

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, epothilones, 5FU, Gemcitabine

Partial sensitivity: inhibitors of topoisomerase II, taxanes, eribulin, alkaloids of vinca, Fudr, UFT

Expression

Over expression: EGF, Ikb(a,b,c), HDAC, HAT, C-MET

Down regulation: 5-LOX, COX2, P180, ESRI, PGR, SS-r, ALK, HSP90, HSP27

NATURAL SUBSTANCES SENSITIVITY

Class I

Cytotoxic Agents

Ascorbic acid, Bio D Mulsion NuMedica D3, C-statin, DCA (dichloroacetate), Doxycycline, GcMAF (Big Harmony), Onkobel Pro, Ribraxx, Super Artemisinin, Ukrain

Class II

Immunostimulants / Immunomodulators

Alpha lipoic Acid, Boswellia Serratta, Fucoidan, Thymex

Class III

PK Inhibitors

Genistein, Indol 3 Carbinol, Polyphenole CA III

* Disclaimer! The natural substances that are tested in our lab facilities are not bonded from restriction for medical use.

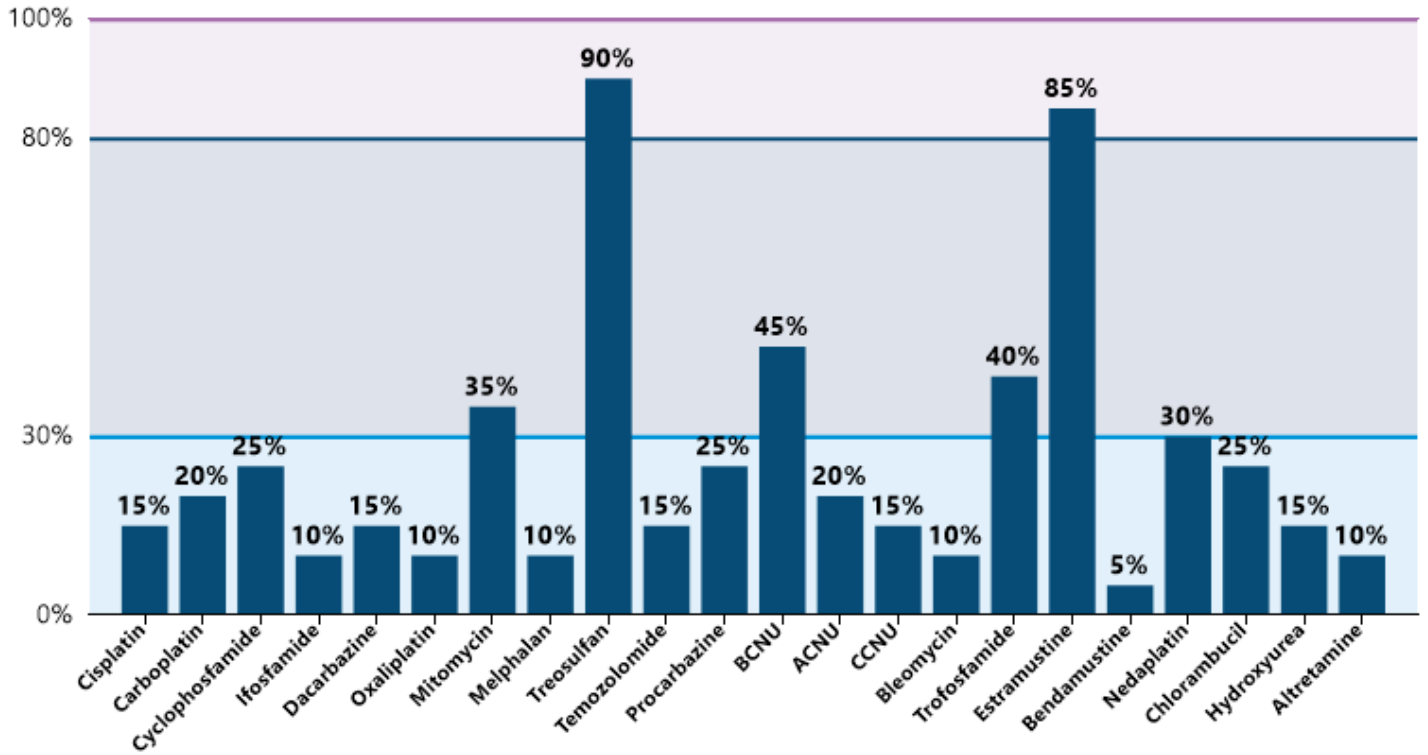
Conclusion Results

- The neoplastic cells have the greatest sensitivity in Treosulfan, Estramustine, Ixabepilone, Abraxane, 5FU, Gemcitabine
- Also can be used 5-azacytidine, Afatinib, Erlotinib, Regorafenib
- 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

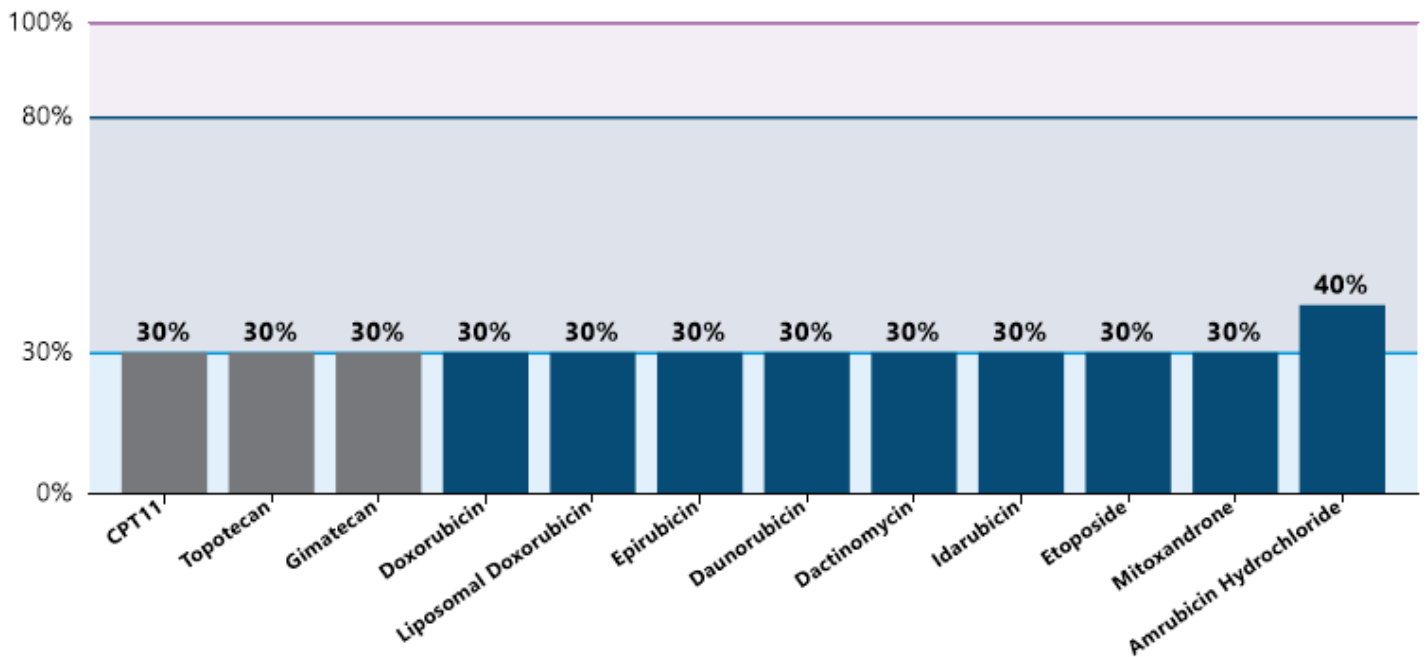
High sensitivity: Treosulfan, Estramustine



Inhibitors of Topoisomerase I & II

High sensitivity:

Inhibitors of Topoisomerase I — Inhibitors of Topoisomerase II —

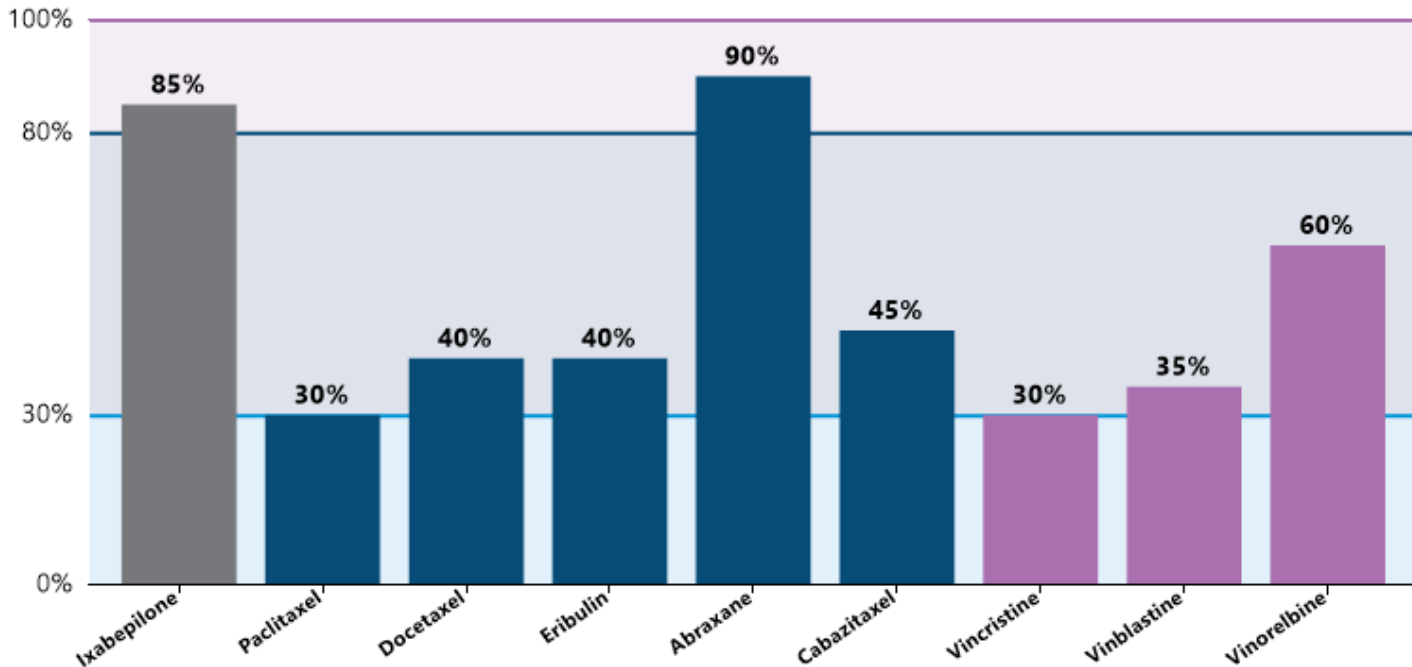


— No sensitivity — Partial sensitivity — High sensitivity

Epothilones & Nucleus Spindle Stabilizer I & II

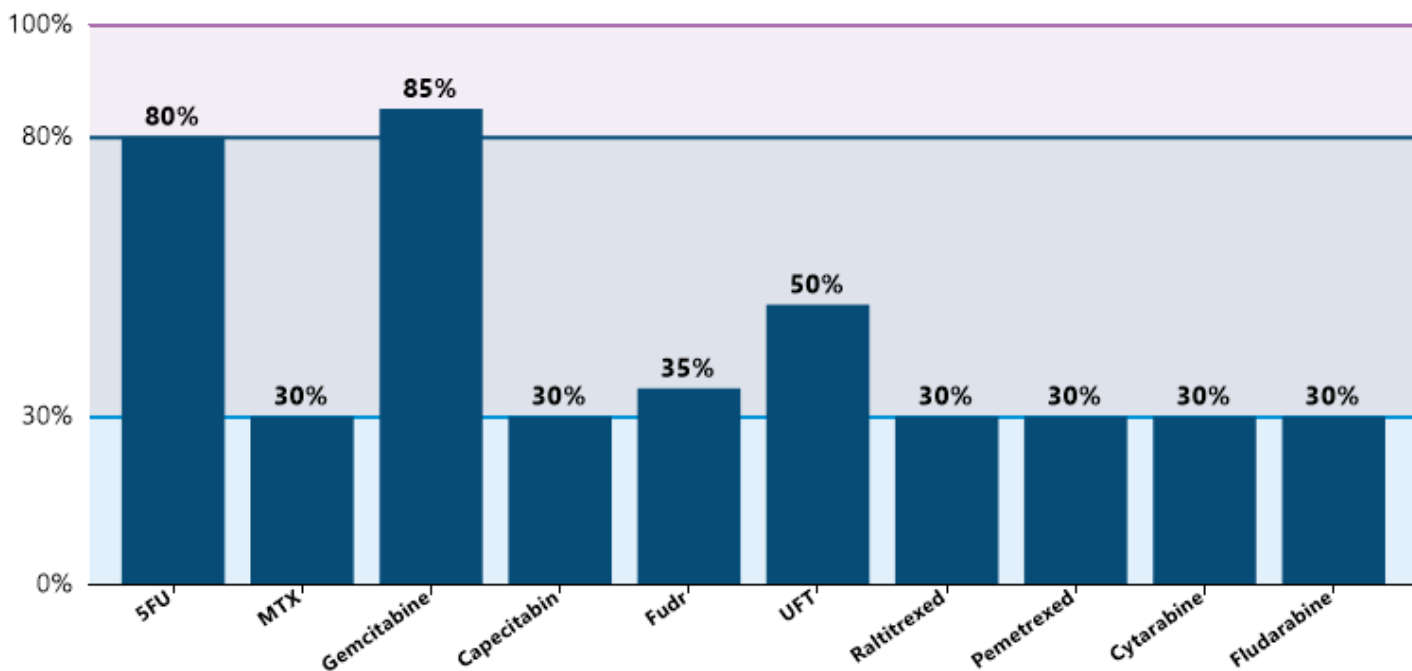
High sensitivity: *Ixabepilone, Abraxane*

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

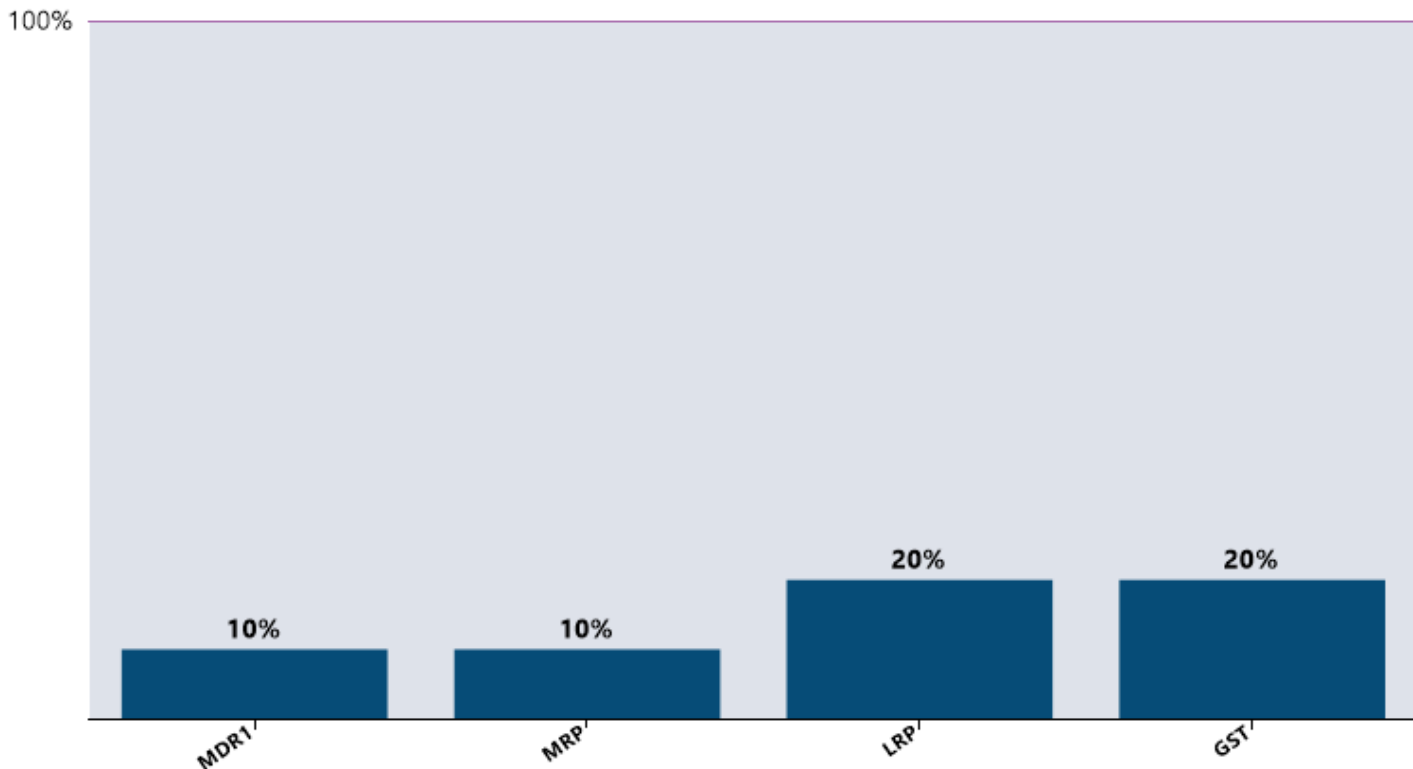


Nucleoside Analogues

High sensitivity: *Gemcitabine*

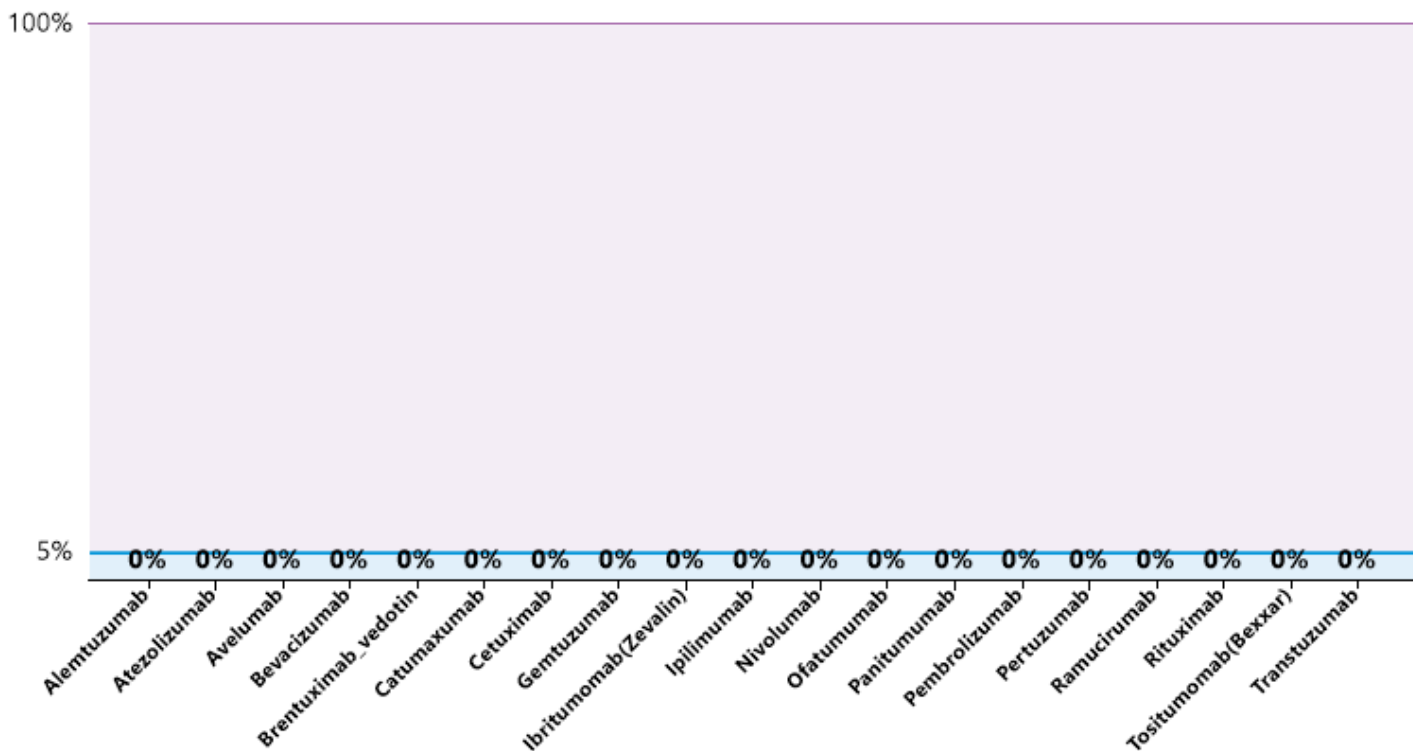


Resistance Factors



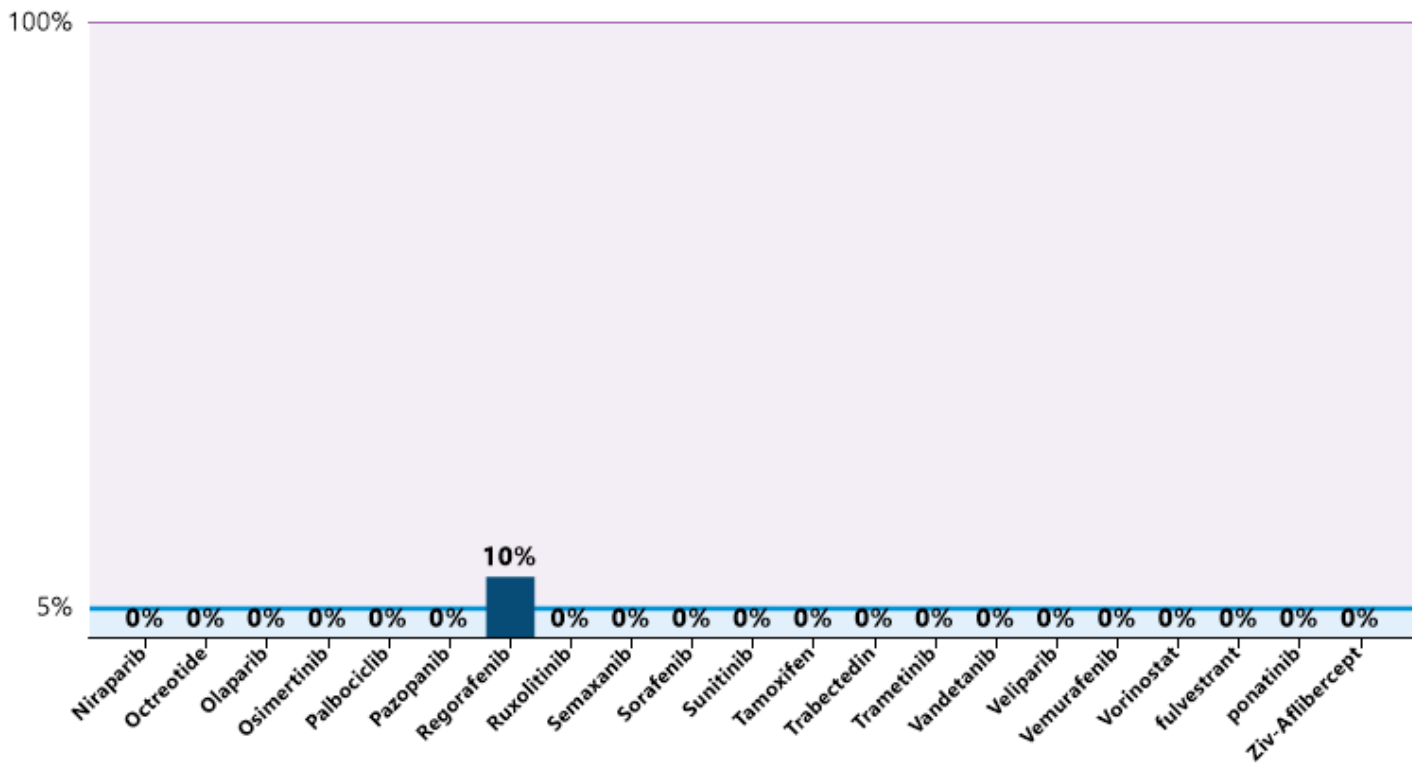
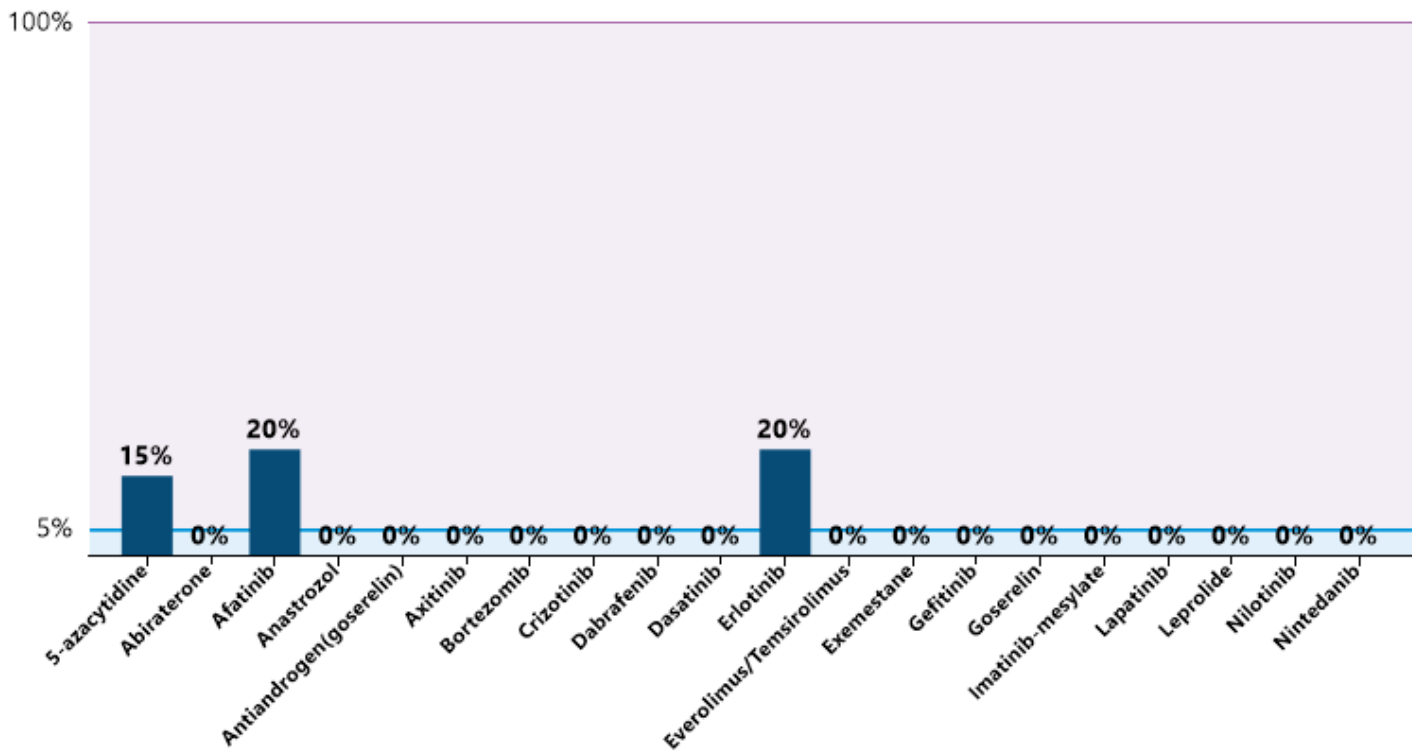
Moab - Monoclonal Antibodies

— 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.	-10	HIGH RISK
Bcr-abl	Fusion Protein	LOW RISK	Resist phenotype	0	LOW RISK
PTEN	Repair Related Gene	LOW RISK	Tumor Suppressor Gene	0	LOW RISK
COX2	Eicosanoid related protein	HIGH RISK	Tumour Growth	-10	HIGH RISK
5-LOX			Tumour Growth	-10	HIGH RISK
NFkB	Proteasome inhibitors	HIGH RISK	Transcription fact	-5	LOW RISK
IkB(a,b,c)			Inhibitor of NFkB	60	HIGH RISK
ALK	Proto-Oncogene	HIGH RISK	Acute Leukemia kinase	-20	HIGH RISK
EML-4-ALK			Fusion EML with ALK	5	LOW RISK
NPM-ALK			Fusion NPM with ALK	5	LOW RISK
RET			Proto-Oncogene	60	HIGH RISK

Preprotein for Cellular stress

-10% p180

Fusion Protein

Bcr-abl | 0%

Repair Related Gene

PTEN | 0%

Eicosanoid related protein

-10% COX2

-10% 5-LOX

Proteasome inhibitors

-5% NFkB

IkB(a,b,c) | 60%

Proto-Oncogene

-20% ALK

EML-4-ALK | 5%

NPM-ALK | 5%

RET | 60%

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	5	LOW RISK
IGF-r 1			Insulin like growth factor receptor	0	LOW RISK
IGF-r-2			Insulin like growth factor receptor	0	LOW RISK
EGF			Tumour Growth	50	HIGH RISK
c-erb-B1			Her1	0	LOW RISK
c-erb-B2			Her/neu2	0	LOW RISK
JAK1/2	Signal Transduction Pathway	HIGH RISK	Single transduction pathway	0	LOW RISK
c-Jun			Proto-Oncogene	0	LOW RISK
c-Fos			Proto-Oncogene	5	LOW RISK
Ras/Raf/MEK/Er k			Transduction pathway	15	HIGH RISK
mTOR			Transduction pathway	0	LOW RISK
Progesterone Receptor	Hormone Receptors	HIGH RISK	Growth Factor Receptor	-10	HIGH RISK
Estrogene Receptor			Growth Factor Receptor	-10	HIGH RISK
NR3C4-A			Nucleous receptor group III Class 4(andro...	0	LOW RISK
NR3C4-B			Nucleous receptor group III Class 4(andro...	0	LOW RISK

Growth Factor Receptor

SS-r	-20%
CD 117(c-kit)	5%
IGF-r 1	0%
IGF-r-2	0%
EGF	50%
c-erb-B1	0%
c-erb-B2	0%

Signal Transduction Pathway

JAK 1/2	0%
c-Jun	0%
c-Fos	5%
Ras/Raf/MEK/Er k	15%
mTOR	0%

Hormone Receptors

Progesterone Receptor	-10%
Estrogene Receptor	-10%
NR3C4-A	0%
NR3C4-B	0%

SELF REPAIR - RESISTANCE

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
TGF-b	Signal transduction	LOW RISK	Tumour Growth	0	LOW RISK
HSP27	Radiotherapy / Hyperthermia sensitivity	SENSITIVE	Heat Shock Protein	-20	SENSITIVE
HSP72			Heat Shock Protein	-5	SENSITIVE
HSP90			Heat Shock Protein	-15	SENSITIVE
DNA methyltransferas el	Resistant Phenotype Markers	HIGH RISK	DNA methylation	20	HIGH RISK
DNA demethylase			DNA methylation	0	LOW RISK
06-methyl-DNA- tran			DNA methylation	-5	LOW RISK
Histone deacetylase			DNA coiling (nucleosome)	15	HIGH RISK
HAT			Histone acetyl transferase	20	HIGH RISK
CXCR4			Resistant Phenotype	20	HIGH RISK
CXCL12			Resistant Phenotype	20	HIGH RISK
Gamma GC			Resist to alkylating drugs	15	HIGH RISK
HDAC			Histone deacetylase	20	HIGH RISK

Signal transduction

TGF-b 0%

Radiotherapy / Hyperthermia sensitivity

-20% HSP27

-5% HSP72

-15% HSP90

Resistant Phenotype Markers

DNA methyltransferas el 20%

DNA demethylase 0%

-5% 06-methyl-DNA- tran

Histone deacetylase 15%

HAT 20%

CXCR4 20%

CXCL12 20%

Gamma GC 15%

HDAC 20%

ANGIOGENESIS - METASTASES

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
VEGF	Angiogenesis	LOW RISK	Angiogenesis	0	LOW RISK
FGF			Angiogenesis	0	LOW RISK
PDGF			Angiogenesis	0	LOW RISK
ANG 1			Angiogenin I	0	LOW RISK
ANG 2			Angiogenin II	0	LOW RISK
c-MET	Migration invasion	HIGH RISK	Mesenchymal to epithelial transition	15	HIGH RISK
67LR			67 Laminin receptor	15	HIGH RISK
KISS-1-r			Metastases regulator	0	LOW RISK
Nm23			Metastases regulator	0	LOW RISK
MMP			Metastases	15	HIGH RISK

Angiogenesis

VEGF	0%
FGF	0%
PDGF	0%
ANG 1	0%
ANG 2	0%

Migration invasion

c-MET	15%
67LR	15%
KISS-1-r	0%
Nm23	0%
MMP	15%

CELL CYCLE REGULATION & IMMORTALIZATION / APOPTOSIS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
E2F1	Increase Protein Synthesis	LOW RISK	Transcr. Fact of TS & topo I	0	LOW RISK
CDC6	Rapid Cell Cycle	LOW RISK	Initiation of DNA replication	0	LOW RISK
h-TERT	Immortalization	HIGH RISK	M2 crisis- aggressive phen	20	HIGH RISK
Bcl-2	Regulation of Apoptosis	LOW RISK	Apoptosis	0	LOW RISK
Bax			Apoptosis	0	LOW RISK
CD95 (fas-r)			Apoptosis related receptor	0	LOW RISK
p27	Cell Cycle Rate	LOW RISK	Cell arrest (G0)	0	LOW RISK
p53			Cell cycle regulator	0	LOW RISK
p16			Apoptosis	0	LOW RISK

Increase Protein Synthesis

E2F1 | 0%

Rapid Cell Cycle

CDC6 | 0%

Immortalization

h-TERT | 20%

Regulation of Apoptosis

Bcl-2 | 0%

Bax | 0%

CD95 (fas-r) | 0%

Cell Cycle Rate

p27 | 0%

p53 | 0%

p16 | 0%

DRUG METABOLISMS & TARGETS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
DPD	Nucleoside Import Transformation	HIGH RISK	Resist to 5FU	0	LOW RISK
UP			Resist to 5FU	-10	HIGH RISK
NP			Resist topyrim. Antagonist	-10	HIGH RISK
TP			Resist to 5FU	-10	HIGH RISK
TS			Rapid cell cycle (THFA)	0	LOW RISK
DHFR			Rapid cell cycle (THFA)	0	LOW RISK
SHMT			Rapid cell cycle (THFA)	15	HIGH RISK
GARFT			Rapid cell cycle (THFA)	0	LOW RISK
Ribonucleosider Eductase			DNA synthesis	0	LOW RISK
CES1&2 (carboxyesterase)			Activation of Camptothecin	LOW RISK	Resist to camptothecin
CypB1	Xenobiotic	LOW RISK	Xenobiotic metabolism	0	LOW RISK
ERCC1	DNA Repair Related Gene	LOW RISK	DNA repair mechanism	0	LOW RISK
RRM1			Nucleotide polymerizations	0	LOW RISK

Nucleoside Import Transformation

DPD	0%
-10%	UP
-10%	NP
-10%	TP
TS	0%
DHFR	0%
SHMT	15%
GARFT	0%
Ribonucleosider Eductase	0%

Activation of Camptothecin

CES1&2 (carboxyesterase)	0%
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Xenobiotic

CypB1	0%
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DNA Repair Related Gene

ERCC1	0%
RRM1	0%

MARKERS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
CD33	Immune system regulation	LOW RISK	Myeloid Cell origin	0	LOW RISK
CD52	Immune system regulation	HIGH RISK	Leukaemia Marker	15	HIGH RISK
CD20	Development and differentiation of B cells into plasma cells	LOW RISK	Lymphoma Related Antigen	0	LOW RISK
EpCAM (EpCAM+ve)	Cell-cell adhesion	LOW RISK	Epithelial Marker (2.7 cells/7.5 ml)	0	LOW RISK
PD-L1	Immune system regulation	HIGH RISK	Immunoregulatory Factor	45	HIGH RISK
PD 1	Immune system regulation	HIGH RISK	Immunoregulatory Factor	45	HIGH RISK
PD-L2	Immune system regulation	HIGH RISK	Immunoregulatory Factor	50	HIGH RISK

Immune system regulation

CD33 | 0%

Immune system regulation

CD52 | 15%

Development and differentiation of B cells into plasma cells

CD20 | 0%

Cell-cell adhesion

EpCAM (EpCAM+ve) | 0%

Immune system regulation

PD-L1 | 45%

Immune system regulation

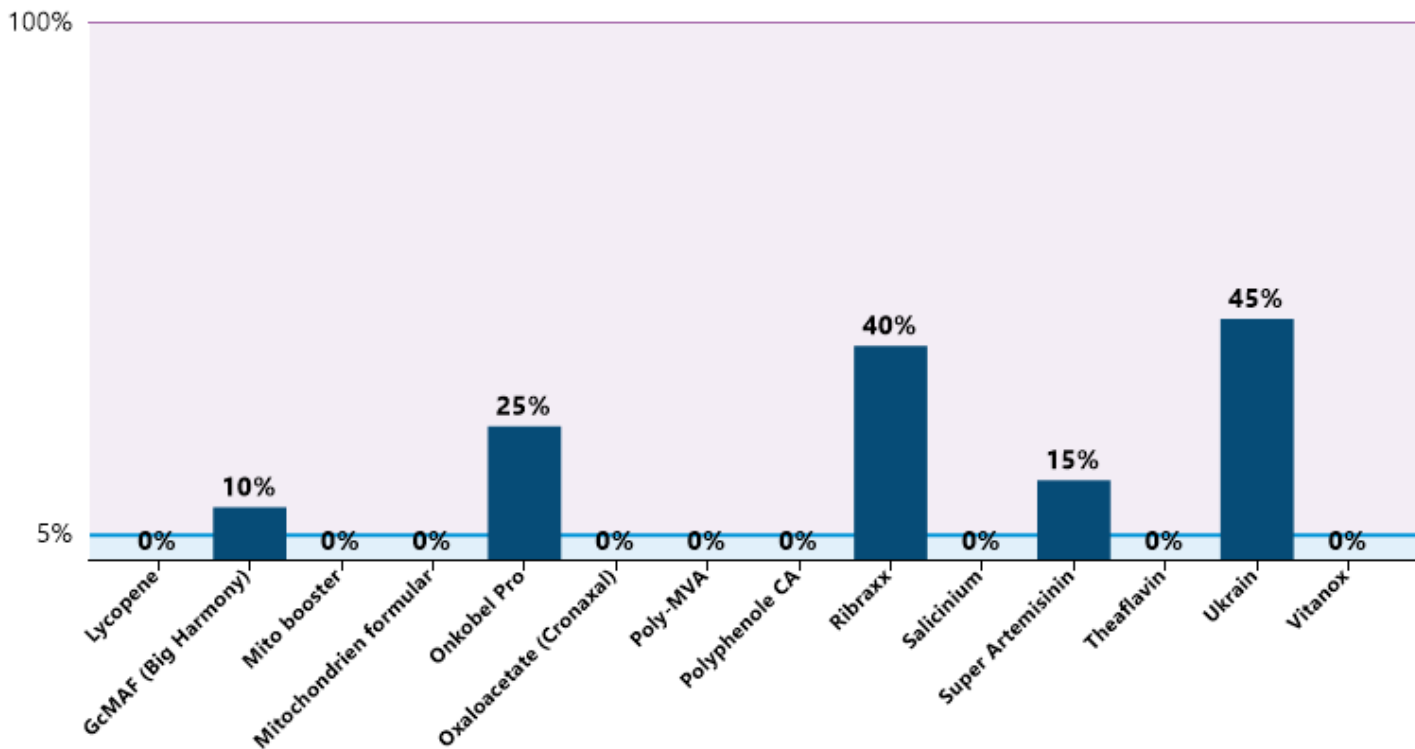
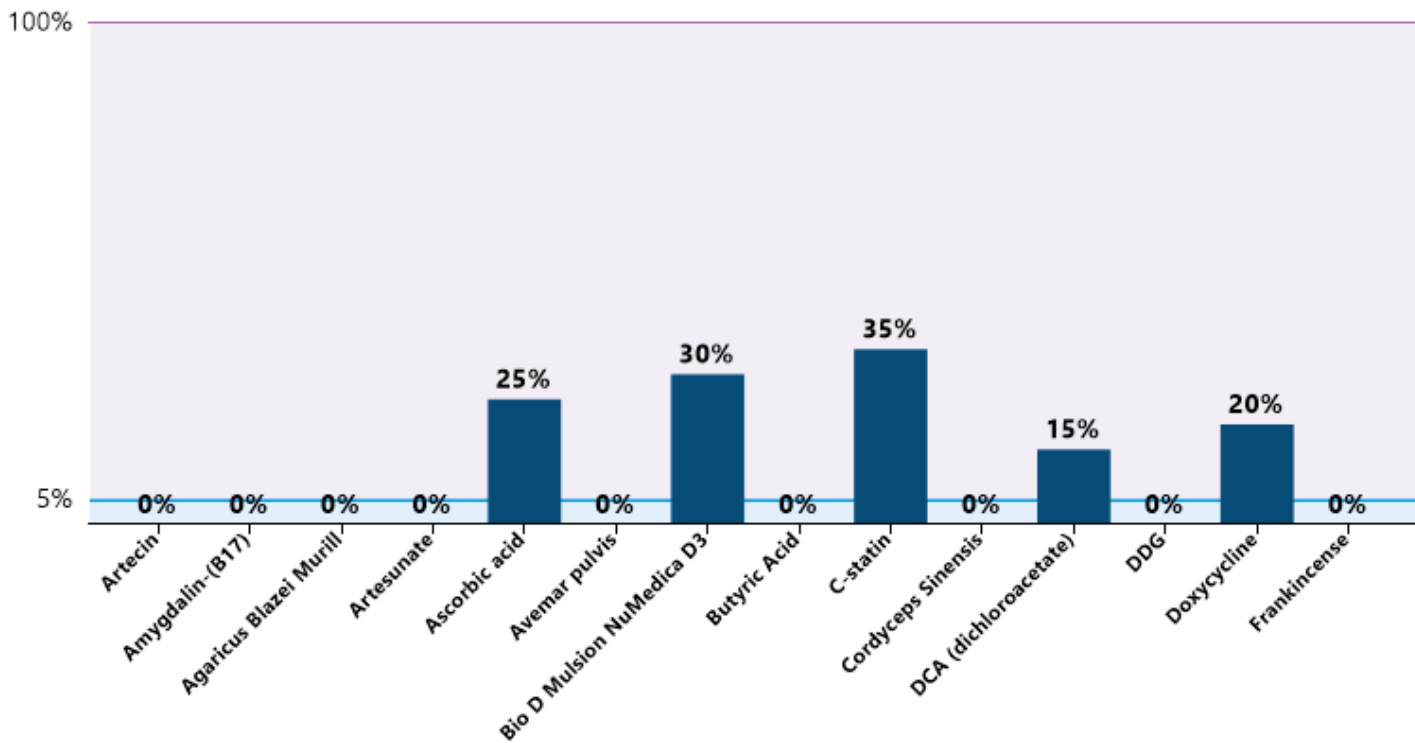
PD 1 | 45%

Immune system regulation

PD-L2 | 50%

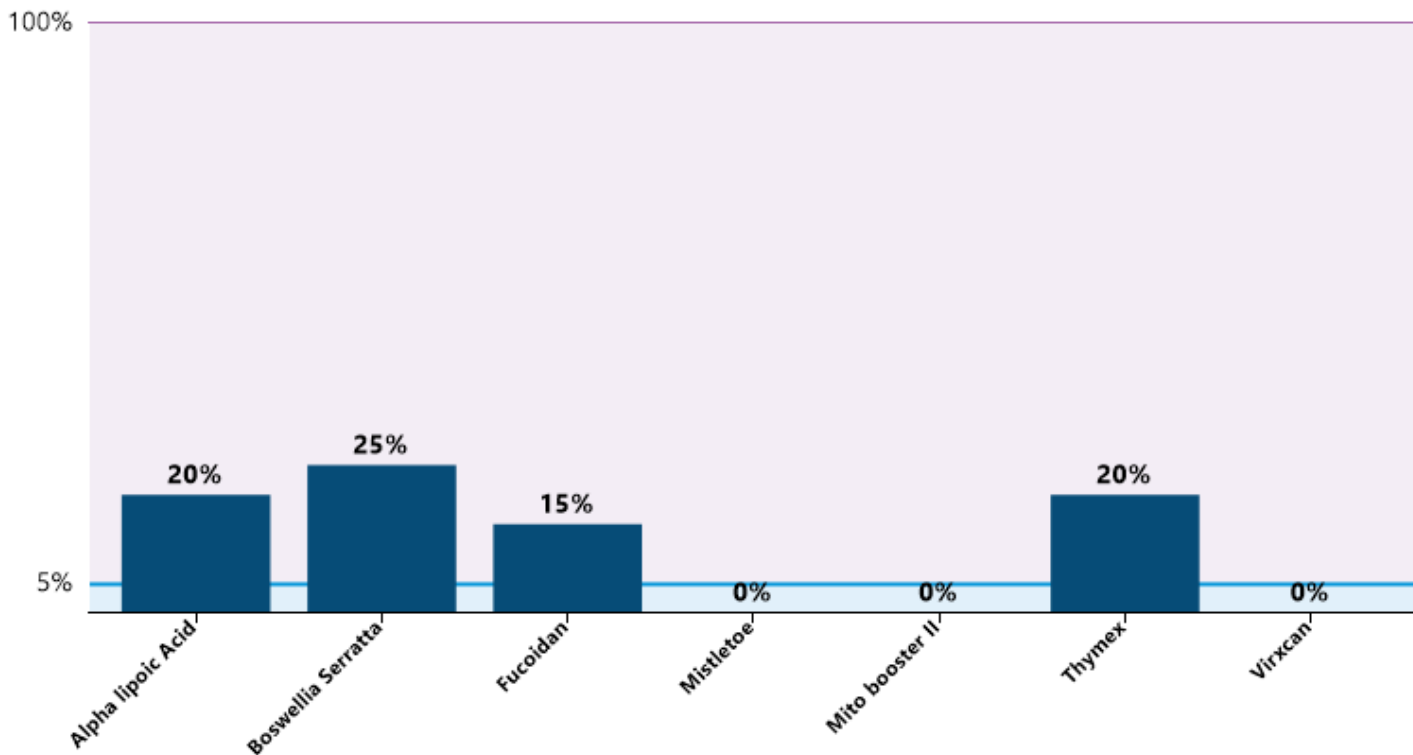
— No sensitivity — Sensitivity

Class I (Cytotoxic Agents)

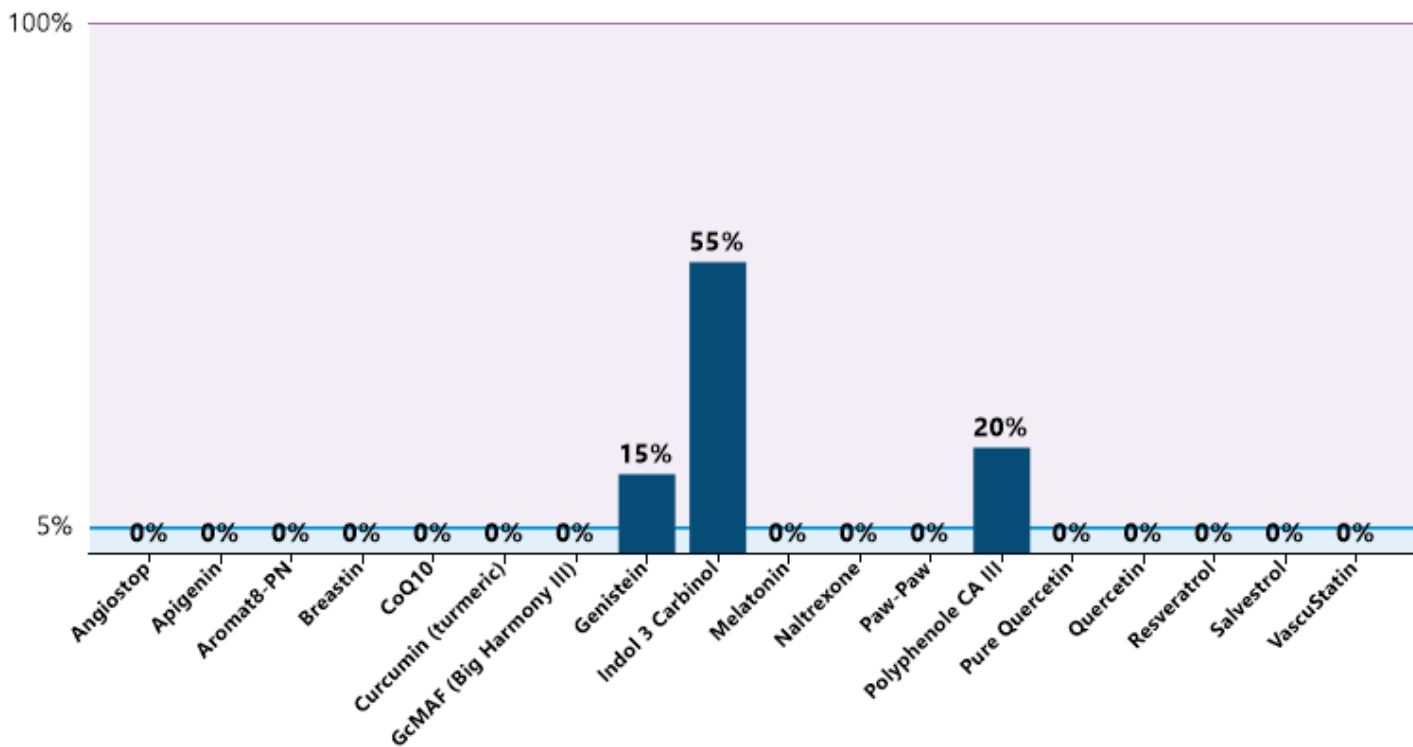


— No sensitivity — Sensitivity

Class II (Immunostimulants / Immunomodulators)



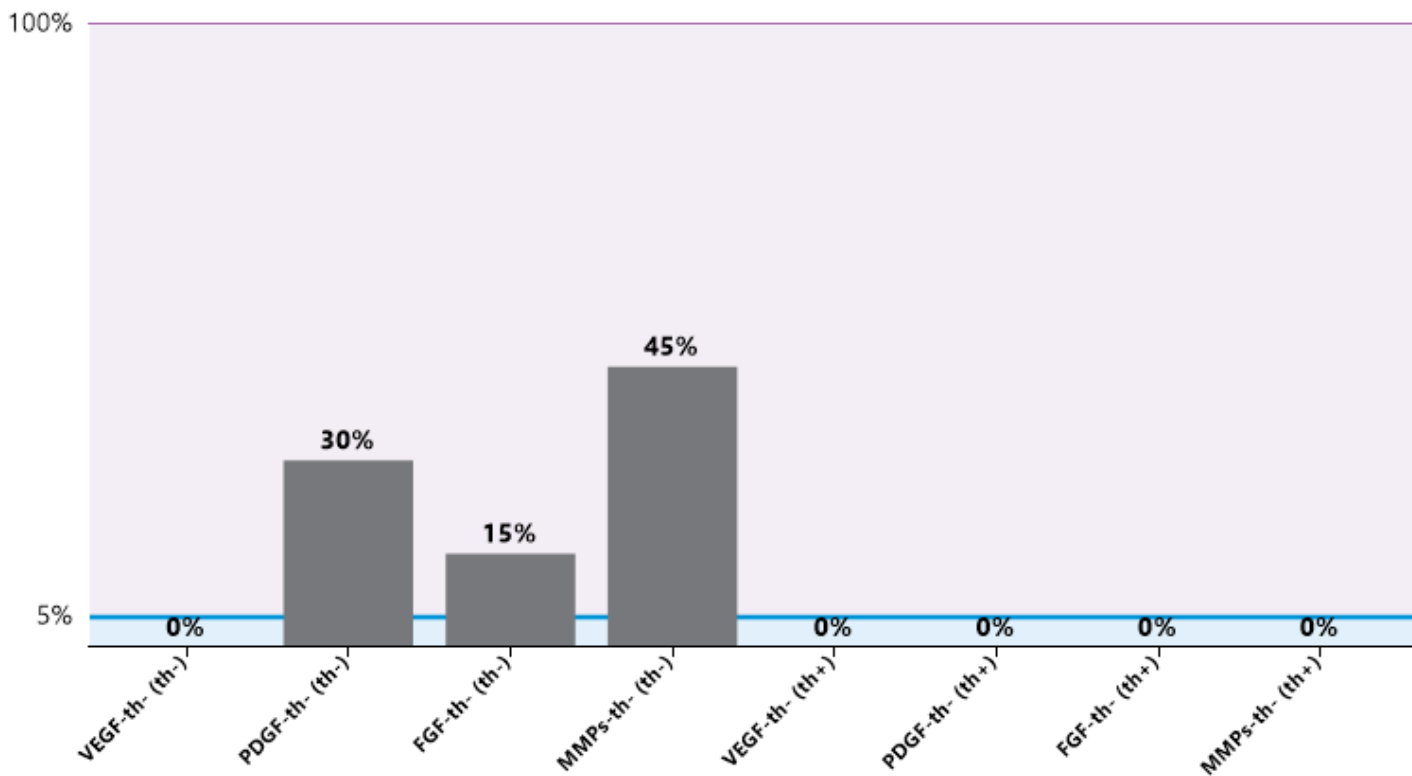
Class III (PK Inhibitors)



No sensitivity Sensitivity

Malignant Cells - Thalidomide

th-
th+



NATURAL SUBSTANCES

SUBSTANCE NAME	VALUE W/O SUBSTANCE	VALUE WITH SUBSTANCE	EFFICACY
Berberine	10	14	Not Effective
Mangosteen	10	17	Effective
Cordyceps	10	15	Not Effective
Graviola	10	14	Not Effective
Honopure 50mg/kg l	11	17	Effective
Teavigo	12	18	Effective
test	10	20	Effective
Graviola	20	10	Not Effective

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 Papisotiriou 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. Papatotiriou 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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