

Patient NAME Ms Jane Doe	DATE OF BIRTH 1992-Jun-12	DISEASE Breast	STAGE II	Physician NAME Administrator
SPECIMEN 20ml Blood	VIAL IDs 1			

REPORT SUMMARY

CTCs COUNT: Isolated 3.3 cells/7.5 ml , SD +/- 0.3 cells

SENSITIVITY - GENE EXPRESSION

Sensitivity

High sensitivity: alkylating factors, inhibitors of topoisomerase I, taxanes

Partial sensitivity: epothilones, inhibitors of topoisomerase II, alkaloids of vinca, 5FU, MTX, Gemcitabine, Capecitabin, Fudr, UFT, Raltitrexed, Pemetrexed, Cytarabine, Fludarabine

Expression

Over expression: C-erb-B2, C-erb-B1, EGF, Ikb(a,b,c), NFkB, 5-LOX, COX2, P180, ESRI, PGR, SS-r, ALK, EML-4-ALK, NPM-ALK, CD 117 (c-kit), IGF-r 1, IGF-r 2, NR3C4-A, NR3C4-B, TGF-b,

Down regulation:

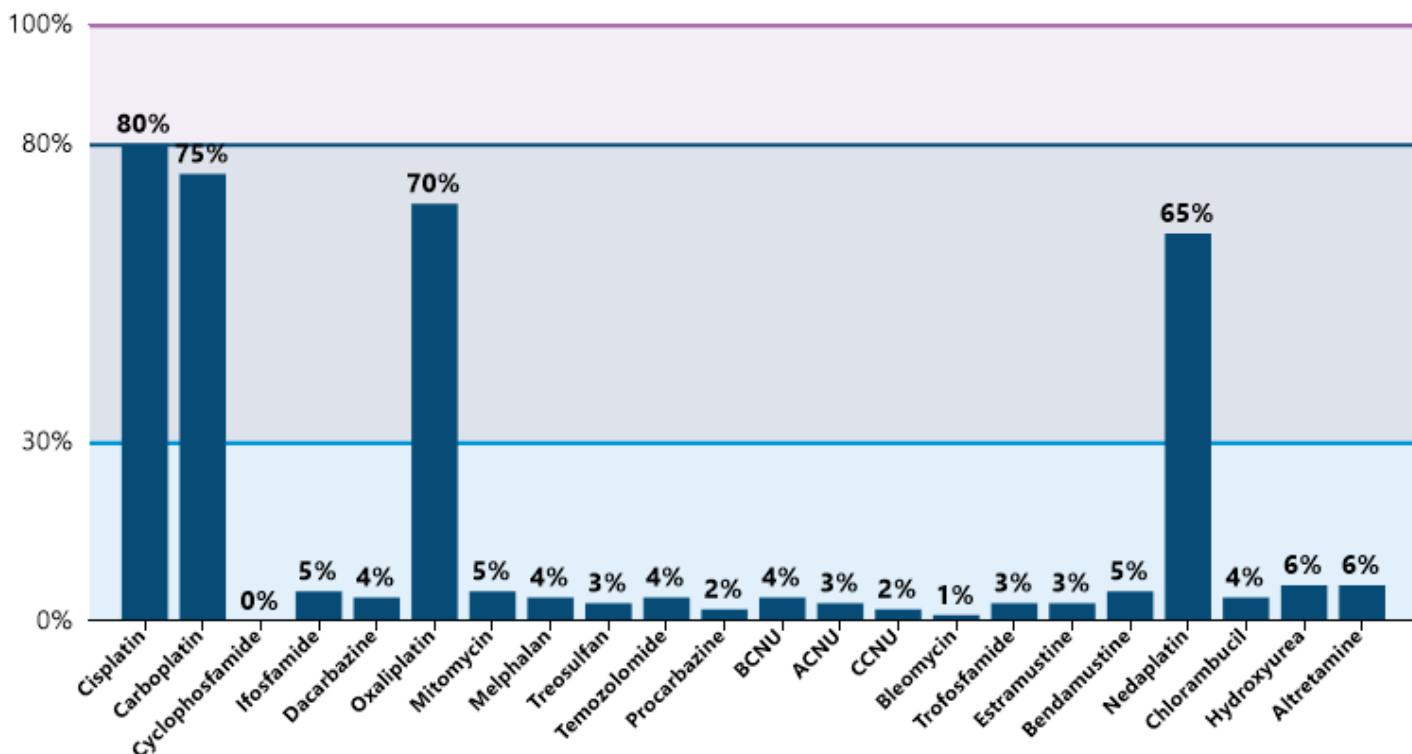
Conclusion Results

- The neoplastic cells have the greatest sensitivity in Cisplatin, CPT11, Topotecan, Gimatecan, Paclitaxel
- Also can be used Alemtuzumab, Atezolizumab, Avelumab, Brentuximab_vedotin, Catumaxumab, Cetuximab, Gemtuzumab, Ibritumomab(Zevalin), Ipilimumab, Nivolumab, Ofatumumab, Panitumumab, Pembrolizumab, Pertuzumab, Rituximab, Tositumomab(Bexxar), Transtuzumab, Abiraterone, Afatinib, Anastrozol, Antiandrogen(goserelin), Crizotinib, Dasatinib, Erlotinib, Exemestane
- The specific tumor appears to have resisting populations because of the MDR1 overexpression that can be reversed by the use of inhibitors of ABCG2 pumps

— No sensitivity — Partial sensitivity — High sensitivity

Alkylating Agents

High sensitivity:

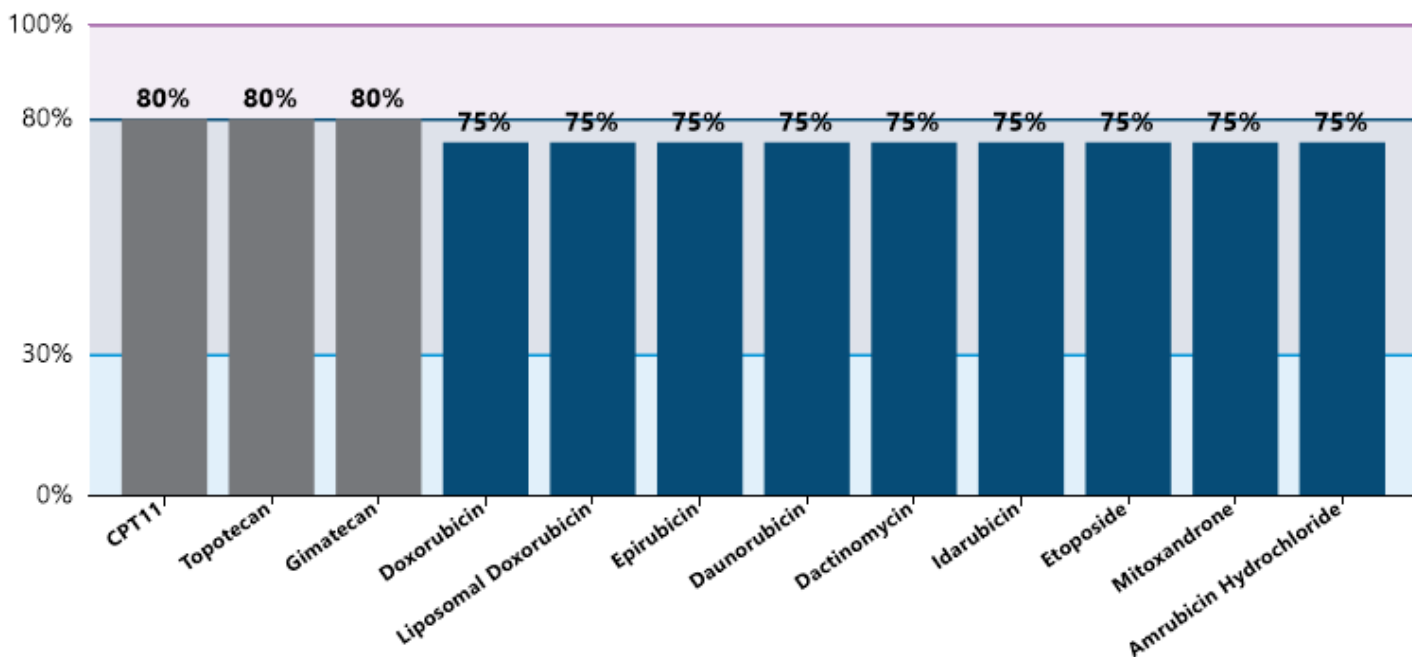


Inhibitors of Topoisomerase I & II

High sensitivity:

Inhibitors of Topoisomerase I

Inhibitors of Topoisomerase II

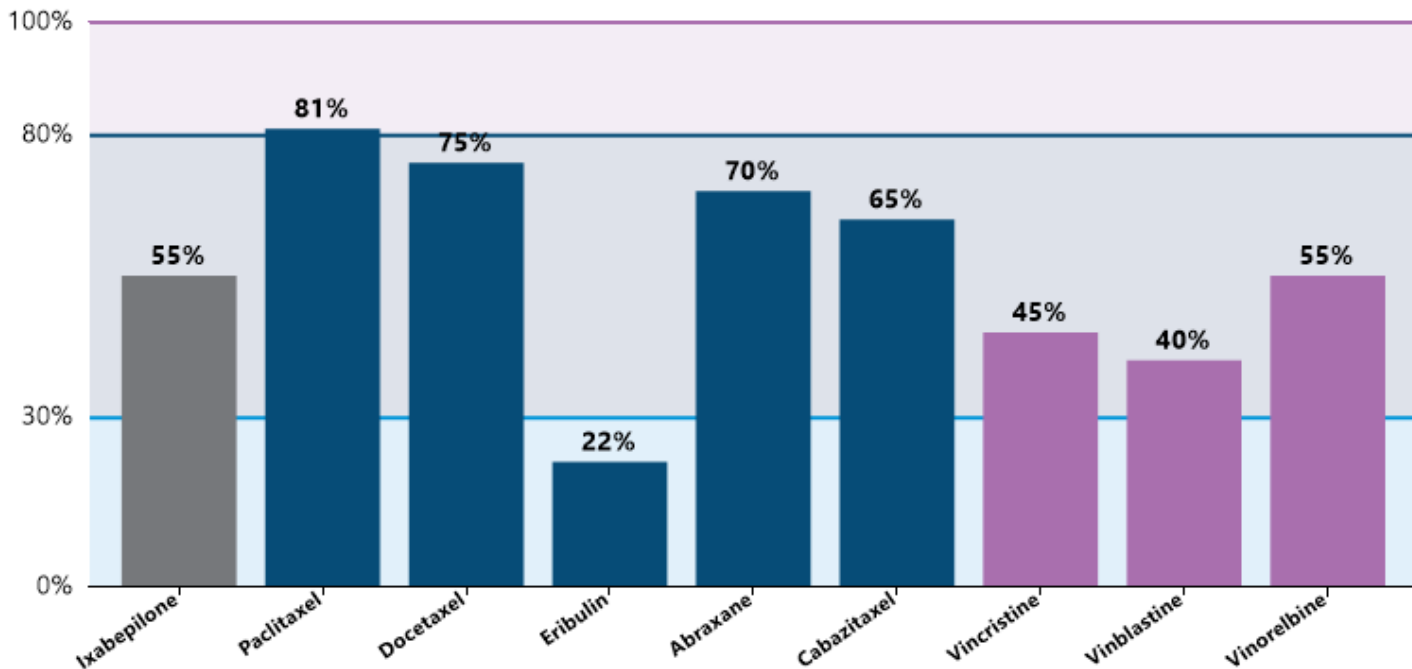


— No sensitivity — Partial sensitivity — High sensitivity

Epothilones & Nucleus Spindle Stabilizer I & II

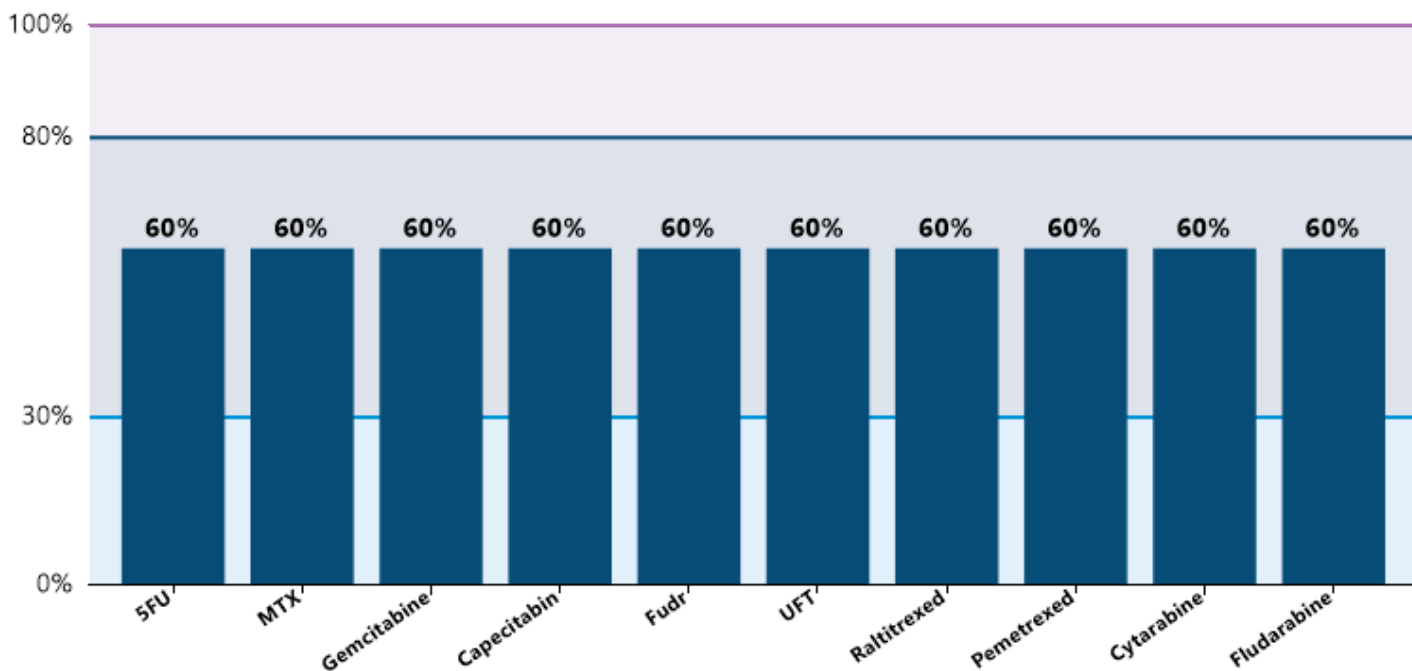
High sensitivity: Paclitaxel

Epothilones —
 Nucleus Spindle Stabilizer I —
 Nucleus Spindle Stabilizer II —

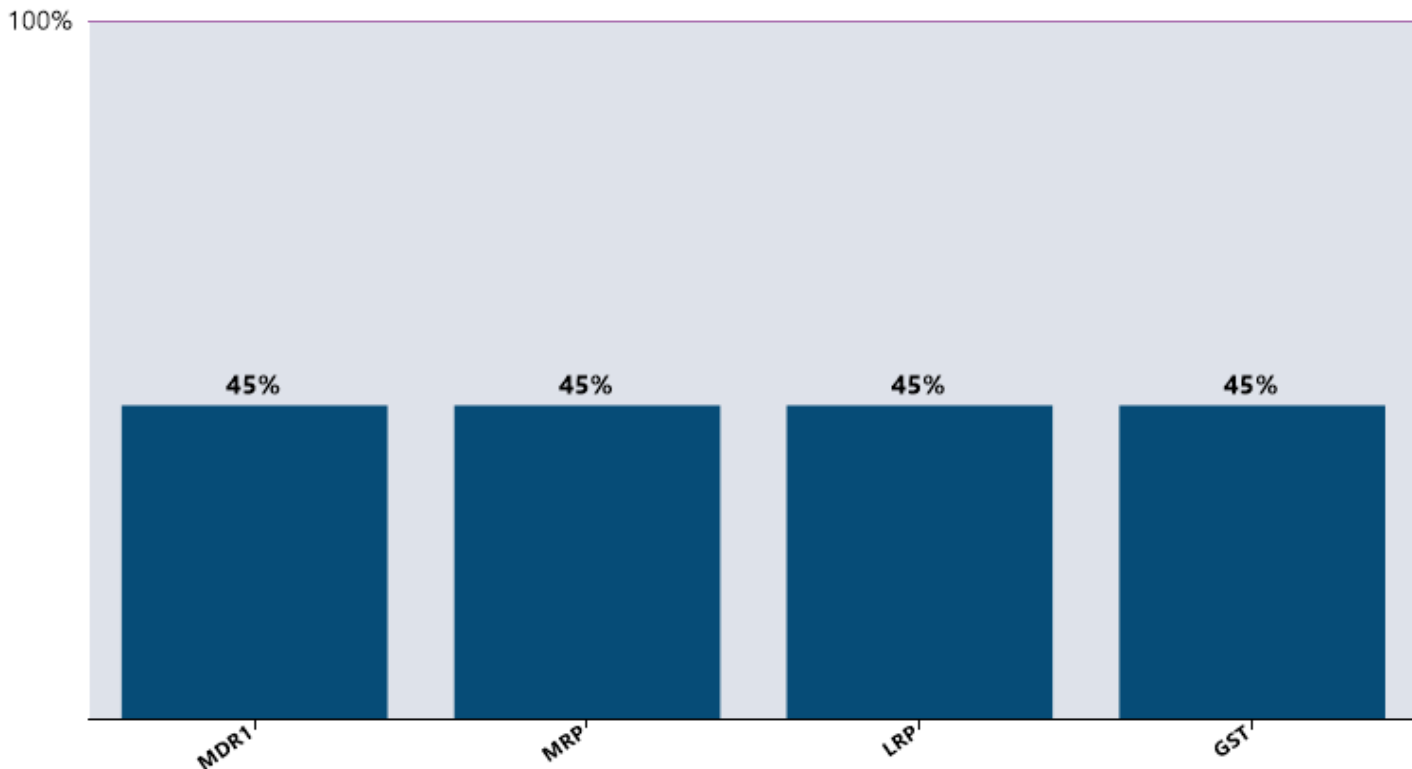


Nucleoside Analogues

High sensitivity:

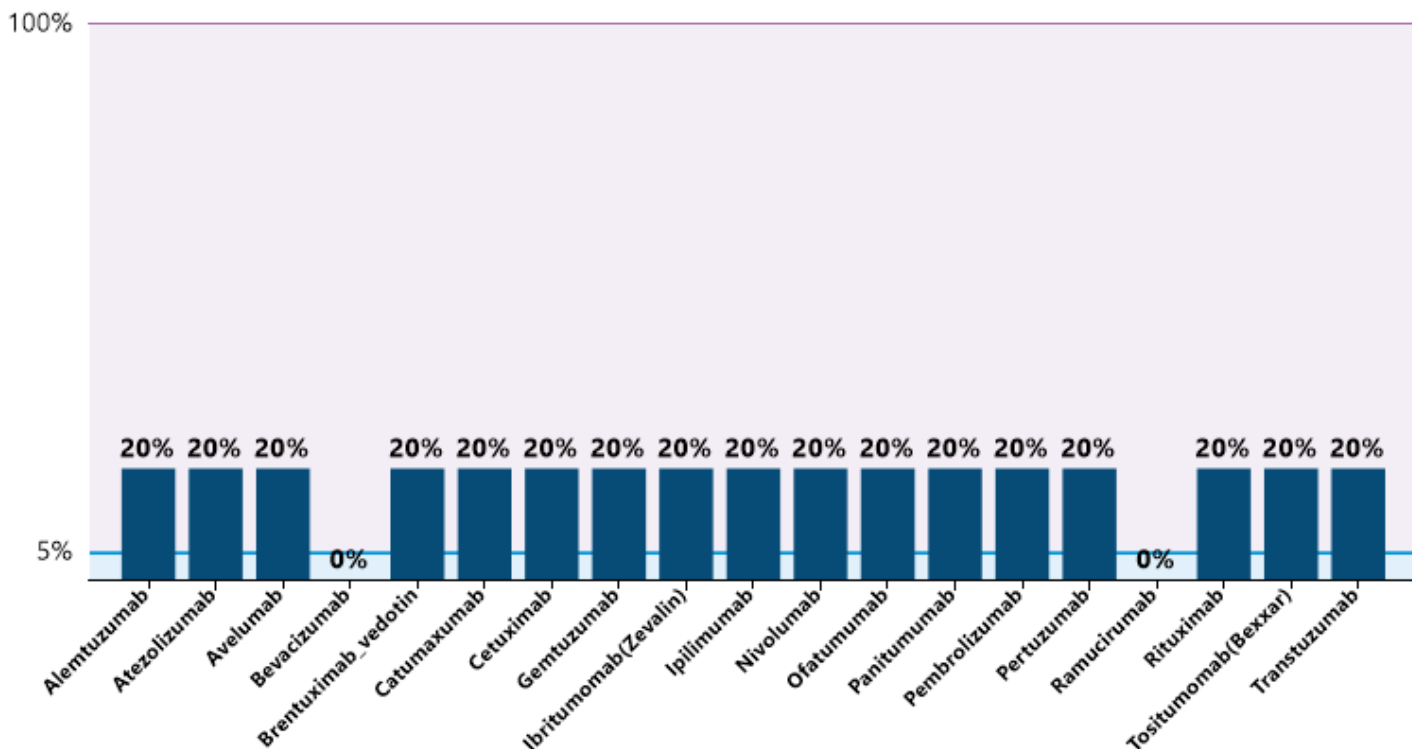


Resistance Factors



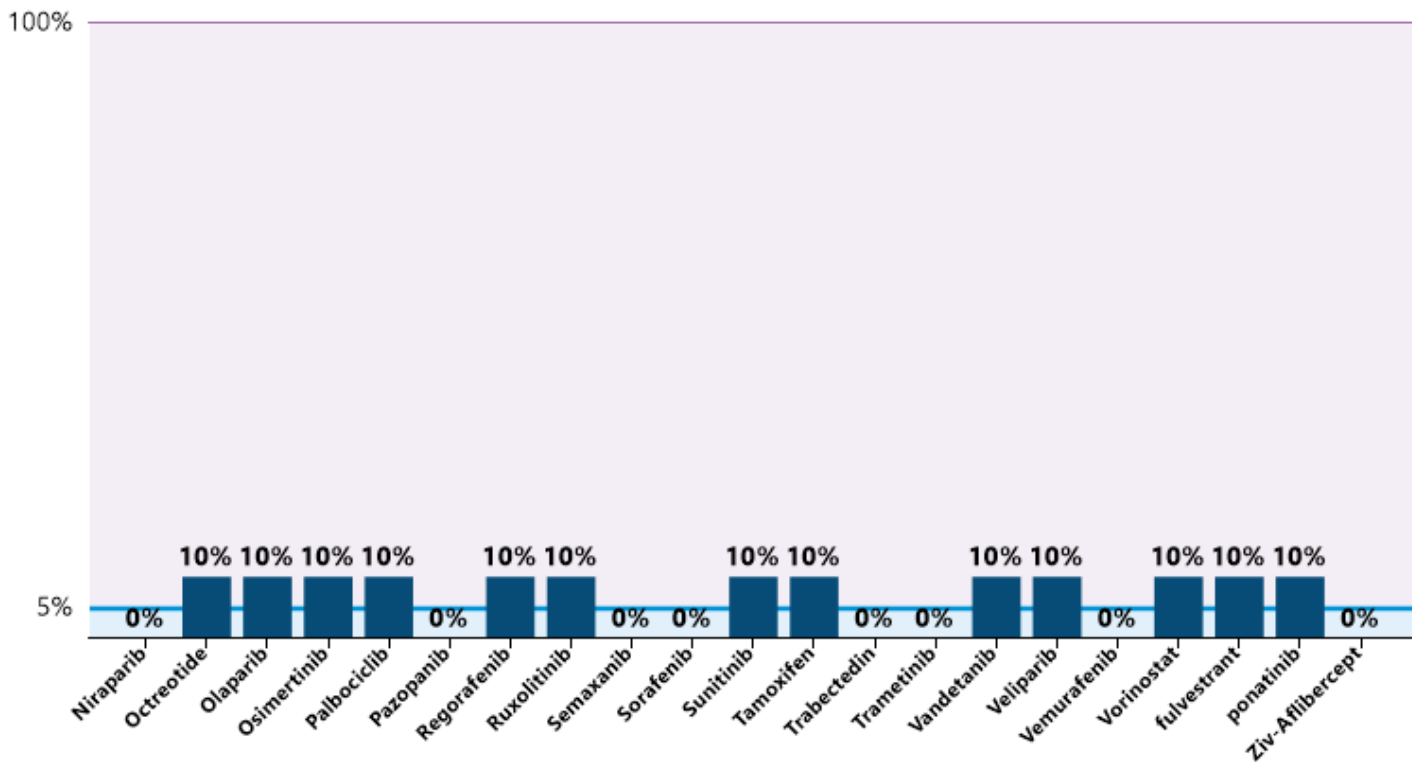
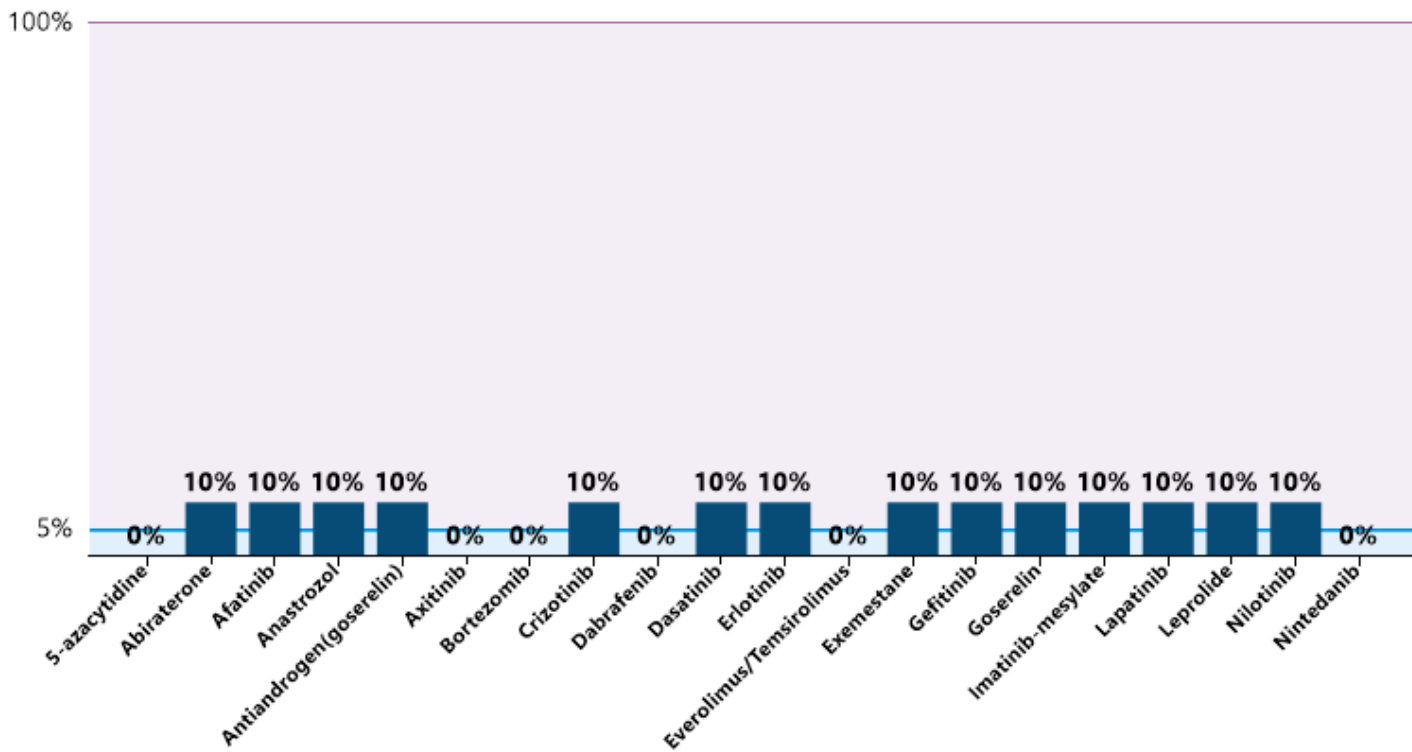
Moab - Monoclonal Antibodies

— No sensitivity — Sensitivity



— No sensitivity — Sensitivity

SMW - Small Molecular weight molecule



Growth Factors Proliferation Stimuli

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
p180	Preprotein for Cellular stress	HIGH RISK	Tyrosin kinase growth f.	20	HIGH RISK
Bcr-abl	Fusion Protein	HIGH RISK	Resist phenotype	20	HIGH RISK
PTEN	Repair Related Gene	HIGH RISK	Tumor Suppressor Gene	20	HIGH RISK
COX2	Eicosanoid related protein	HIGH RISK	Tumour Growth	20	HIGH RISK
5-LOX			Tumour Growth	20	HIGH RISK
NFkB	Proteasome inhibitors	HIGH RISK	Transcription fact	20	HIGH RISK
IkB(a,b,c)			Inhibitor of NFkB	20	HIGH RISK
ALK	Proto-Oncogene	HIGH RISK	Acute Leukemia kinase	20	HIGH RISK
EML-4-ALK			Fusion EML with ALK	20	HIGH RISK
NPM-ALK			Fusion NPM with ALK	20	HIGH RISK
RET			Proto-Oncogene	20	HIGH RISK

Preprotein for Cellular stress

p180 20%

Fusion Protein

Bcr-abl 20%

Repair Related Gene

PTEN 20%

Eicosanoid related protein

COX2 20%

5-LOX 20%

Proteasome inhibitors

NFkB 20%

IkB(a,b,c) 20%

Proto-Oncogene

ALK 20%

EML-4-ALK 20%

NPM-ALK 20%

RET 20%

Growth Factors Proliferation Stimuli

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
SS-r	Growth Factor Receptor	HIGH RISK	Somatostatin receptor	20	HIGH RISK
CD 117(c-kit)			Proliferate growth factor receptor	20	HIGH RISK
IGF-r 1			Insulin like growth factor receptor	20	HIGH RISK
IGF-r-2			Insulin like growth factor receptor	20	HIGH RISK
EGF			Tumour Growth	20	HIGH RISK
c-erb-B1			Her1	20	HIGH RISK
c-erb-B2			Her/neu2	20	HIGH RISK
JAK1/2	Signal Transduction Pathway	HIGH RISK	Single transduction pathway	20	HIGH RISK
c-Jun			Proto-Oncogene	20	HIGH RISK
c-Fos			Proto-Oncogene	20	HIGH RISK
Ras/Raf/MEK/Er k			Transduction pathway	20	HIGH RISK
mTOR			Transduction pathway	20	HIGH RISK
Progesterone Receptor	Hormone Receptors	HIGH RISK	Growth Factor Receptor	20	HIGH RISK
Estrogene Receptor			Growth Factor Receptor	20	HIGH RISK
NR3C4-A			Nucleous receptor group III Class 4(androg...	20	HIGH RISK
NR3C4-B			Nucleous receptor group III Class 4(androg...	20	HIGH RISK

Growth Factor Receptor

SS-r	20%
CD 117(c-kit)	20%
IGF-r 1	20%
IGF-r-2	20%
EGF	20%
c-erb-B1	20%
c-erb-B2	20%

Signal Transduction Pathway

JAK 1/2	20%
c-Jun	20%
c-Fos	20%
Ras/Raf/MEK/Er k	20%
mTOR	20%

Hormone Receptors

Progesterone Receptor	20%
Estrogene Receptor	20%
NR3C4-A	20%
NR3C4-B	20%

SELF REPAIR - RESISTANCE

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
TGF-b	Signal transduction	HIGH RISK	Tumour Growth	25	HIGH RISK
HSP27	Radiotherapy / Hyperthermia sensitivity	RESISTANT	Heat Shock Protein	25	RESISTANT
HSP72			Heat Shock Protein	25	RESISTANT
HSP90			Heat Shock Protein	25	RESISTANT
DNA methyltransferas el	Resistant Phenotype Markers	HIGH RISK	DNA methylation	25	HIGH RISK
DNA demethylase			DNA methylation	25	HIGH RISK
06-methyl-DNA- tran			DNA methylation	25	HIGH RISK
Histone deacetylase			DNA coiling (nucleosome)	25	HIGH RISK
HAT			Histone acetyl transferase	25	HIGH RISK
CXCR4			Resistant Phenotype	25	HIGH RISK
CXCL12			Resistant Phenotype	25	HIGH RISK
Gamma GC			Resist to alkylating drugs	25	HIGH RISK
HDAC			Histone deacetylase	25	HIGH RISK

Signal transduction

TGF-b 25%

Radiotherapy / Hyperthermia sensitivity

HSP27 25%

HSP72 25%

HSP90 25%

Resistant Phenotype Markers

DNA methyltransferas el 25%

DNA demethylase 25%

06-methyl-DNA- tran 25%

Histone deacetylase 25%

HAT 25%

CXCR4 25%

CXCL12 25%

Gamma GC 25%

HDAC 25%

ANGIOGENESIS - METASTASES

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
VEGF	Angiogenesis	HIGH RISK	Angiogenesis	30	HIGH RISK
FGF			Angiogenesis	30	HIGH RISK
PDGF			Angiogenesis	30	HIGH RISK
ANG 1			Angiogenin I	30	HIGH RISK
ANG 2			Angiogenin II	30	HIGH RISK
c-MET	Migration invasion	HIGH RISK	Mesenchymal to epithelial transition	10	HIGH RISK
67LR			67 Laminin receptor	10	HIGH RISK
KISS-1-r			Metastases regulator	10	HIGH RISK
Nm23			Metastases regulator	10	HIGH RISK
MMP			Metastases	10	HIGH RISK

Angiogenesis

VEGF	30%
FGF	30%
PDGF	30%
ANG 1	30%
ANG 2	30%

Migration invasion

c-MET	10%
67LR	10%
KISS-1-r	10%
Nm23	10%
MMP	10%

CELL CYCLE REGULATION & IMMORTALIZATION / APOPTOSIS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
E2F1	Increase Protein Synthesis	HIGH RISK	Transcr. Fact of TS & topo I	35	HIGH RISK
CDC6	Rapid Cell Cycle	HIGH RISK	Initiation of DNA replication	35	HIGH RISK
h-TERT	Immortalization	HIGH RISK	M2 crisis- aggressive phen	35	HIGH RISK
Bcl-2	Regulation of Apoptosis	HIGH RISK	Apoptosis	35	HIGH RISK
Bax			Apoptosis	35	HIGH RISK
CD95 (fas-r)			Apoptosis related receptor	35	HIGH RISK
p27	Cell Cycle Rate	HIGH RISK	Cell arrest (G0)	35	HIGH RISK
p53			Cell cycle regulator	35	HIGH RISK
p16			Apoptosis	35	HIGH RISK

Increase Protein Synthesis

E2F1 35%

Rapid Cell Cycle

CDC6 35%

Immortalization

h-TERT 35%

Regulation of Apoptosis

Bcl-2 35%

Bax 35%

CD95 (fas-r) 35%

Cell Cycle Rate

p27 35%

p53 35%

p16 35%

DRUG METABOLISMS & TARGETS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
DPD	Nucleoside Import Transformation	HIGH RISK	Resist to 5FU	15	HIGH RISK
UP			Resist to 5FU	15	HIGH RISK
NP			Resist topyrim. Antagonist	15	HIGH RISK
TP			Resist to 5FU	15	HIGH RISK
TS			Rapid cell cycle (THFA)	15	HIGH RISK
DHFR			Rapid cell cycle (THFA)	15	HIGH RISK
SHMT			Rapid cell cycle (THFA)	15	HIGH RISK
GARFT			Rapid cell cycle (THFA)	15	HIGH RISK
Ribonucleosider Eductase			DNA synthesis	15	HIGH RISK
CES1&2 (carboxyesterase)			Activation of Camptothecin	HIGH RISK	Resist to camptothecin
CypB1	Xenobiotic	HIGH RISK	Xenobiotic metabolism	15	HIGH RISK
ERCC1	DNA Repair Related Gene	HIGH RISK	DNA repair mechanism	15	HIGH RISK
RRM1			Nucleotide polymerizations	15	HIGH RISK

Nucleoside Import Transformation

DPD	15%
UP	15%
NP	15%
TP	15%
TS	15%
DHFR	15%
SHMT	15%
GARFT	15%
Ribonucleosider Eductase	15%

Activation of Camptothecin

CES1&2 (carboxyesterase)	15%
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Xenobiotic

CypB1	15%
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DNA Repair Related Gene

ERCC1	15%
RRM1	15%

MARKERS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
CD33	Immune system regulation	HIGH RISK	Myeloid Cell origin	20	HIGH RISK
CD52	Immune system regulation	HIGH RISK	Leukaemia Marker	20	HIGH RISK
CD20	Development and differentiation of B cells into plasma cells	HIGH RISK	Lymphoma Related Antigen	20	HIGH RISK
EpCAM (EpCAM+ve)	Cell-cell adhesion	HIGH RISK	Epithelial Marker (2.7 cells/7.5 ml)	20	HIGH RISK
PD-L1	Immune system regulation	HIGH RISK	Immunoregulatory Factor	20	HIGH RISK
PD 1	Immune system regulation	HIGH RISK	Immunoregulatory Factor	20	HIGH RISK
PD-L2	Immune system regulation	HIGH RISK	Immunoregulatory Factor	20	HIGH RISK

Immune system regulation

CD33 20%

Immune system regulation

CD52 20%

Development and differentiation of B cells into plasma cells

CD20 20%

Cell-cell adhesion

EpCAM (EpCAM+ve) 20%

Immune system regulation

PD-L1 20%

Immune system regulation

PD 1 20%

Immune system regulation

PD-L2 20%

Information

Laboratory Process

- Isolation of the malignant cells using flow cytometry and negative selection. The isolated cells were expanded and they splitter in two, from which, one part is going to viability assays and the other is going for transcriptomic micro-Arrays
- Isolation of mRNA
- Quality control of integrity of mRNA
- Reversed transcription of mRNA to cDNA
- Hybridisation of cDNA with micro-Arrays all genome transcriptomic micro-Arrays slide
- Analysis of the data and detection of repeatable patterns
- Normalization and assessment of clinical relevant probes

This Test report is issued based on testing the sample / specimen examined by the Laboratory. Modification of data, selective breeding and using portions of this test report is forbidden. The laboratory assumes no liability for improper use or improper interpretation of the results.

Expression Rates

Clinical relevant genes related with:

Isolation of mRNA	p53, p21, p16, DHFR, TS, SHMT
Drug targets	Topo I & II, TS, DHFR, ribonucleotide reductase etc.
Signal Transduction Pathway	EGFr, PDGFr, etc.
Epigenetic aberration	Dnmt1, DNA demethylase, etc.
Angiogenesis	VEGF-r, FGFr, PDGFr
Growth signal	c-erb-B1, c-erb-B2, bar-abl, etc
Repair after physical application (radiation, hyperthermia)	HSP27, HSP70, HSP90, HIF1a, etc.

Sincerely,

Dr. Ioannis Papatiriu MD, PhD, SCym

GROWTH FACTORS PROLIFERATION STIMULI

FUNCTION	NAME	NAME OFFICIAL	RELATED
Preprotein for Cellular stress	p180	RRBP1	Tyrosine kinase growth factor
Fusion Protein	Bcr-abl	BCR-ABL	Resist phenotype
Repair Related Gene	PTEN	PTEN	Tumor Suppressor Gene
Eicosanoid related protein	COX2 5-LOX	PTGS2 ALOX5	Tumour Growth Tumour Growth
Proteasome inhibitors	NFkB Ikb (a,b,c)	NFKB1 NFKBIA/B	Transcription Factor NFkB Inhibitors
Proto-Oncogene	ALK EML-4-ALK NPM-ALK RET	ALK EML4-ALK NPM-ALK RET	Acute Leukemia kinase Fused EML-ALK Fused NPM-ALK Proto-Oncogene
Growth Factor Receptor	SS-r CD 117 (c-kit) IGF-r 1 IGF-r 2 EGF C-erb-B2 C-erb-B1	SSTR3/5 KIT IGF1R IGF2R EGF ERBB2 EGFR	Somatostatin receptor Proliferate growth factor receptor Insulin like growth factor receptor Insulin like growth factor receptor Tumour Growth Receptor tyrosine-protein kinase Epithermal Growth Factor Recept...
Signal Transduction Pathway	JAK1/2 c-Jun c-Fos Ras-Raf-MEK-ERK mTOR	JAK1/2 FOS JUN ERK1/2 MTOR	Single transduction pathway Proto-Oncogene Proto-Oncogene Single transduction pathway Single transduction pathway
Hormone Receptors	Progesterone-Receptor Estrogen-Receptor NR3C4-A NR3C4-B	PGR ESR1 NR3C4A NR3C4B	Growth Factor Receptor Growth Factor Receptor Androgen Receptor Androgen Receptor

SELF REPAIR - RESISTANCE

FUNCTION	NAME	NAME OFFICIAL	RELATED
Signal transduction	TGF-b	TGFB2	Tumour Growth
Radiotherapy / Hyperthermia se...	HSP27 HSP72 HSP90	HSPB1 HSPA1A HSP90AA1	Heat Shock Protein Heat Shock Protein Heat Shock Protein
Resistant Phenotype Markers	DNA methyltransferase I DNA-demethylase 06-methyl-DNA-tran Histone-deacetylase-dipeptide HAT CXCR4 HDAC CXCL12 Gamma GC	DNMT1 TET1 MGMT HDAC1 HAT1 CXCR4 HDAC2 CXCL12 GGCX	DNA methylation DNA methylation DNA methylation DNA Coiling Histone acetyl transferase Resist phenotype Histone deacetylase Resist phenotype Resist to alkylating drugs

ANGIOGENESIS

FUNCTION	NAME	NAME OFFICIAL	RELATED
Angiogenesis	VEGF	VEGFA	Angiogenesis
	FGF	FGF1(3)	Angiogenesis
	PDGF	PDGFA(2)	Angiogenesis
	ANG 1	ANGPT1	Angiopoietin
	ANG 2	ANGPT2	Angiopoietin

DRUG METABOLISMS & TARGETS

FUNCTION	NAME	NAME OFFICIAL	RELATED
Nucleoside Import Transformation	DPD	DPYD	Resist to 5FU
	UP	UPP1	Resist to 5FU
	NP	PNP	Purine Nucleoside Phosphorylase
	TP	TYMP	Resist to 5FU
	TS	TYMS	Rapid cell cycle (THFA)
	DHFR	DHFR	Rapid cell cycle (THFA)
	SHMT	SHMT1	Rapid cell cycle (THFA)
	GARFT	GART	Rapid cell cycle (THFA)
	Ribonucleoside reductase	RRM1	DNA synthesis
Activation of Camptothecin	CES1-2	CES1-2	Resist to camptothecin
Xenobiotic	CypB1	CYB1B1	Xenobiotic metabolism
DNA Repair Related Gene	ERCC1	ERCC1	DNA repair mechanism
	RRM1	RRM1	Nucleotide polymerizations

MARKERS

FUNCTION	NAME	NAME OFFICIAL	RELATED
markers	CD33	CD33	Myeloid Cell origin
	CD52	CD52	Leukaemia Marker
	CD20	CD20	Lymphoma Related Antigen
	EpCAM	EPCAM	Epithelial Marker
	PD-L1	CD274	Immunoregulatory Factor
	PD 1	PDCD1	Immunoregulatory Factor
	PD-L2	PDCD1LG2	Immunoregulatory Factor

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- c. Papatirou I, et al. Detection of Circulating Tumor Cells in Patients with Breast, Prostate, Pancreatic, Colon and Melanoma Cancer: A Blinded Comparative Study Using Healthy Donors. *Journal of Cancer Therapy*. 2015;6:543-553. <http://dx.doi.org/10.4236/jct.2015.67059>.
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