ONCONOMICS PLUS RGCC®

Patient				Physician
NAME	DATE OF BIRTH	DISEASE	STAGE	NAME
Mr John Doe	1992-Jun-12	Prostate	II	Administrator
SPECIMEN	VIAL IDs			
	4			

REPORT SUMMARY

CTCs COUNT: Isolated 3.4 cells/ml , SD +/- 0.3 cells

SENSITIVITY - GENE EXPRESSION

Sensitivity

High sensitivity: alkylating factors

Partial sensitivity: inhibitors of topoisomerase I, inhibitors of topoisomerase II, taxanes, alkaloids of vinca, Raltitrexed, Cytarabine

Expression

Over expression: HDAC

Down regulation: COX2, IGF-r 2, HSP90, HSP72, HSP27

NATURAL SUBSTANCES SENSITIVITY

Class I

Cytotoxic Agents

Artecin, Artesunate, Bio D Mulsion NuMedica D3, Butyric Acid, DCA (dichloroacetate), Doxycycline, Frankincense, Lycopene, Colloidal Silver

Class II

Immunostimulants / Immunomodulators

Boswellia Serratta, Fucoidan, Astaxanthin, Reishi Pure, Sodium Bicarbonate

Class III

PK Inhibitors

Apigenin, Indol 3 Carbinol, Melatonin, IP6 (Inositol)

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

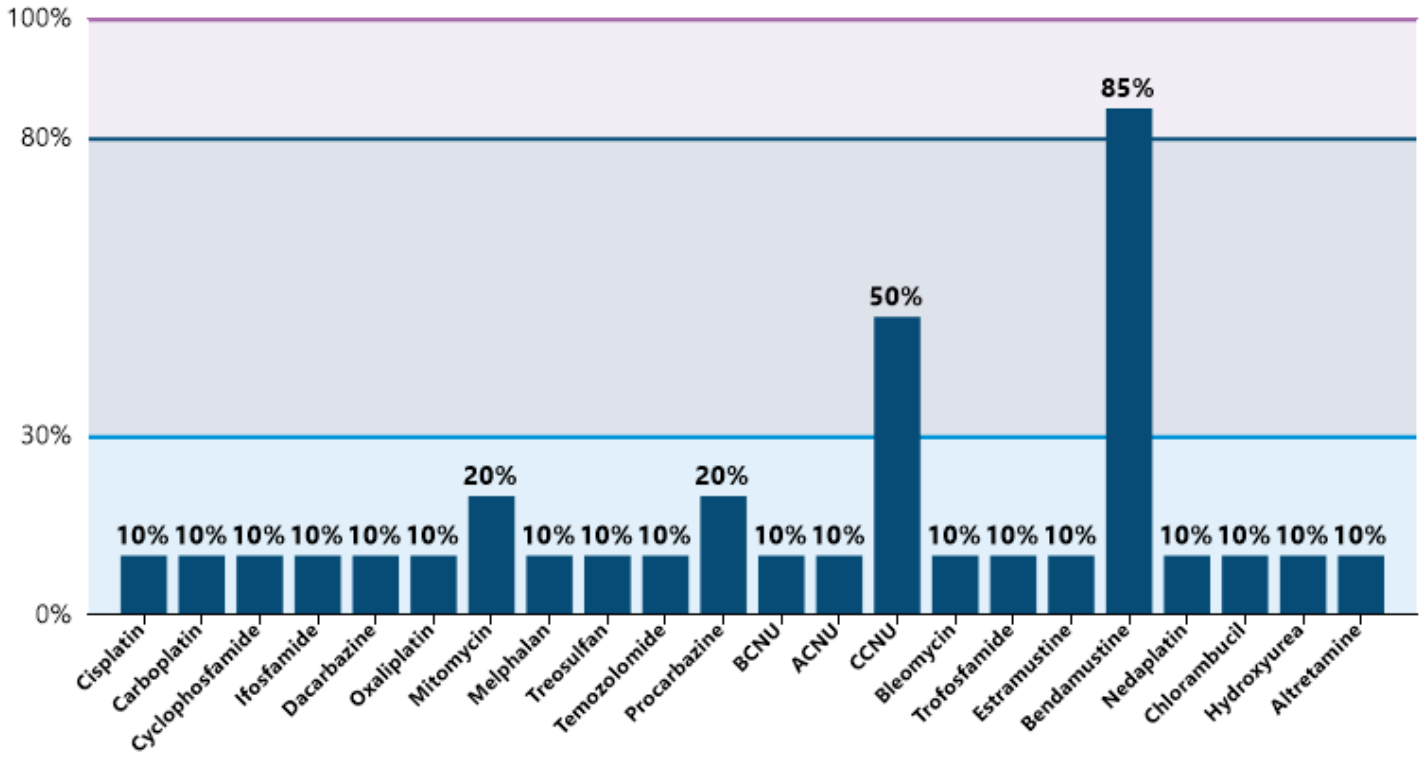
Conclusion Results

- The neoplasmatic cells have the greatest sensitivity in Bendamustine
- Also can be used Everolimus/Temsirolimus, Trabectedin, Vemurafenib
- 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

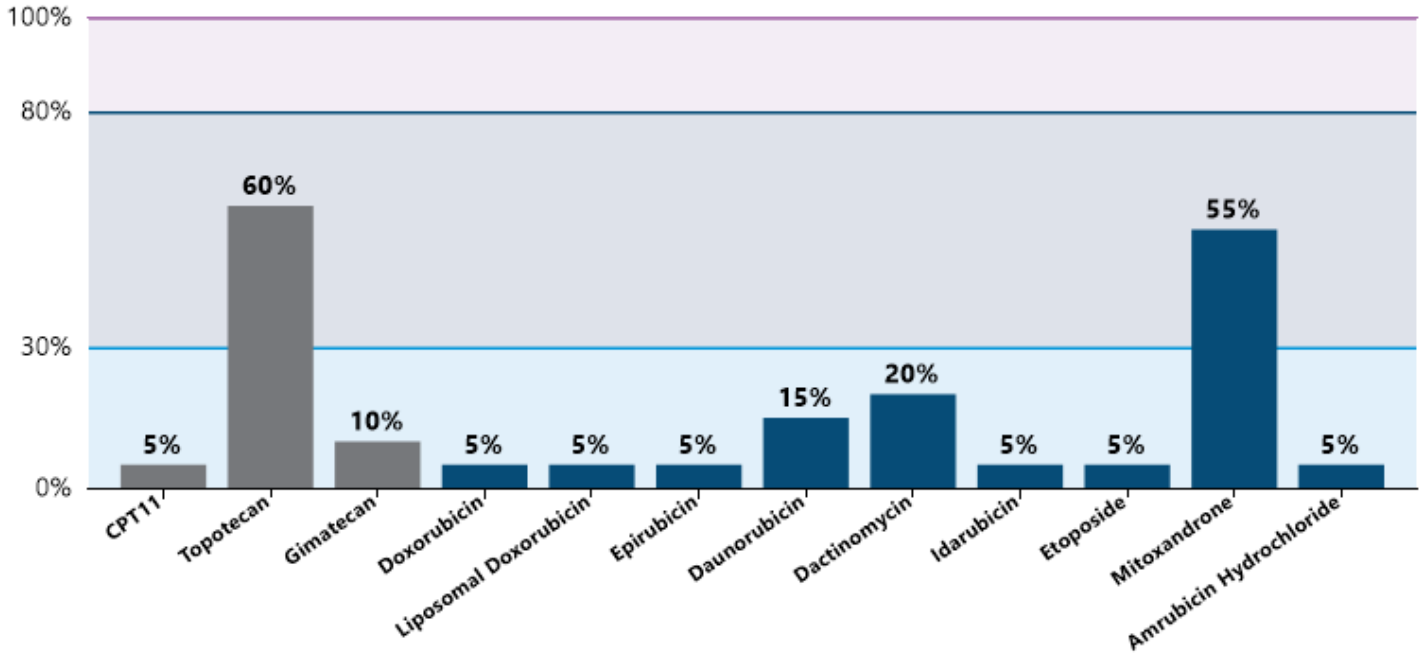
High sensitivity: Bendamustine



Inhibitors of Topoisomerase I & II

Inhibitors of Topoisomerase I
Inhibitors of Topoisomerase II

High sensitivity:

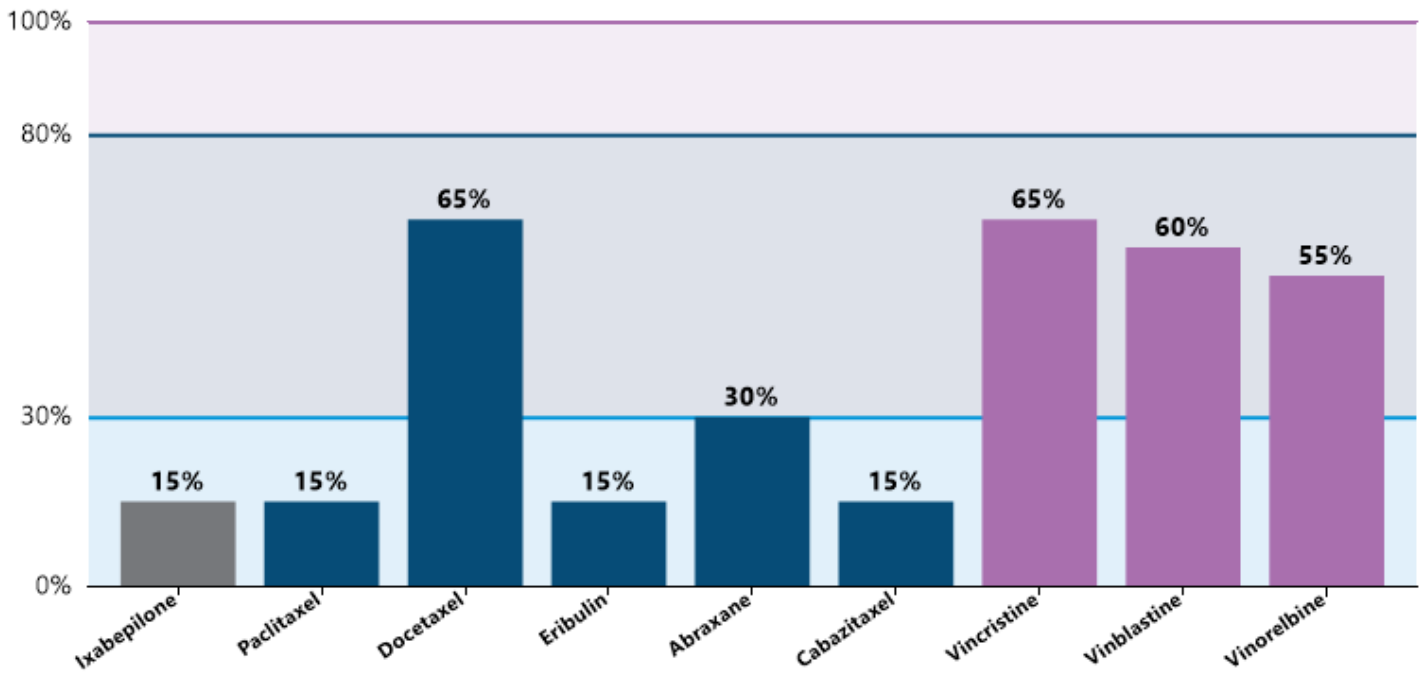


No sensitivity Partial sensitivity High sensitivity

Epothilones & Nucleus Spindle Stabilizer I & II

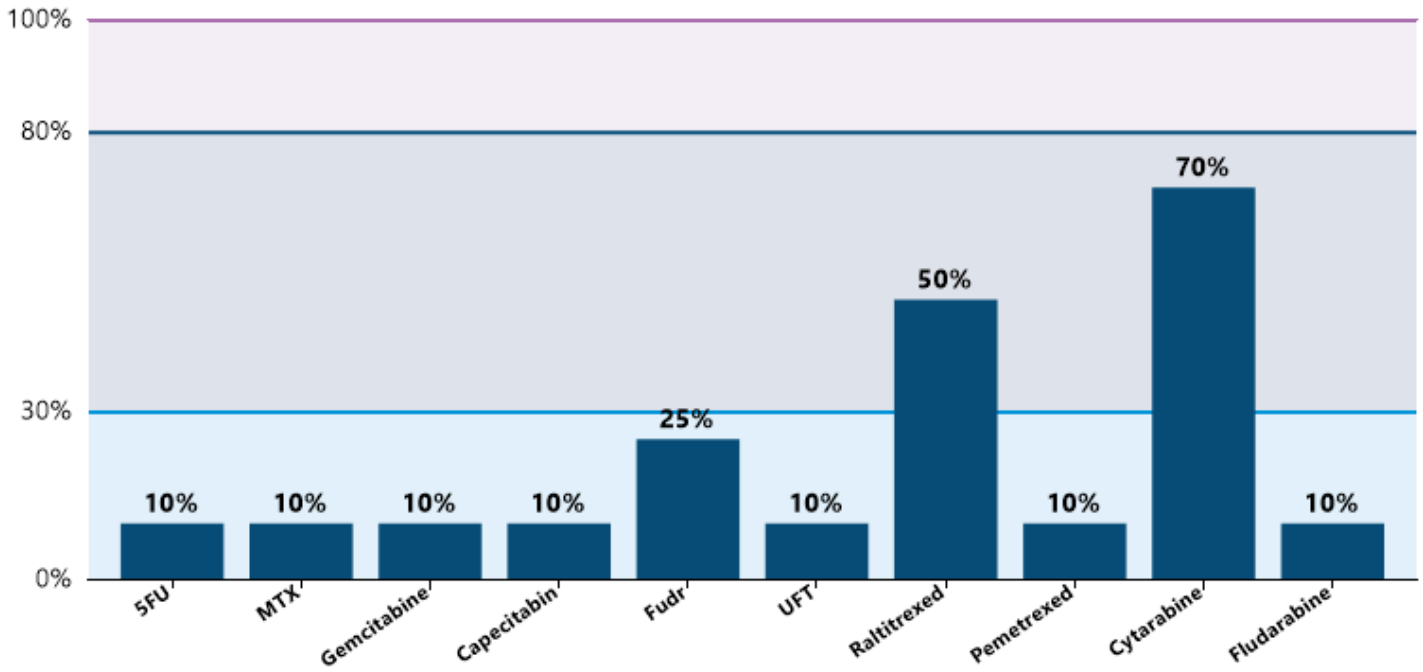
High sensitivity:

Epothilones
Nucleus Spindle Stabilizer I
Nucleus Spindle Stabilizer II

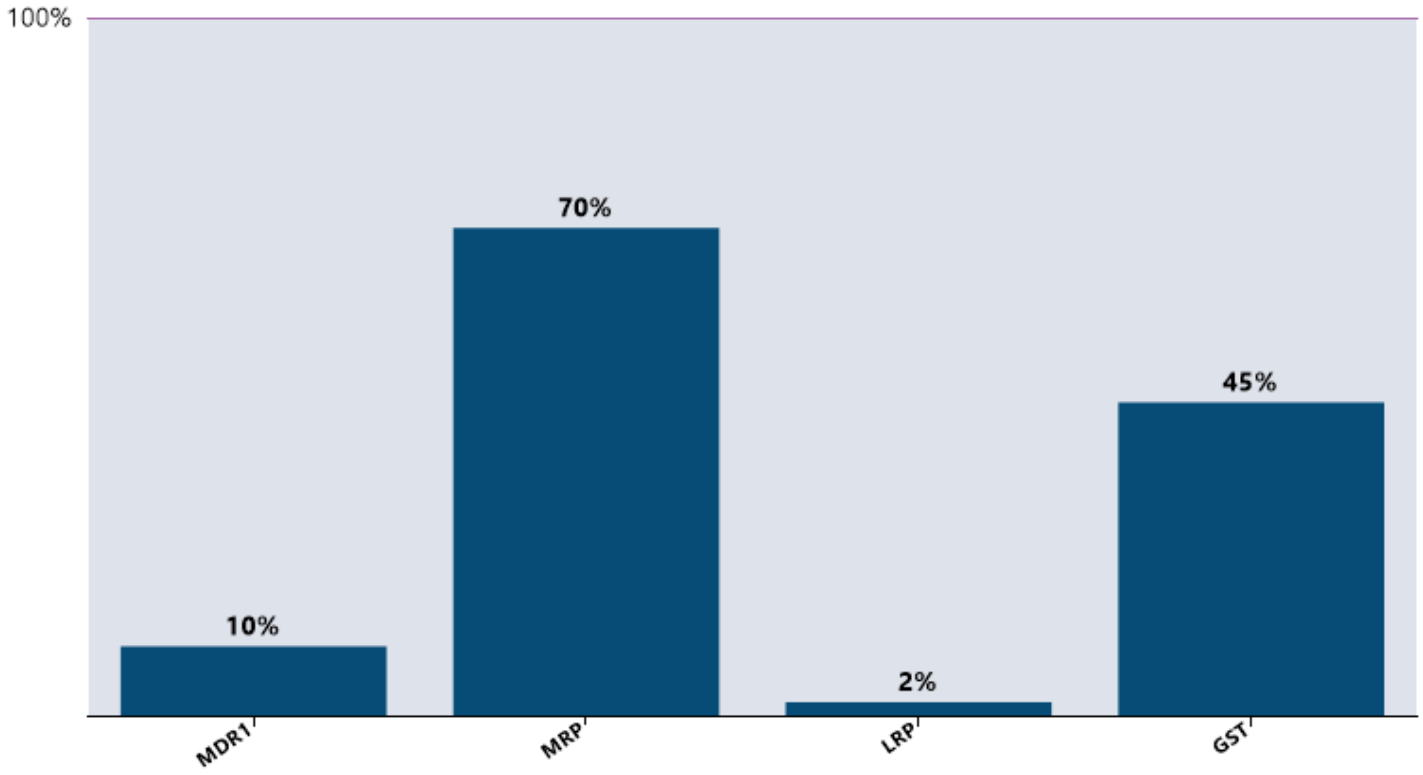


Nucleoside Analogues

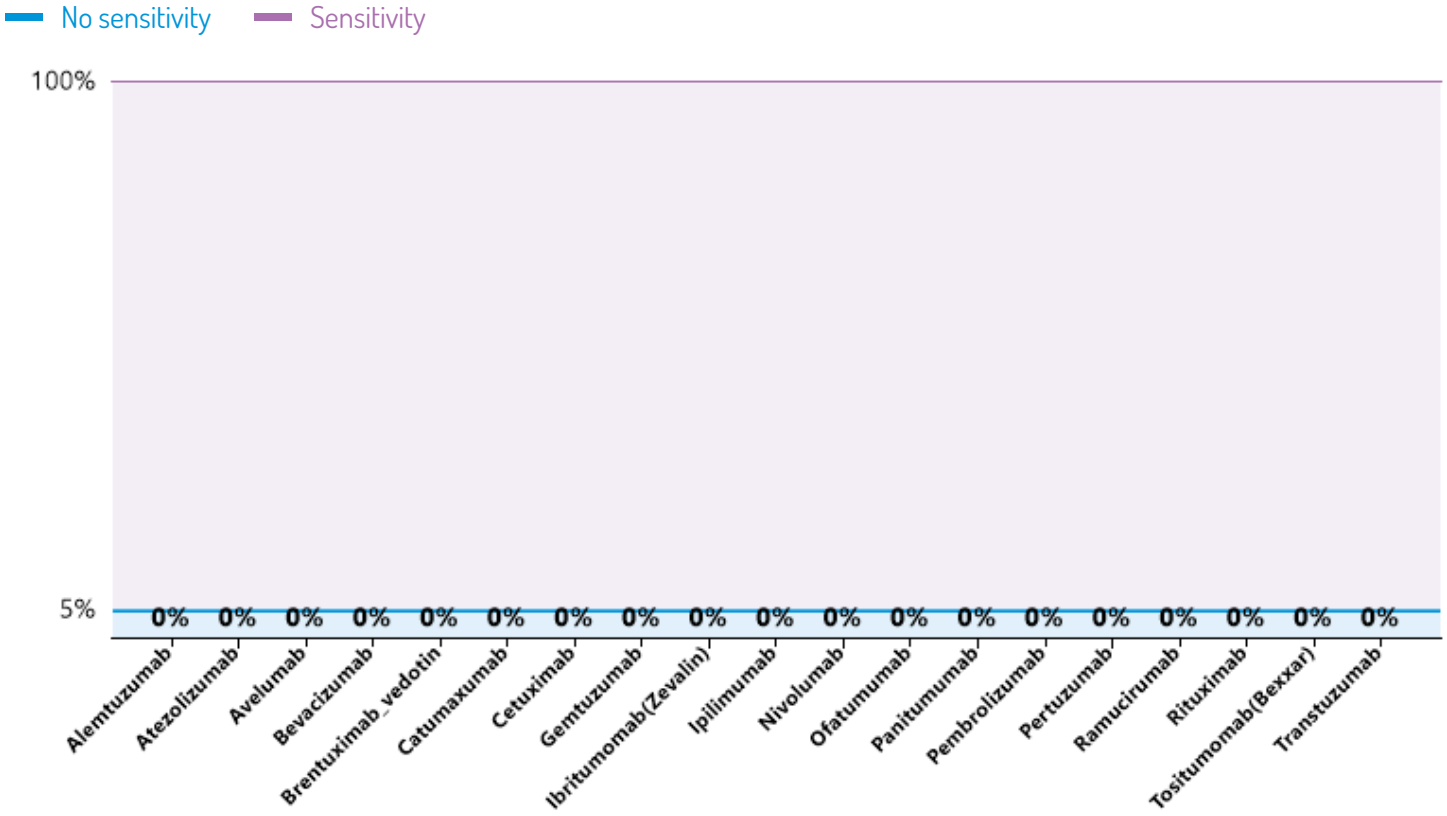
High sensitivity:



Resistance Factors

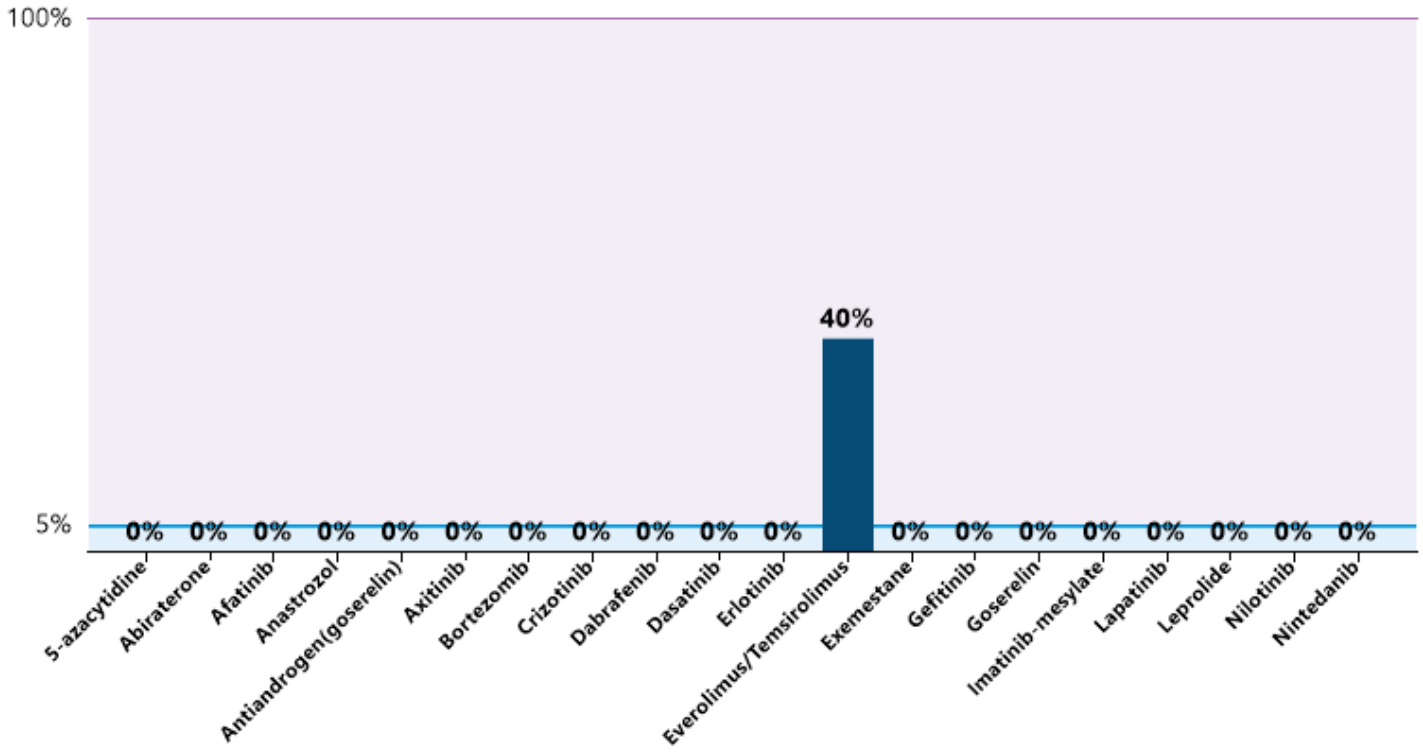


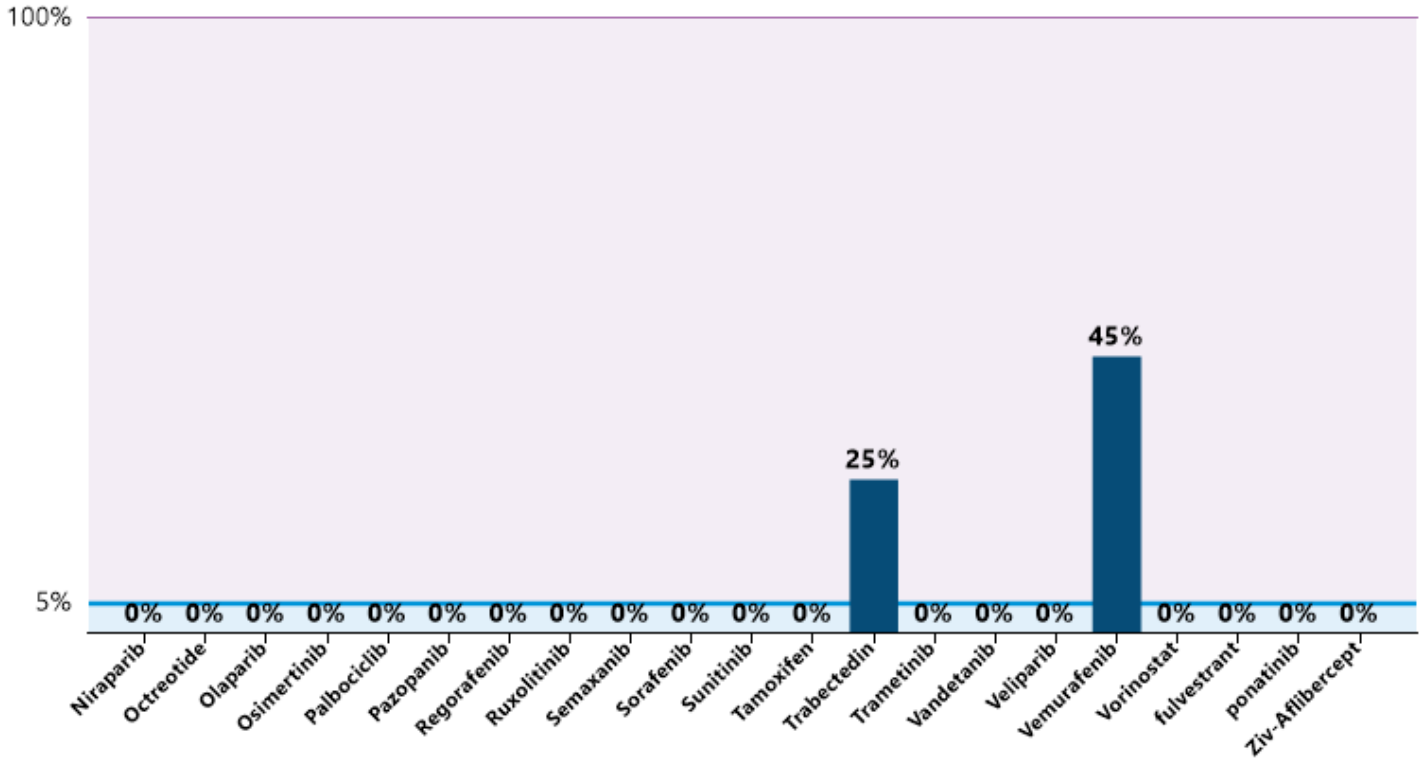
Moab -Monoclonal Antibodies



No sensitivity Sensitivity

SMW - Small Molecular weight molecule





Growth Factors Proliferation Stimuli

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
p180	Preprotein for Cellular stress	LOW RISK	Tyrosin kinase growth f.	0	LOW RISK
Bcr-abl	Fusion Protein	LOW RISK	Resist phenotype	0	LOW RISK
PTEN	Repair Related Gene	HIGH RISK	Tumor Suppressor Gene	-50	HIGH RISK
COX2	Eicosanoid related protein	HIGH RISK	Tumour Growth	-45	HIGH RISK
5-LOX			Tumour Growth	0	LOW RISK
NFkB	Proteasome inhibitors	LOW RISK	Transcription fact	0	LOW RISK
IkB(a,b,c)			Inhibitor of NFkB	0	LOW RISK
ALK	Proto-Oncogene	LOW RISK	Acute Leukemia kinase	0	LOW RISK
EML-4-ALK			Fusion EML with ALK	0	LOW RISK
NPM-ALK			Fusion NPM with ALK	0	LOW RISK
RET			Proto-Oncogene	0	LOW RISK

Preprotein for Cellular stress

p180 0%

Fusion Protein

Bcr-abl 0%

Repair Related Gene

-50% PTEN

Eicosanoid related protein

-45% COX2

5-LOX 0%

Proteasome inhibitors

NFkB 0%

IkB(a,b,c) 0%

Proto-Oncogene

ALK 0%

EML-4-ALK 0%

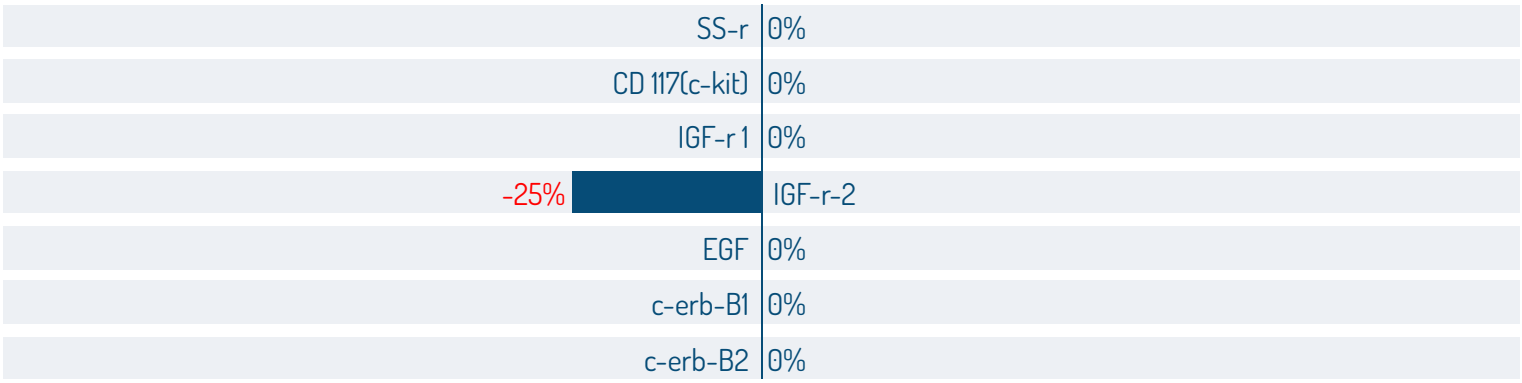
NPM-ALK 0%

RET 0%

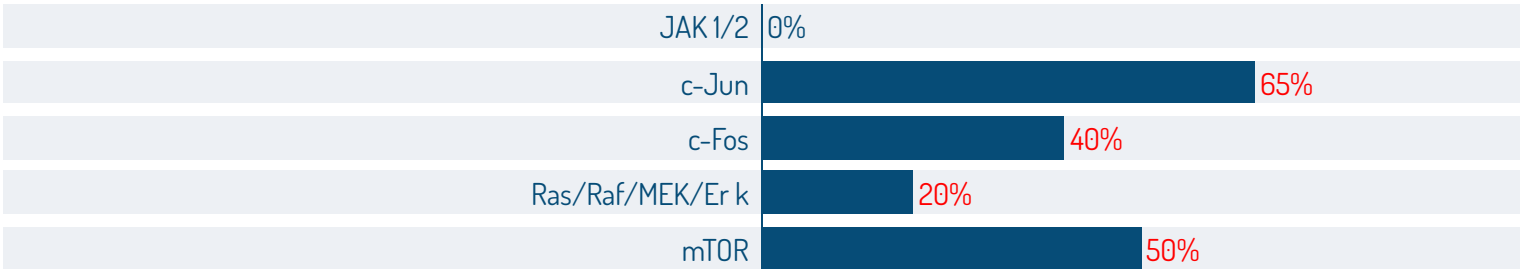
Growth Factors Proliferation Stimuli

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
SS-r	Growth Factor Receptor	HIGH RISK	Somatostatin receptor	0	LOW RISK
CD 117(c-kit)			Proliferate growth factor receptor	0	LOW RISK
IGF-r 1			Insulin like growth factor receptor	0	LOW RISK
IGF-r-2			Insulin like growth factor receptor	-25	HIGH RISK
EGF			Tumour Growth	0	LOW RISK
c-erb-B1			Her1	0	LOW RISK
c-erb-B2			Her/neu2	0	LOW RISK
JAK 1/2	Signal Transduction Pathway	HIGH RISK	Single transduction pathway	0	LOW RISK
c-Jun			Proto-Oncogene	65	HIGH RISK
c-Fos			Proto-Oncogene	40	HIGH RISK
Ras/Raf/MEK/Er k			Transduction pathway	20	HIGH RISK
mTOR			Transduction pathway	50	HIGH RISK
Progesterone Receptor	Hormone Receptors	LOW RISK	Growth Factor Receptor	0	LOW RISK
Estrogene Receptor			Growth Factor Receptor	0	LOW RISK
NR3C4-A			Nucleous receptor group III Class 4(androg...	0	LOW RISK
NR3C4-B			Nucleous receptor group III Class 4(androg...	0	LOW RISK

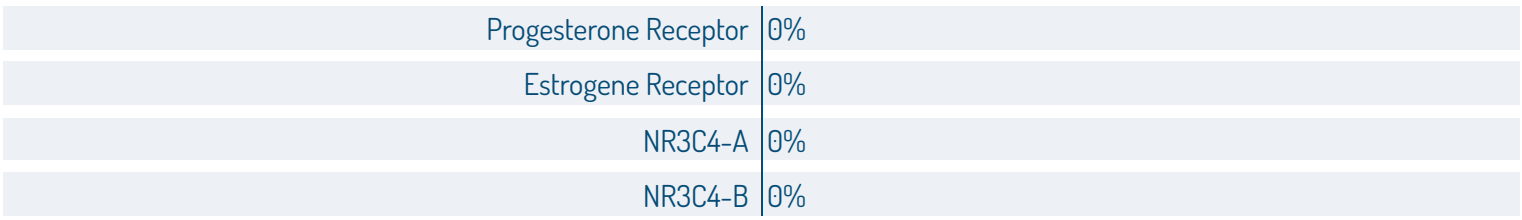
Growth Factor Receptor



Signal Transduction Pathway



Hormone Receptors

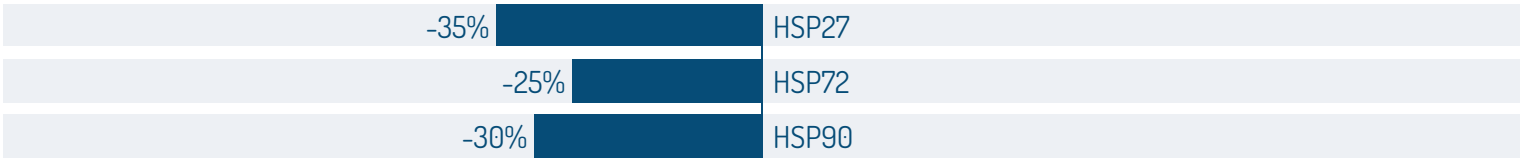


SELF REPAIR - RESISTANCE

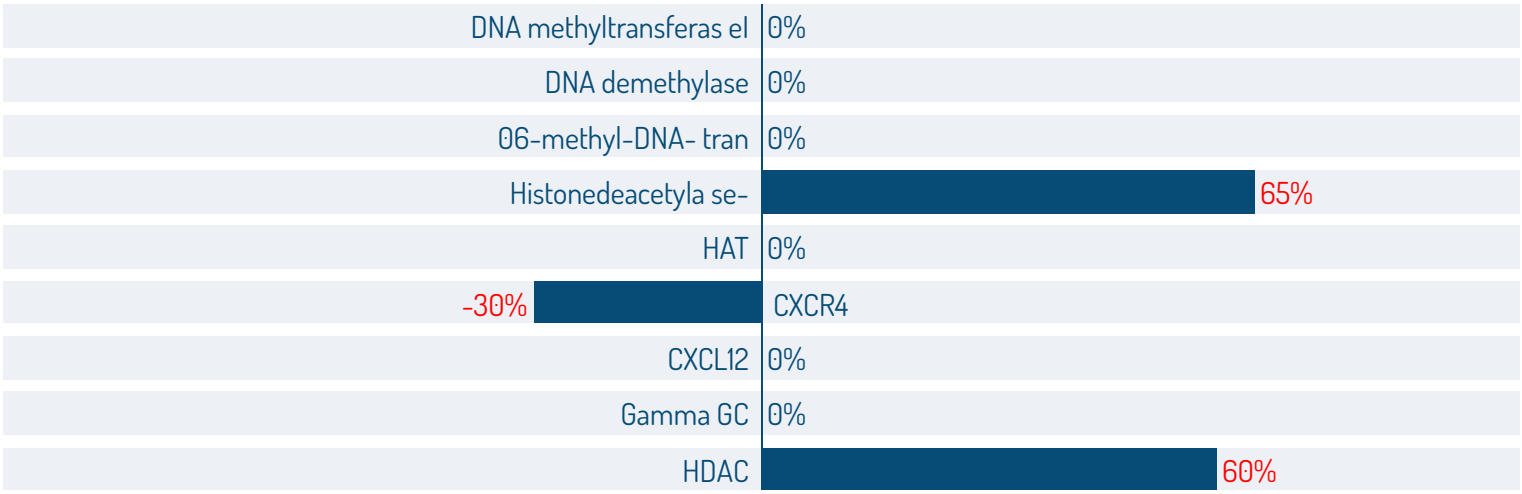
NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
TGF-b	Signal transduction	LOW RISK	Tumour Growth	0	LOW RISK
HSP27	Radiotherapy / Hyperthermia sensitivity	SENSITIVE	Heat Shock Protein	-35	SENSITIVE
HSP72			Heat Shock Protein	-25	SENSITIVE
HSP90			Heat Shock Protein	-30	SENSITIVE
DNA methyltransferas el	Resistant Phenotype Markers	HIGH RISK	DNA methylation	0	LOW RISK
DNA demethylase			DNA methylation	0	LOW RISK
06-methyl-DNA- tran			DNA methylation	0	LOW RISK
Histonedeacetyla se-			DNA coiling (nucleosome)	65	HIGH RISK
HAT			Histone acetyl transferase	0	LOW RISK
CXCR4			Resistant Phenotype	-30	HIGH RISK
CXCL12			Resistant Phenotype	0	LOW RISK
Gamma GC			Resist to alkylating drugs	0	LOW RISK
HDAC			Histone deacetylase	60	HIGH RISK
PARP (1-17)	DNA Repair Related Gene	HIGH RISK	DNA repair mechanism	40	HIGH RISK

Signal transduction

Radiotherapy / Hyperthermia sensitivity



Resistant Phenotype Markers

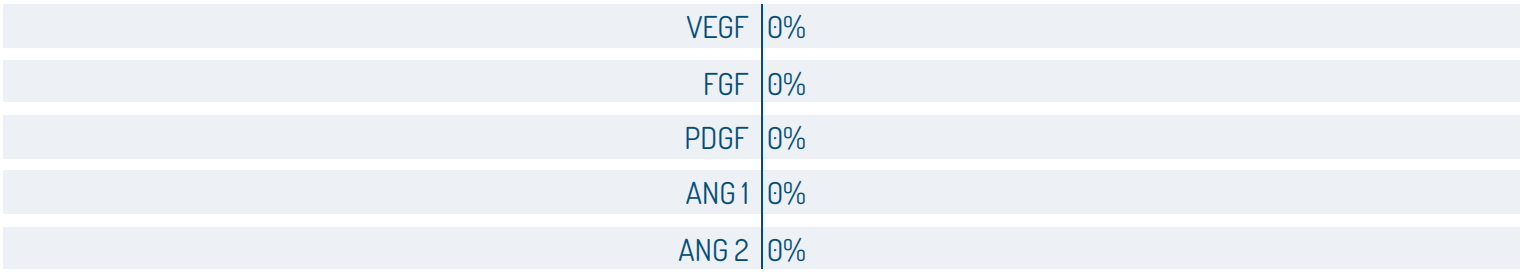


DNA Repair Related Gene

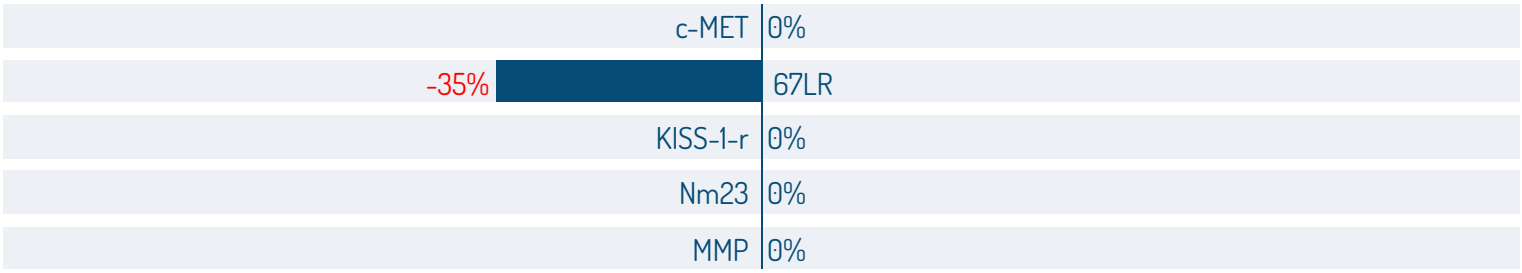
ANGIOGENESIS - METASTASES

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	0	LOW RISK
67LR			67 Laminin receptor	-35	HIGH RISK
KISS-1-r			Metastases regulator	0	LOW RISK
Nm23			Metastases regulator	0	LOW RISK
MMP			Metastases	0	LOW RISK

Angiogenesis



Migration invasion



CELL CYCLE REGULATION & IMMORTALIZATION / APOPTOSIS

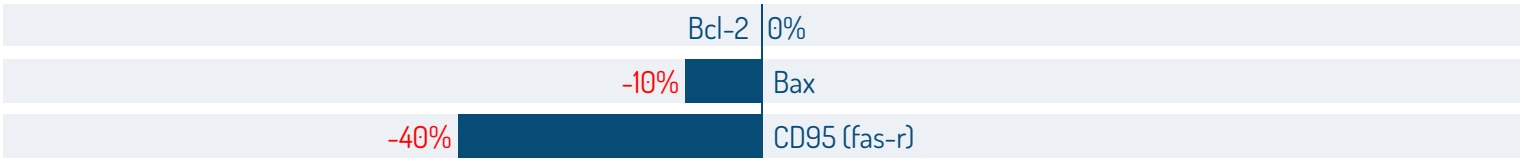
NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
E2F1	Increase Protein Synthesis	LOW RISK	Transcr. Fact of TS & topo I	0	LOW RISK
CDC6	Rapid Cell Cycle	LOW RISK	Initiation of DNA replication	0	LOW RISK
h-TERT	Immortalization	LOW RISK	M2 crisis- aggressive phen	0	LOW RISK
Bcl-2	Regulation of Apoptosis	HIGH RISK	Apoptosis	0	LOW RISK
Bax			Apoptosis	-10	HIGH RISK
CD95 (fas-r)			Apoptosis related receptor	-40	HIGH RISK
p27	Cell Cycle Rate	HIGH RISK	Cell arrest (G0)	-15	HIGH RISK
p53			Cell cycle regulator	45	HIGH RISK
p16			Apoptosis	0	LOW RISK
CDK4/6	Cell cycle regulator	LOW RISK	Cyclin-dependent kinase	0	LOW RISK

Increase Protein Synthesis

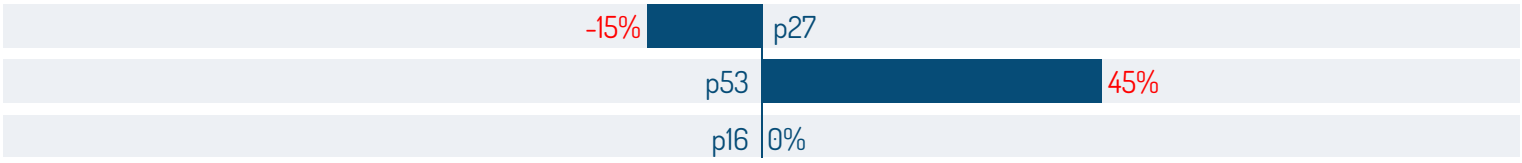
Rapid Cell Cycle

Immortalization

Regulation of Apoptosis



Cell Cycle Rate

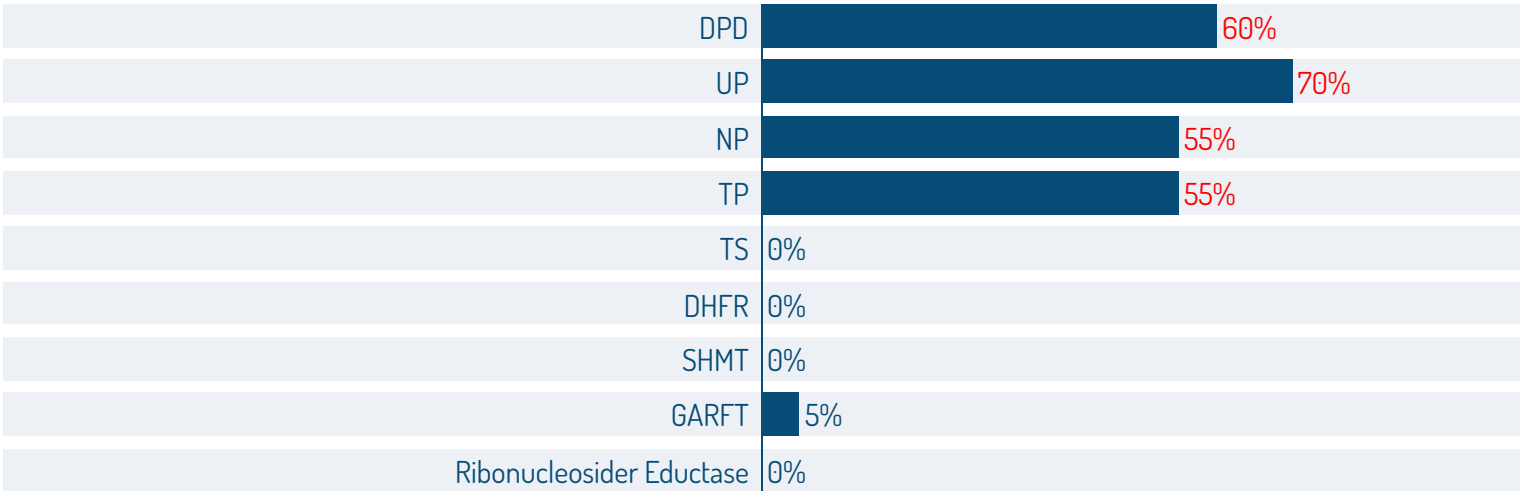


Cell cycle regulator

DRUG METABOLISMS & TARGETS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
DPD	Nucleoside Import Transformation	HIGH RISK	Resist to 5FU	60	HIGH RISK
UP			Resist to 5FU	70	HIGH RISK
NP			Resist topyrim. Antagonist	55	HIGH RISK
TP			Resist to 5FU	55	HIGH RISK
TS			Rapid cell cycle (THFA)	0	LOW RISK
DHFR			Rapid cell cycle (THFA)	0	LOW RISK
SHMT			Rapid cell cycle (THFA)	0	LOW RISK
GARFT			Rapid cell cycle (THFA)	5	LOW RISK
Ribonucleosider Eductase			DNA synthesis	0	LOW RISK
CES1&2 (carboxyesterase)	Activation of Camptothecin	HIGH RISK	Resist to camptothecin	40	HIGH RISK
CypB1	Xenobiotic	LOW RISK	Xenobiotic metabolism	0	LOW RISK
ERCC1	DNA Repair Related Gene	HIGH RISK	DNA repair mechanism	50	HIGH RISK
RRM1			Nucleotide polymerizations	0	LOW RISK

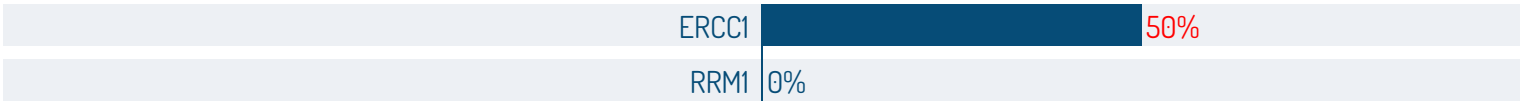
Nucleoside Import Transformation



Activation of Camptothecin

Xenobiotic

DNA Repair Related Gene



MARKERS

NAME	FUNCTION	CLINICAL RISK	RELATED	RESULTS %	OUTCOME
CD33	Immune system regulation	LOW RISK	Myeloid Cell origin	0	LOW RISK
CD52	Immune system regulation	LOW RISK	Leukaemia Marker	0	LOW 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 (2.8 cells/ml)	0	LOW RISK
PD-L1	Immune system regulation	LOW RISK	Immunoregulatory Factor	0	LOW RISK
PD 1	Immune system regulation	LOW RISK	Immunoregulatory Factor	0	LOW RISK
PD-L2	Immune system regulation	LOW RISK	Immunoregulatory Factor	0	LOW RISK

Immune system regulation

CD33	0%

Immune system regulation

CD52	0%

Development and differentiation of B cells into plasma cells

CD20	0%

Cell–cell adhesion

EpCAM (EpCAm+ve)	0%

Immune system regulation

PD-L1	0%

Immune system regulation

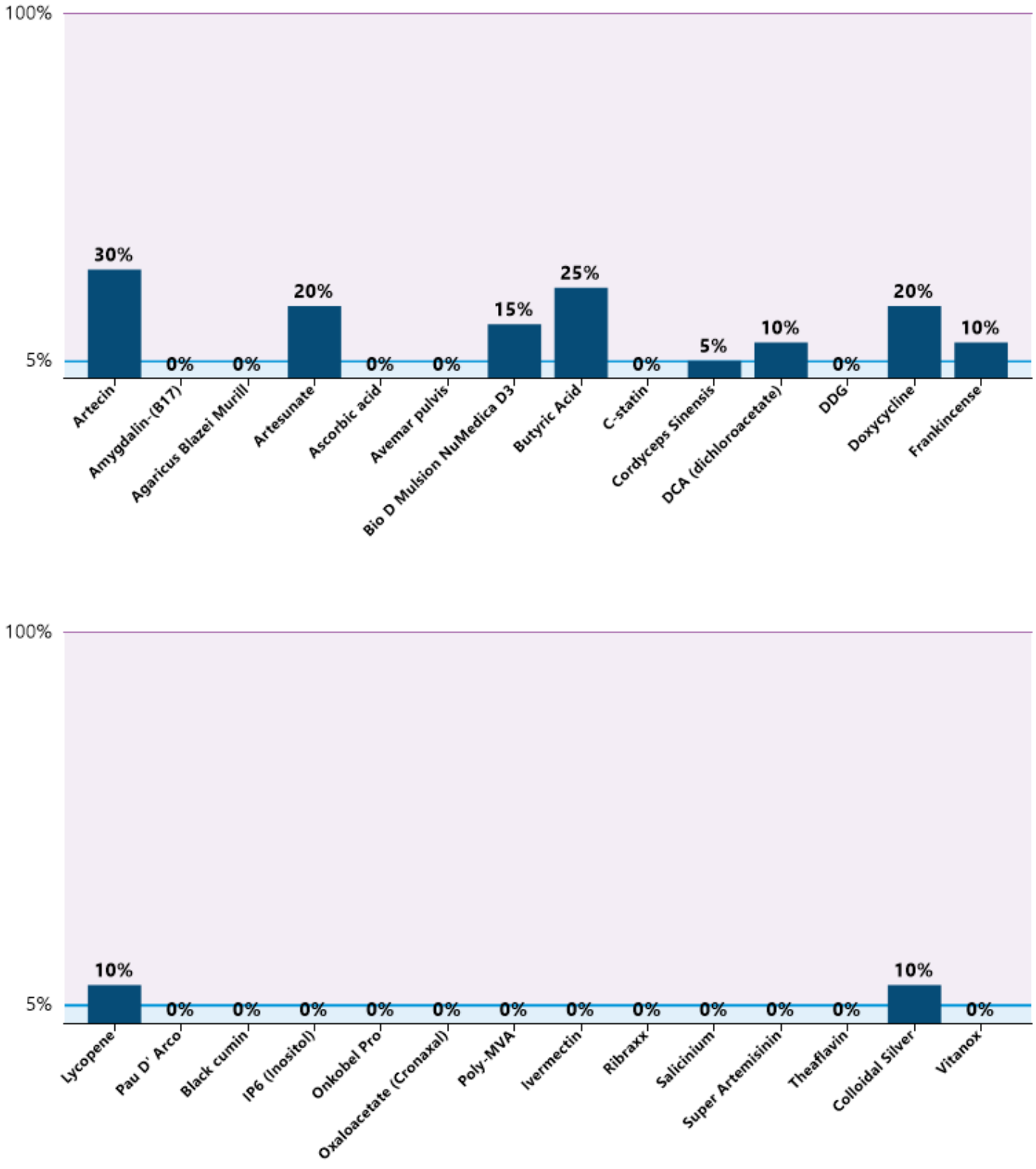
PD 1	0%

Immune system regulation

PD-L2	0%

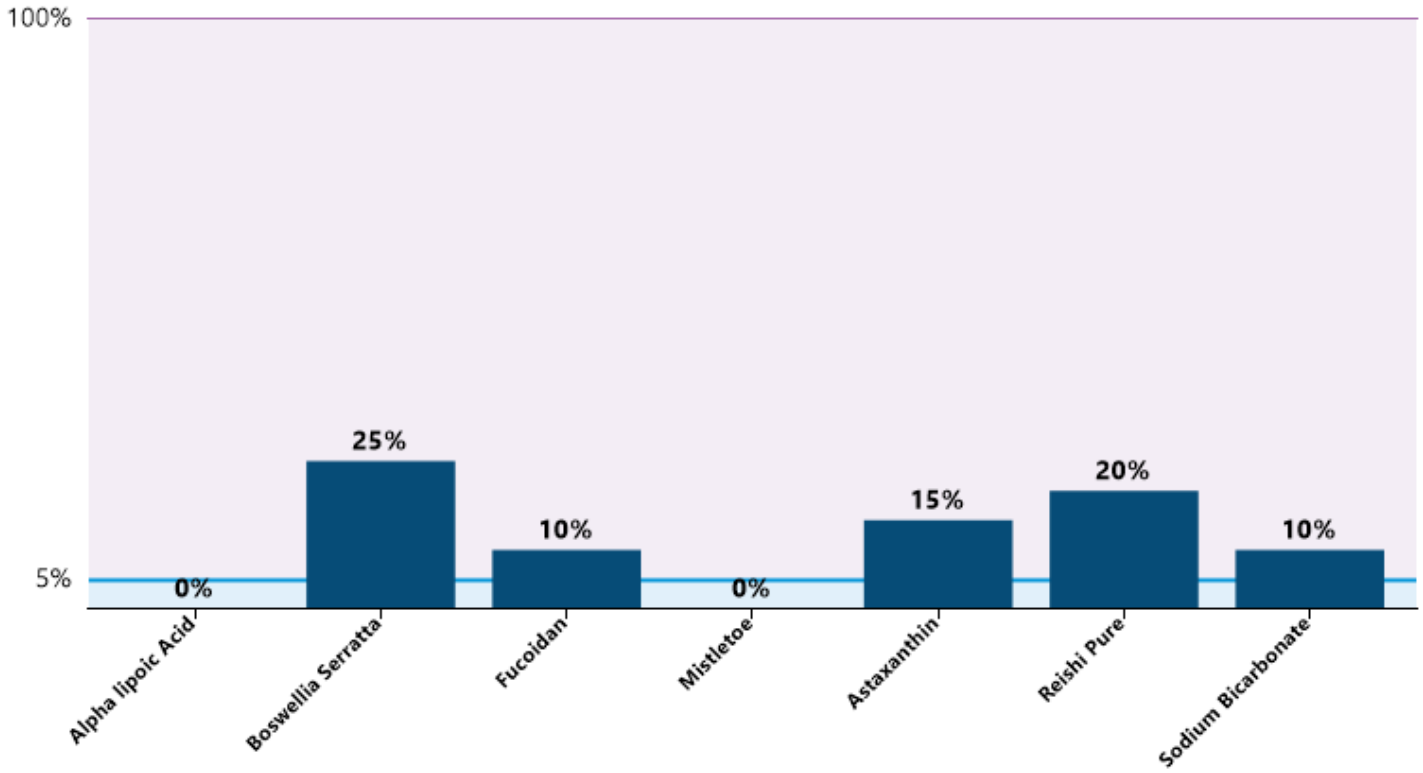
No sensitivity Sensitivity

Class I (Cytotoxic Agents)

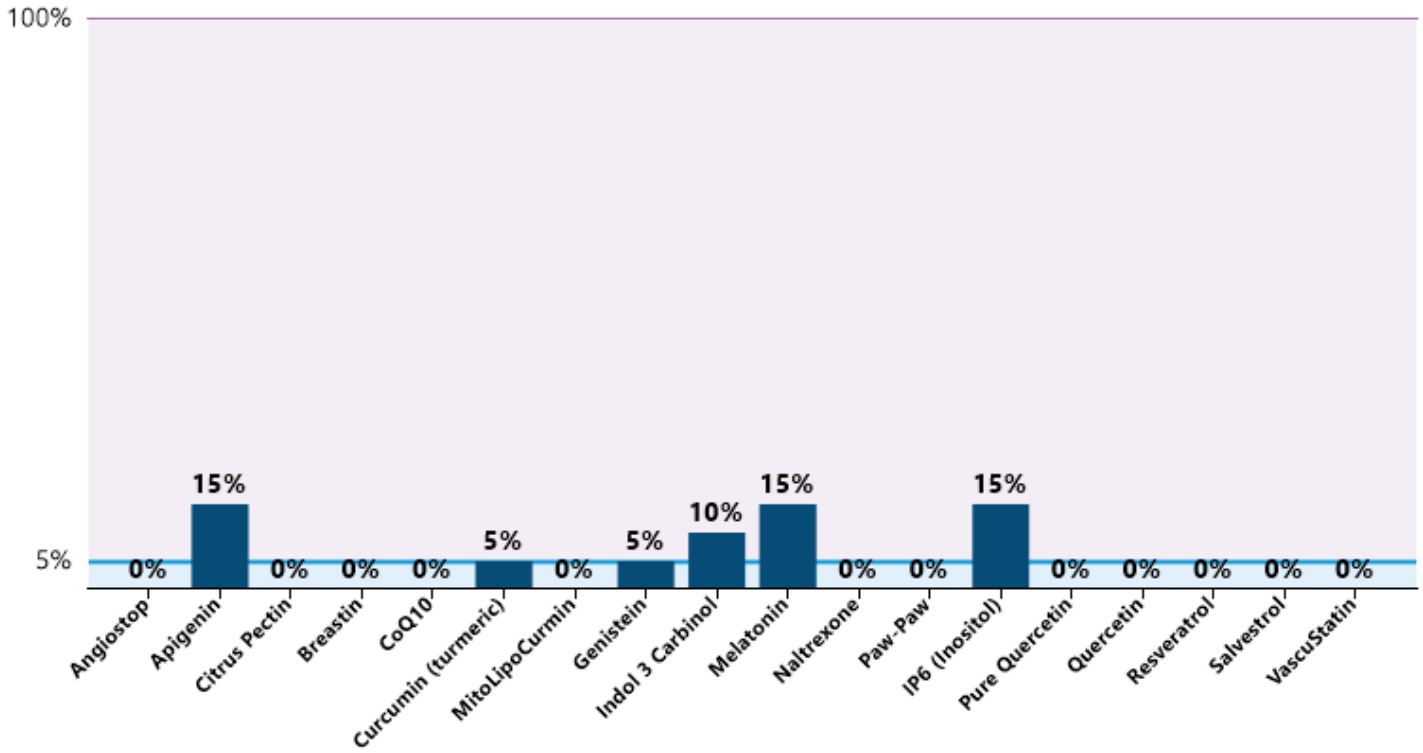


No sensitivity Sensitivity

Class II (Immunostimulants / Immunomodulators)

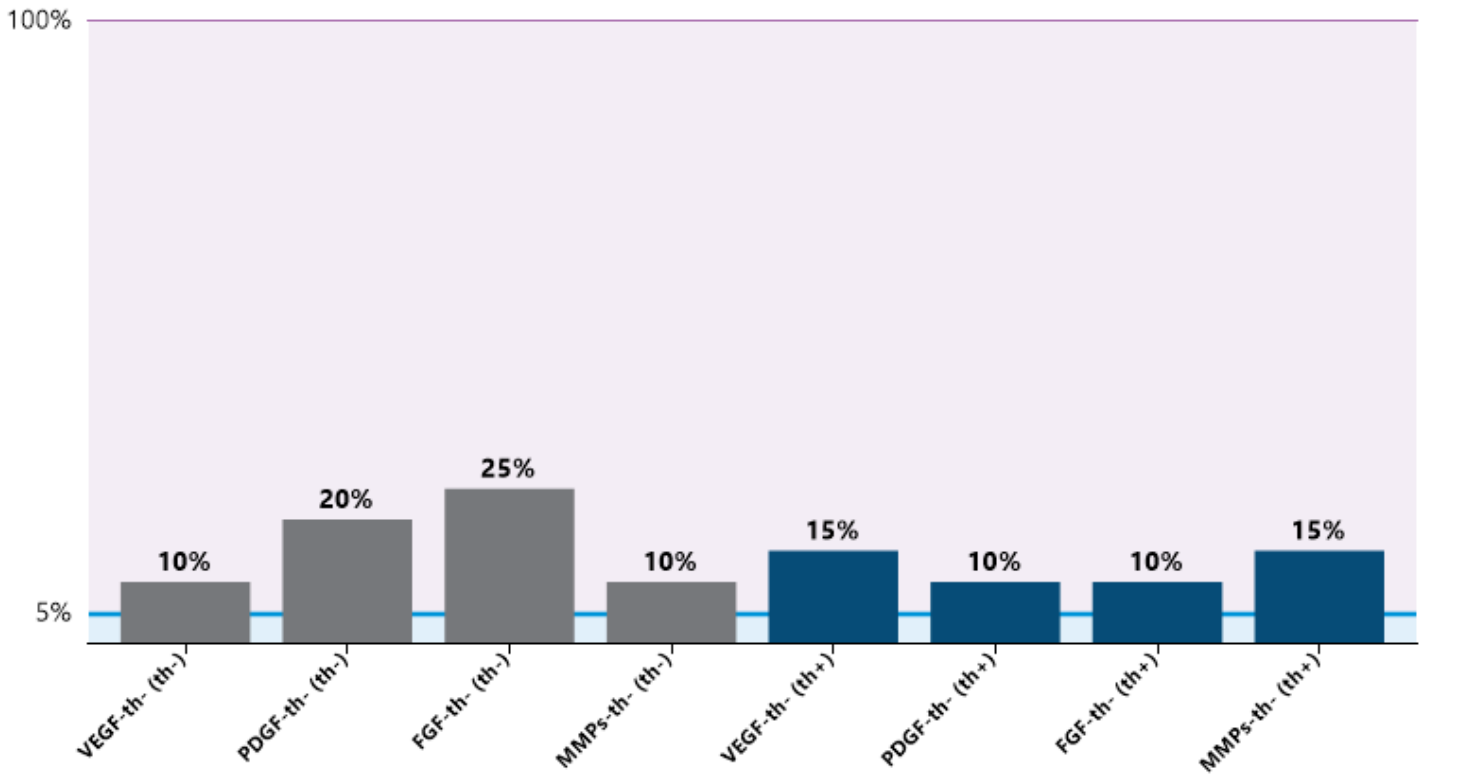


Class III (PK Inhibitors)



No sensitivity Sensitivity

Malignant Cells - Thalidomide



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

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 Papasotiriou 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	PTGS2	Tumour Growth
	5-LOX	ALOX5	Tumour Growth
Proteasome inhibitors	NFkB	NFKB1	Transcription Factor
	IkB (a,b,c)	NFKBIA/B	NFkB Inhibitors
Proto-Oncogene	ALK	ALK	Acute Leukemia kinase
	EML-4-ALK	EML4-ALK	Fused EML-ALK
	NPM-ALK	NPM-ALK	Fused NPM-ALK
	RET	RET	Proto-Oncogene
Growth Factor Receptor	SS-r	SSTR3/5	Somatostatin receptor
	CD 117 (c-kit)	KIT	Proliferate growth factor receptor
	IGF-r 1	IGF1R	Insulin like growth factor receptor
	IGF-r 2	IGF2R	Insulin like growth factor receptor
	EGF	EGF	Tumour Growth
	C-erb-B2	ERBB2	Receptor tyrosine-protein kinase
	C-erb-B1	EGFR	Epithermal Growth Factor Recept...
Signal Transduction Pathway	JAK1/2	JAK1/2	Single transduction pathway
	c-Jun	FOS	Proto-Oncogene
	c-Fos	JUN	Proto-Oncogene
	Ras-Raf-MEK-ERK	ERK1/2	Single transduction pathway
	mTOR	MTOR	Single transduction pathway
Hormone Receptors	Progesterone-Receptor	PGR	Growth Factor Receptor
	Estrogen-Receptor	ESR1	Growth Factor Receptor
	NR3C4-A	NR3C4A	Androgen Receptor
	NR3C4-B	NR3C4B	Androgen Receptor

SELF REPAIR - RESISTANCE

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

a. Lin D, Shen L, Luo M, Zhang K, Li J, Yang Q, Zhu F, Zhou D, Zheng S, Chen Y, Zhou J. Circulating tumor cells: biology and clinical significance. Signal Transduct Target Ther. 2021 Nov 22;6(1):404. doi: 10.1038/s41392-021-00817-8. PMID: 34803167; PMCID: PMC8606574.

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