associated genesas per NCCN and mycancergenome.org are reported here.

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References

Lloye M. Dillon and Todd W. Miller "Therapeutic targeting of cancers with loss of PTEN function" Curr Drug Targets. 2014 Jan; 15(1): 6579.

Kaufman, Bella, et al. "Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation." Journal of clinical oncology 33.3 (2014): 244-250.

Du, Yan, et al. "Associations of polymorphisms in DNA repair genes and MDR1 gene with chemotherapy response and survival of non-small cell lung cancer." PloS one 9.6 (2014): e99843.

Jeselsohn, Rinath, et al. "Emergence of constitutively active estrogen receptor- mutations in pretreated advanced estrogen receptor positive breast cancer." Clinical Cancer Research 20.7 (2014): 1757-1767.

Nagata, Yoichi, et al. "PTEN activation contributes to tumor inhibition by Trastuzumab, and loss of PTEN predicts Trastuzumab resistance in patients." Cancer cell 6.2 (2004): 117-127.

Bergmann, Troels K., et al. "Impact of ABCB1 variants on neutrophil depression: a pharmacogenomic study of paclitaxel in 92 women with ovarian cancer." Basic & clinical pharmacology & toxicology 110.2 (2012):199-204.

Wu, Chaohui, et al. "Prognostic role of microRNA polymorphisms in patients with advanced esophageal squamous cell carcinoma receiving platinum-based chemotherapy." Cancer chemotherapy and pharmacology 73.2 (2014): 335-341.

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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 Match covers identification of all four types of genomic alterations viz. Single Nucleotide Variation (SNV), Copy Number Variations (CNV), Indels and Structural Variations (SV). This test also reports on possibility towards usage of off-label drugs and 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	CYP19A1	ERCC2	JAK2	PARP1
ABCC1	CYP1A1	ERCC3	JAK3	PDCD1
ABCC2	CYP1A2	ERCC4	KDR	PDGFRA
ABCC3	CYP1B1	ERCC5	KIT	PDGFRB
ABCC4	CYP24A1	ESR1	KRAS	PGR
ABCG2	CYP27B1	EWSR1	LINS1	PIK3CA
ABL1	CYP2B6	EZH2	MAP2K1	PTEN
AKT1	CYP2C19	F2R	MAP2K2	REL
ALK	CYP2C9	FGFR1	MAPK1	RET
AR	CYP2E1	FGFR2	MET	ROS1
BCR	CYP3A4	FGFR4	MLH1	RRM1
BRAF	CYP3A5	FLT3	MSH2	STAT3
BRCA1	DCK	GSTA1	MSH6	TERT
BRCA2	DDB1	GSTP1	MTHFD1	TOP1
BTK	DDR2	HIF1A	MTHFR	TP53
CCND1	DYNC2H1	HRAS	MTOR	TSC1
CCND2	EGFR	IDH1	NF1	TSC2
CDA	EML4	IGF1R	NR1I2	VEGFA
CDK4	ERBB2	IL6	NR1I3	VHL
CDK6	ERCC1	JAK1	NRAS	XRCC1

Rearrangements

ALK
FGFR2
RET
ROS1

Amplifications

AR	BRAF
CCND1	CDK4
CCND2	EGFR
ERBB2	FGFR1
FGFR2	KIT
KRAS	MET
PIK3CA	PDGFRA

Insertion/Deletions (Indels)

BRCA1	MTOR
EGFR	NF1
ERBB2	PDGFRA
KIT	PTEN
MET	TP53
MLH1	TSC1
	VHL

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