

Onconomics RGCC™

Results



Results Analysis Report



The sample that was sent to us for analysis was a sample of 20ml Blood that contains anti-coagulant, and packed with an ice pack.

Laboratory Process

Isolation of the malignant cells using flow cytometry and negative selection (isolated 4.4 cells/7.5 ml, SD +/- 0.3 cells). The isolated cells were expanded and they were split 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.

The following were defined

Expression rates of the following clinical relevant genes

Related with cell cycle regulation

p53, p21, p16, DHFR, TS, SHMT

Related with drug targets

Topo I & II, TS, DHFR, ribonucleotide reductase etc.

Related with signal transduction pathway

IGFr, EGFr, PDGFr, etc.

Related with epigenetic aberration

Dnmt1, DNA demethylase, etc.

Related with angiogenesis

VEGF-r, FGFr, PDGFr

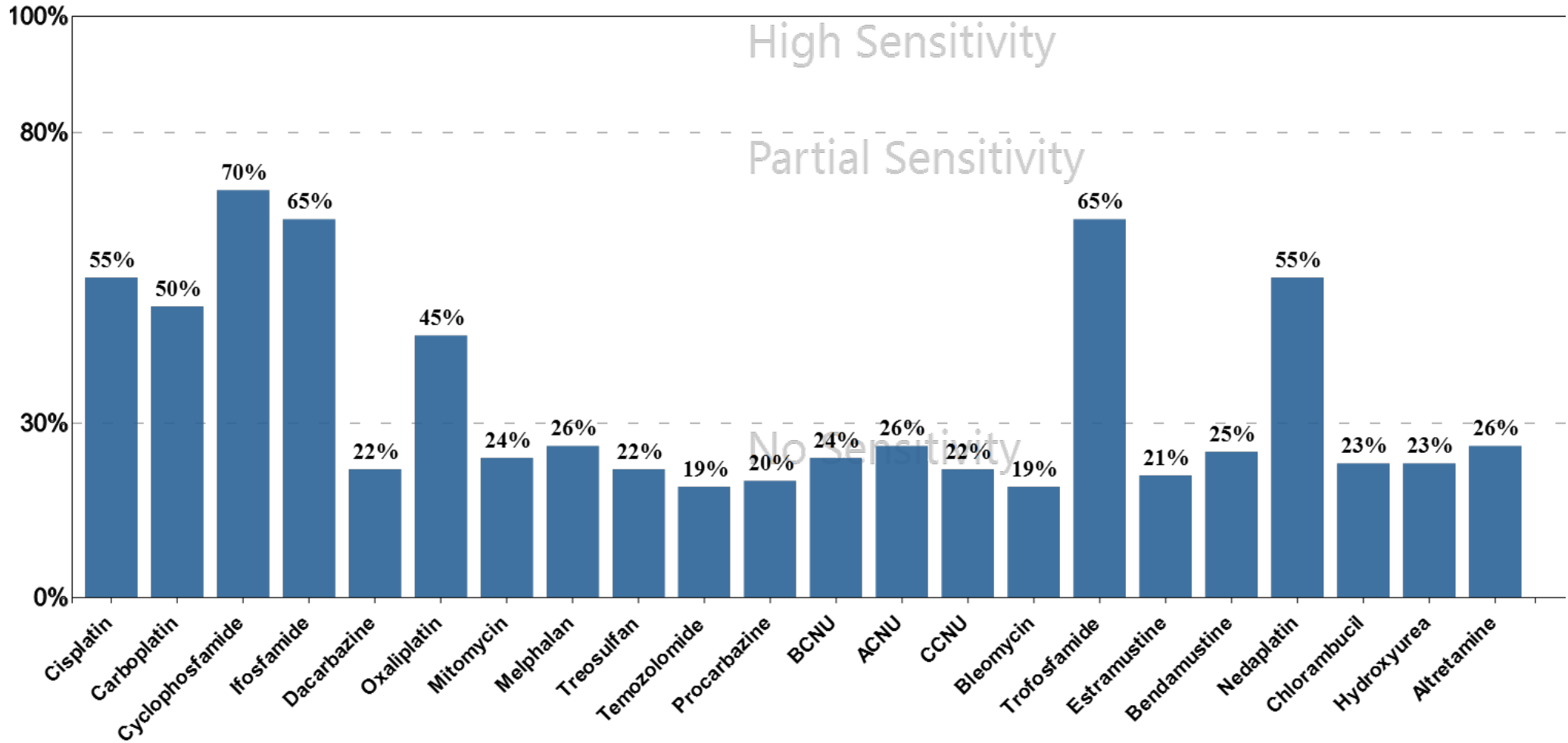
Related with growth signal

c-erb-B1, c-erb-B2, bar-abl, etc.

Related with repair after physical application (radiation, hyperthermia)

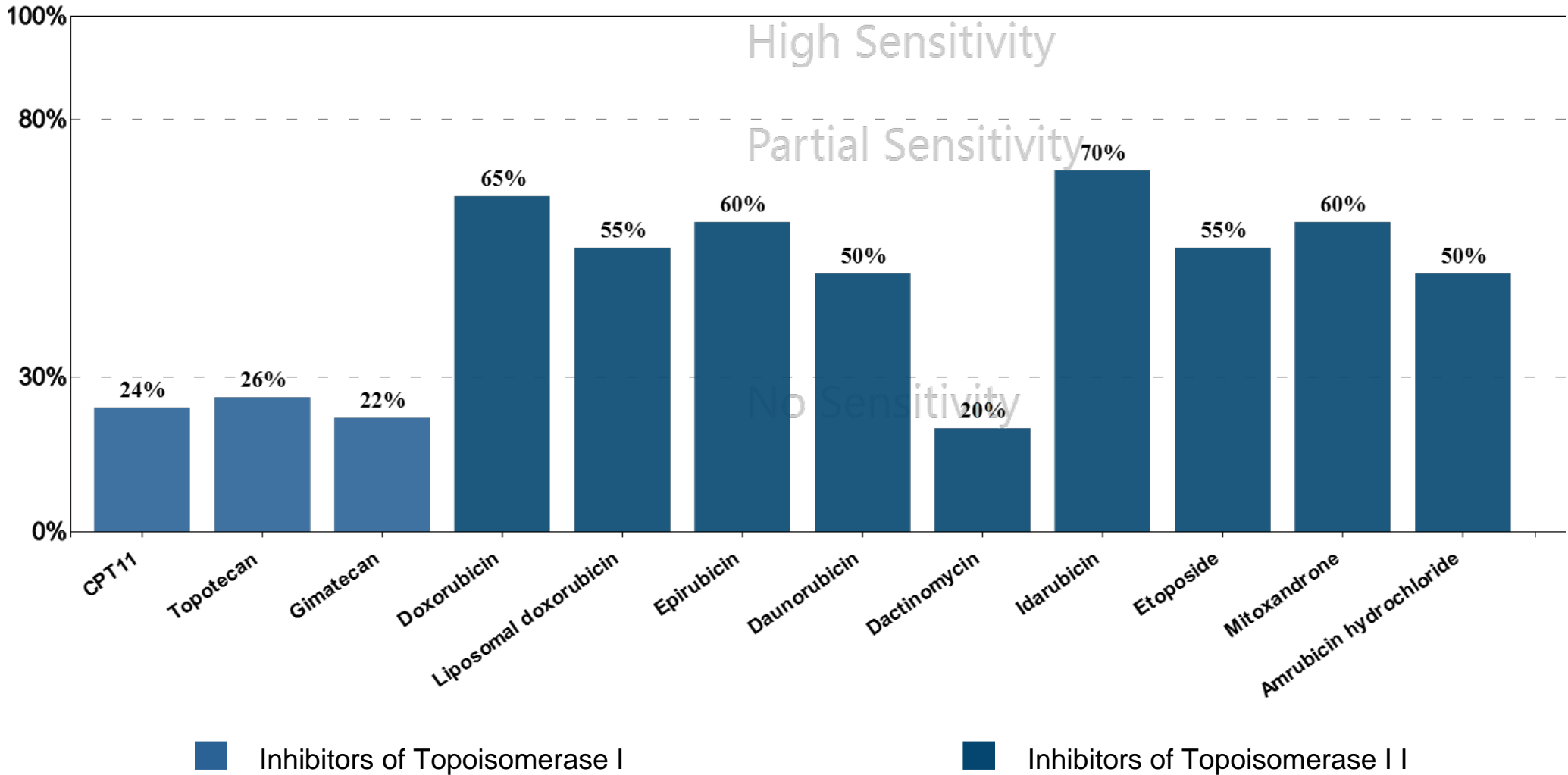
HSP27, HSP70, HSP90, HIF1a, etc.

Alkylating Agents



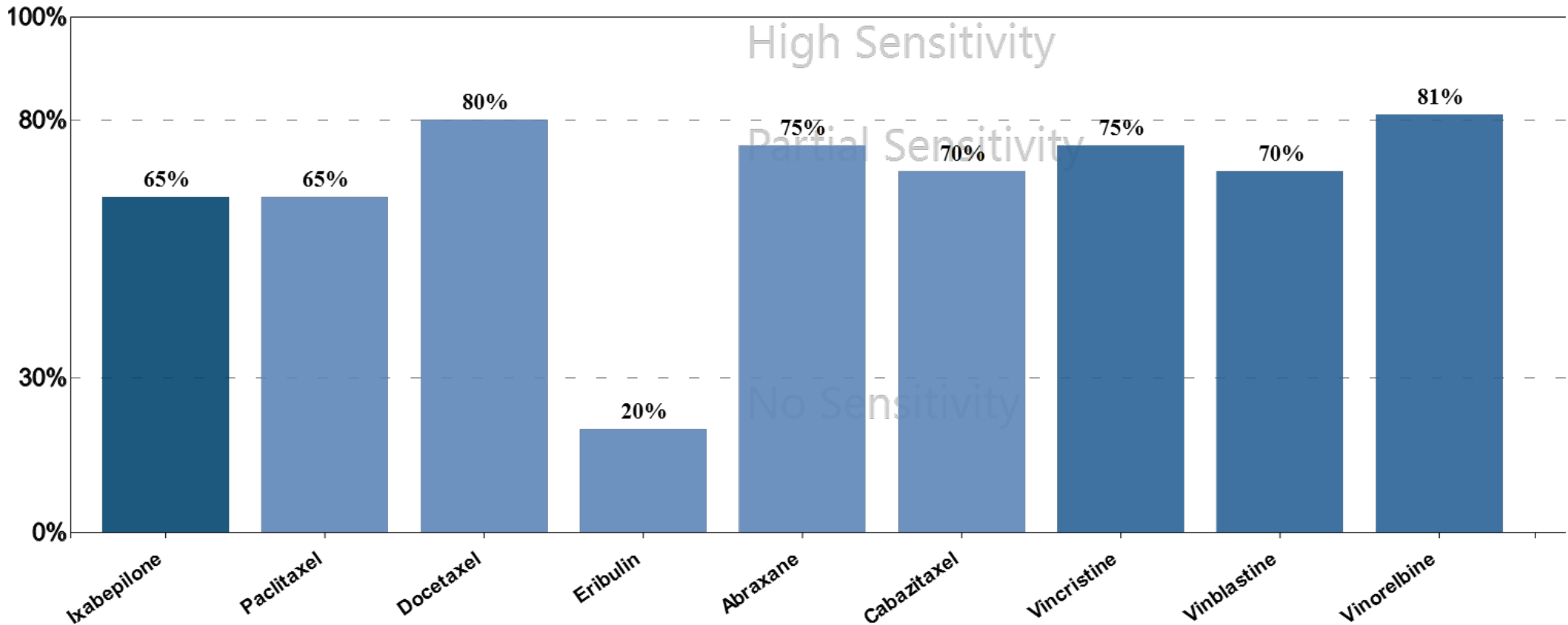
High Sensitivity:

Inhibitors of Topoisomerase I & II



High Sensitivity:

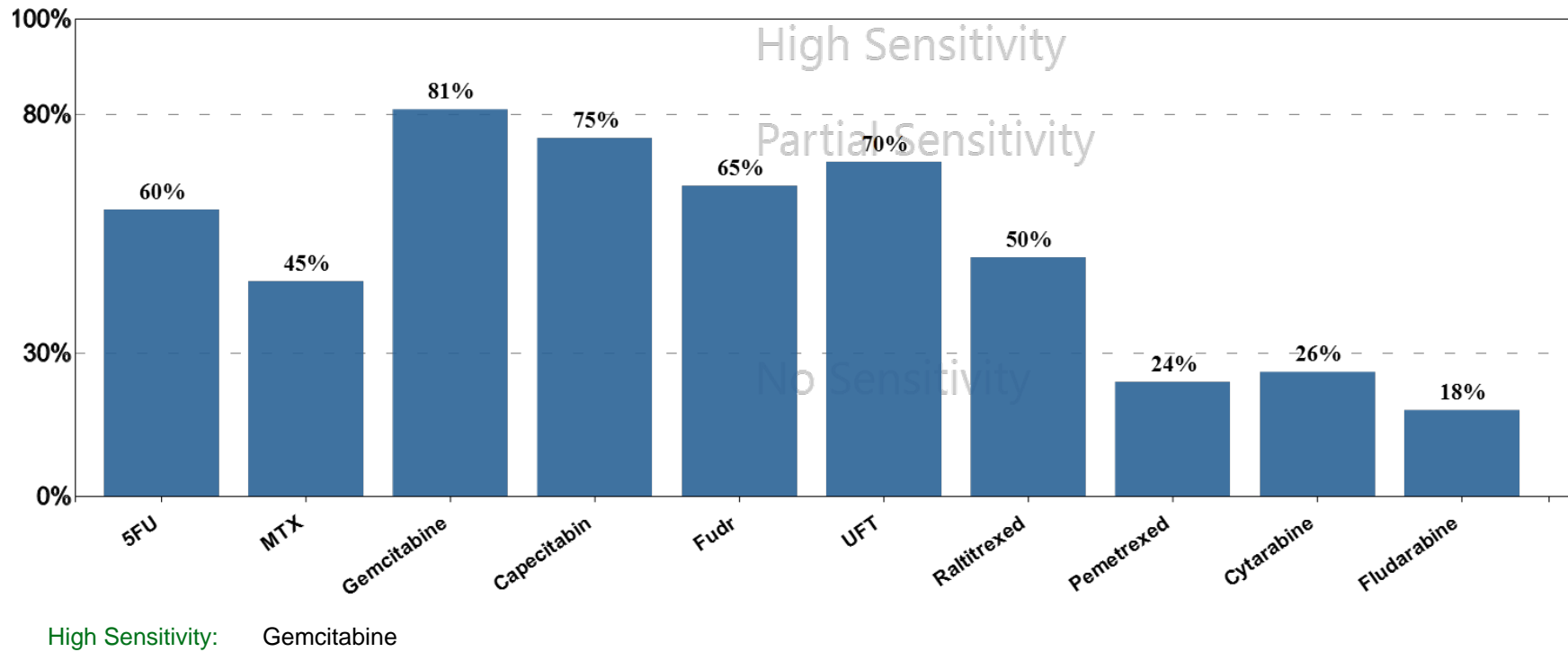
Epothilones & Nucleus Spindle Stabilizer I & II



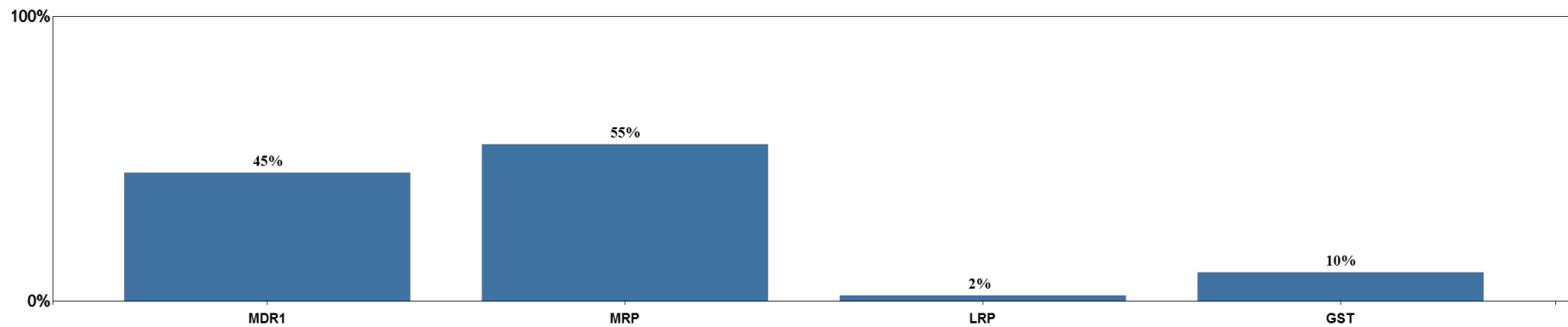
Epothilones
 Nucleus Spindle Stabilizer I
 Nucleus Spindle Stabilizer II

High Sensitivity: Docetaxel, Vinorelbine

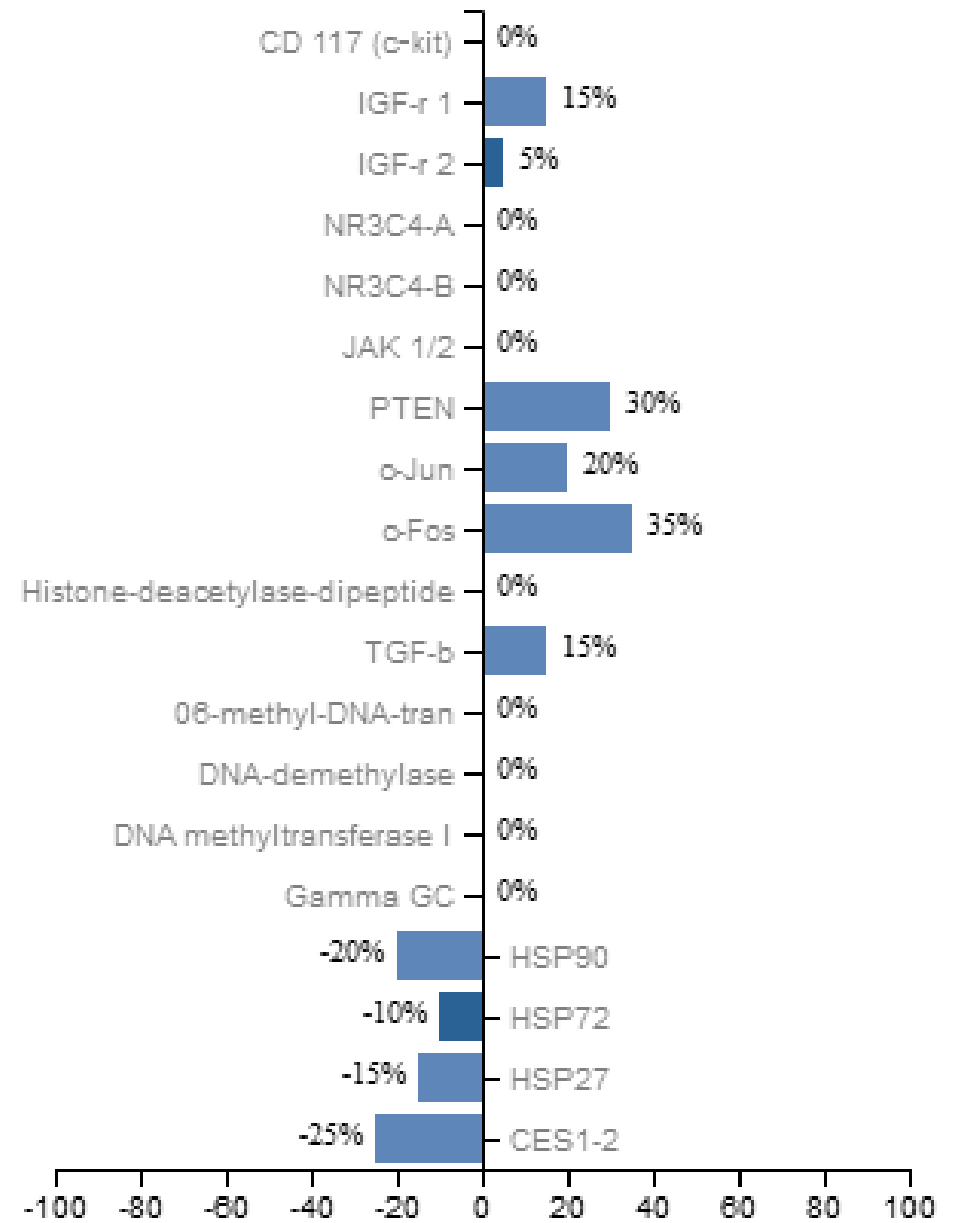
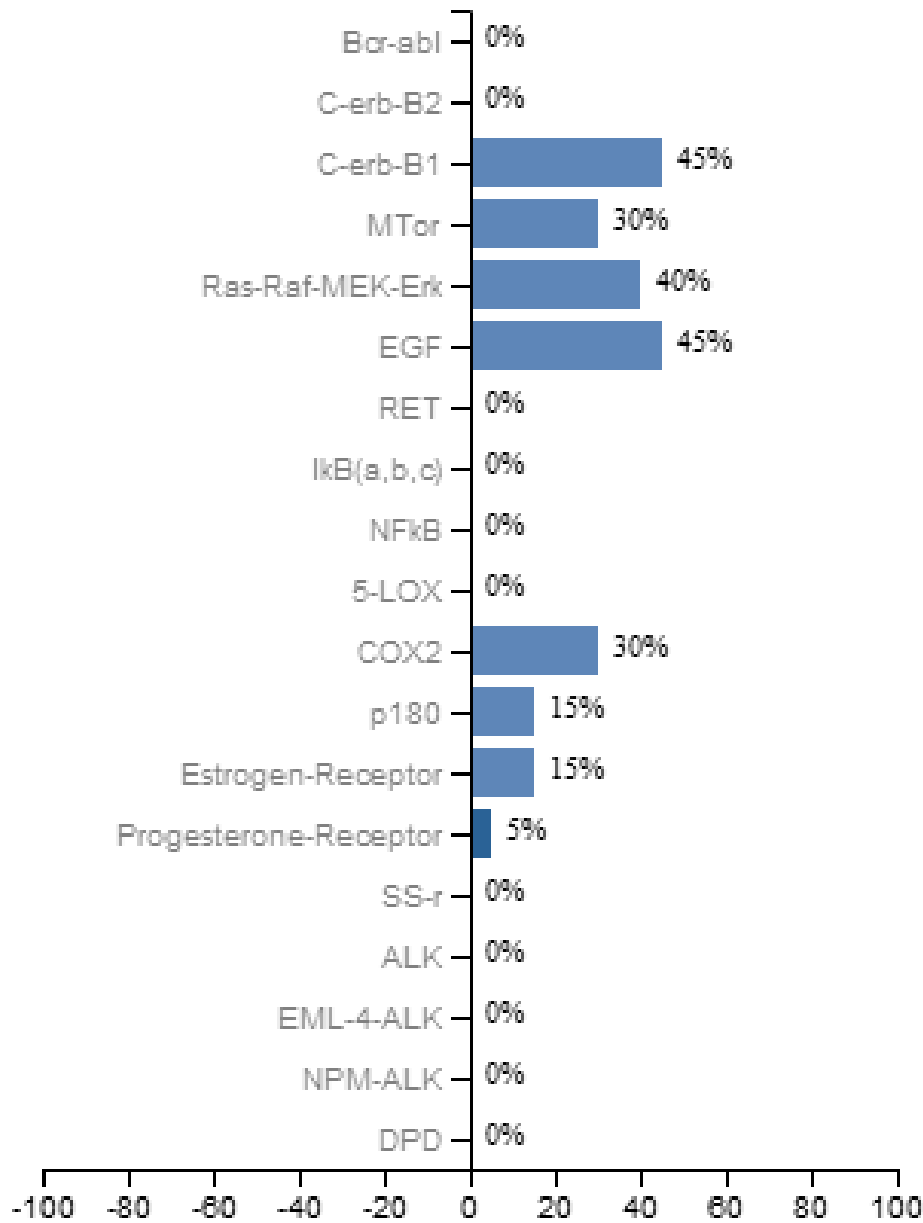
Nucleoside Analogues



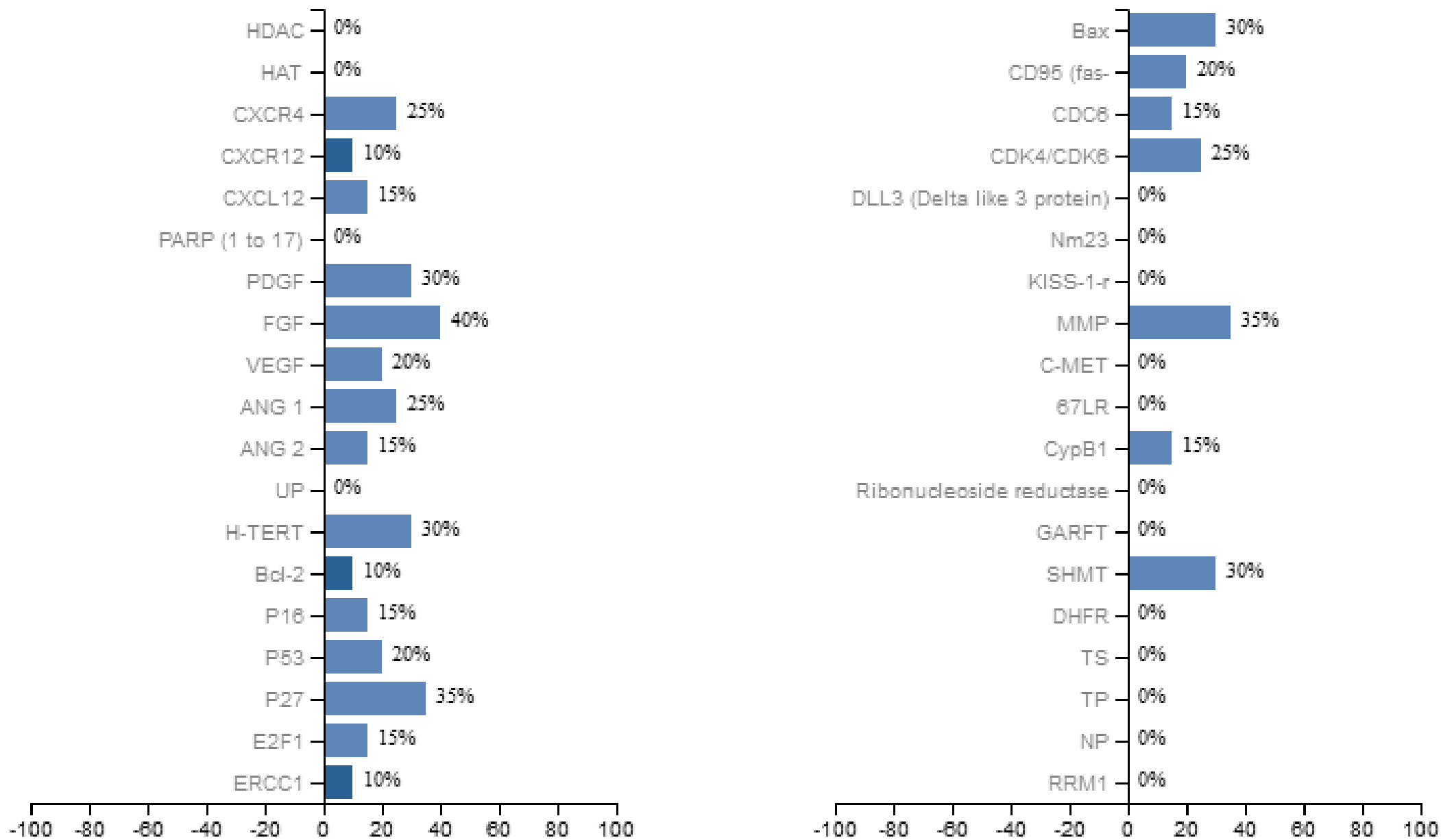
Resistance Factors



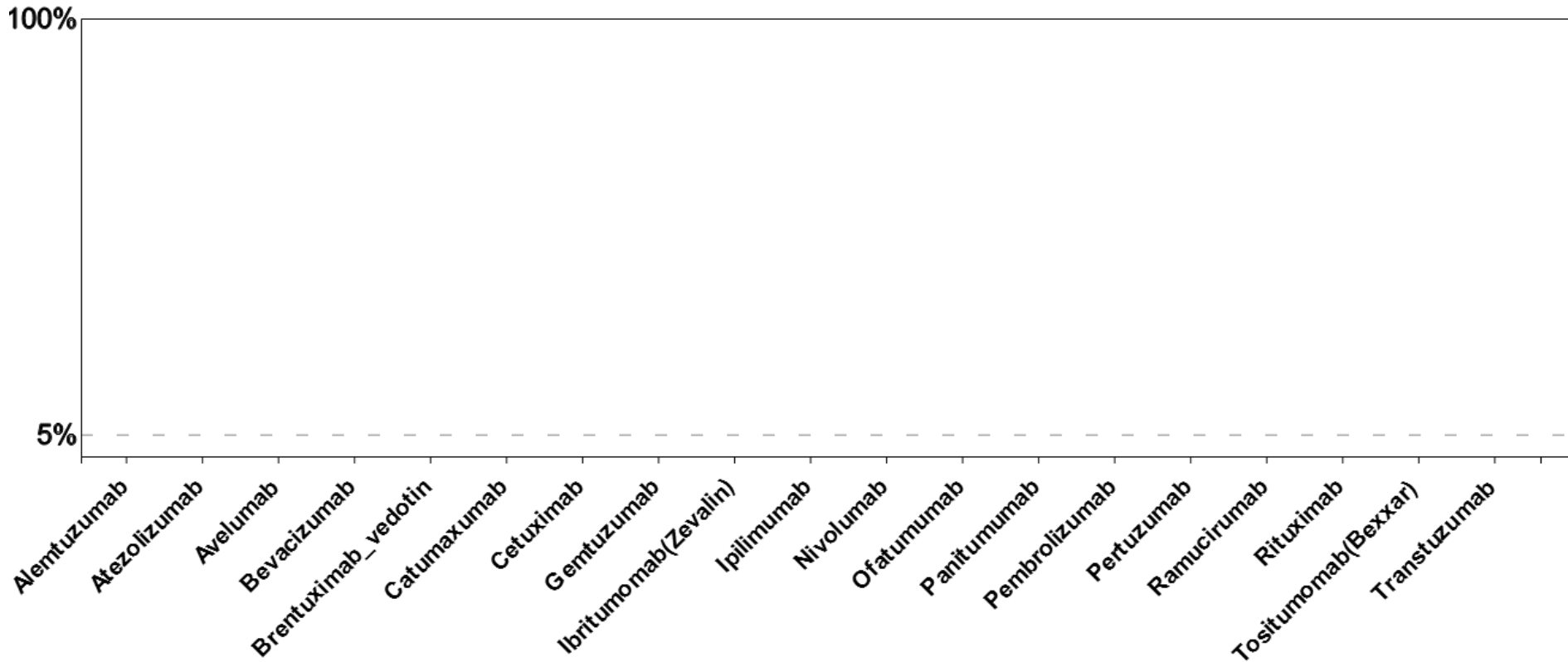
Tumor Related Genes I



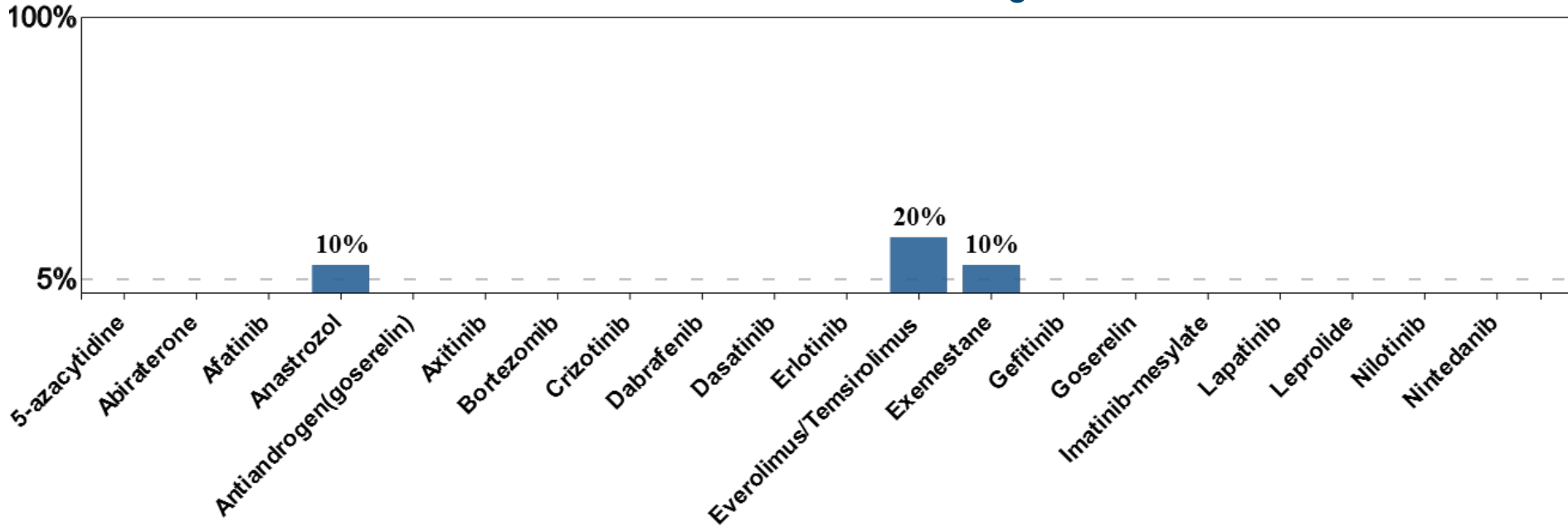
Tumor Related Genes II



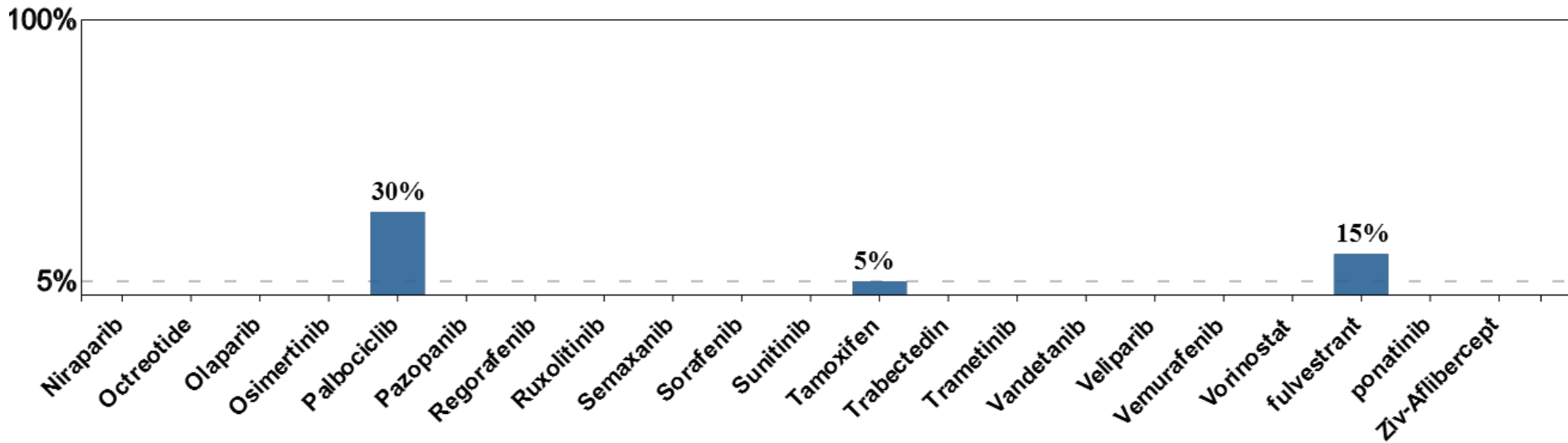
Moab -Monoclonal Antibodies



SMW - Small Molecular weight molecule



SMW - Small Molecular weight molecule



GROWTH FACTORS PROLIFERATION STIMULI

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Preprotein for Cellular stress	HIGH RISK	p180	Tyrosin kinase growth f.	15	HIGH RISK
Fusion Protein	LOW RISK	Bcr-abl	Resist phenotype	Normal	LOW RISK
Repair Related Gene	HIGH RISK	PTEN	Tumor Suppressor Gene	30	HIGH RISK
Eicosanoid related protein	HIGH RISK	COX2	Tumour Growth	30	HIGH RISK
		5-LOX	Tumour Growth	Normal	LOW RISK
Proteasome inhibitors	LOW RISK	NFkB	Transcription fact	Normal	LOW RISK
		IkB(a,b,c)	Inhibitor of NFkB	Normal	LOW RISK
Proto-Oncogene	LOW RISK	ALK	Acute Leukemia kinase	Normal	LOW RISK
		EML-4-ALK	Fusion EML with ALK	Normal	LOW RISK
		NPM-ALK	Fusion NPM with ALK	Normal	LOW RISK
		RET	Proto-oncogene	Normal	LOW RISK

GROWTH FACTORS PROLIFERATION STIMULI

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Growth Factor Receptor	HIGH RISK	SS-r	Somatostatin receptor	Normal	LOW RISK
		CD 117(c-kit)	Proliferate growth factor receptor	Normal	LOW RISK
		IGF-r 1	Insulin like growth factor receptor	15	HIGH RISK
		IGF-r-2	Insulin like growth factor receptor	Normal	LOW RISK
		EGF	Tumour Growth	45	HIGH RISK
		c-erb-B1	Her1	45	HIGH RISK
		c-erb-B2	Her/neu2	Normal	LOW RISK
Signal transduction pathway	HIGH RISK	JAK 1/2	Single transduction pathway	Normal	LOW RISK
		c-Jun	Proto-Oncogene	20	HIGH RISK
		c-Fos	Proto-Oncogene	35	HIGH RISK
		Ras/Raf/MEK/Er k	Transduction pathway	40	HIGH RISK
		mTOR	Transduction pathway	30	HIGH RISK
Hormone Receptors	HIGH RISK	Progesterone Receptor	Growth Factor receptor	Normal	LOW RISK
		Estrogene Receptor	Growth Factor receptor	15	HIGH RISK
		NR3C4-A	Nucleous receptor group III Class 4 (androgen receptor A)	Normal	LOW RISK
		NR3C4-B	Nucleous receptor group III Class 4 (androgen receptor B)	Normal	LOW RISK

SELF REPAIR - RESISTANCE

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Signal transduction	HIGH RISK	TGF-b	Tumour Growth	15	HIGH RISK
Radiotherapy / Hyperthermia sensitivity	SENSITIVE	HSP27	Heat Shock Protein	-15	SENSITIVE
		HSP72	Heat Shock Protein	-10	SENSITIVE
		HSP90	Heat Shock Protein	-20	SENSITIVE
Resistant Phenotype Markers	HIGH RISK	DNA methyltransferas el	DNA methylation	Normal	LOW RISK
		DNA demethylase	DNA methylation	Normal	LOW RISK
		06-methyl-DNA- tran.	DNA methylation	Normal	LOW RISK
		Histonedeacetyla se-	DNA coiling (nucleosome)	Normal	LOW RISK
		HAT	Histone acetyl transferase	Normal	LOW RISK
		CXCR4	Resistant Phenotype	25	HIGH RISK
		CXCR12	Resistant Phenotype	10	HIGH RISK
		CXCL12	Resistant Phenotype	15	HIGH RISK
		Gamma GC	Resist to alkylating drug	Normal	LOW RISK
HDAC	Histone deacetylase	Normal	LOW RISK		

ANGIOGENESIS

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Angiogenesis	HIGH RISK	VEGF	Angiogenesis	20	HIGH RISK
		FGF	Angiogenesis	40	HIGH RISK
		PDGF	Angiogenesis	30	HIGH RISK
		ANG 1	Angiogenin I	25	HIGH RISK
		ANG 2	Angiogenin II	15	HIGH RISK

CELL CYCLE REGULATION & IMMORTALIZATION / APOPTOSIS

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Increase protein Synthesis	HIGH RISK	E2F1	Transcr. Fact of TS & topo I	15	HIGH RISK
Rapid Cell Cycle	HIGH RISK	CDC6	Initiation of DNA replication	15	HIGH RISK
Immortalization	HIGH RISK	h-TERT	M2 crisis- aggressive phen.	30	HIGH RISK
Regulation of apoptosis	HIGH RISK	Bcl-2	Apoptosis	10	HIGH RISK
		Bax	Apoptosis	30	HIGH RISK
		CD95 (fas-r)	Apoptosis related receptor	20	HIGH RISK
Cell cycle Rate	HIGH RISK	p27	Cell arrest (G0)	35	HIGH RISK
		p53	Cell cycle regulator	20	HIGH RISK
		p16	Apoptosis	15	HIGH RISK

ANGIOGENESIS - METASTASES

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Migration invasion	HIGH RISK	c-MET	Mesenchymal to epithelial transition	Normal	LOW RISK
		67LR	67 Laminin receptor	Normal	LOW RISK
		KISS-1-r	Metastases regulator	Normal	LOW RISK
		Nm23	Metastases regulator	Normal	LOW RISK
		MMP	Metastases	35	HIGH RISK

DRUG METABOLISMS & TARGETS

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Nucleoside Import transformation	HIGH RISK	DPD	Resist to 5FU	Normal	LOW RISK
		UP	Resist to 5FU	Normal	LOW RISK
		NP	Resist topyrim. Antagonist	Normal	LOW RISK
		TP	Resist to 5FU	Normal	LOW RISK
		TS	Rapid cell cycle (THFA)	Normal	LOW RISK
		DHFR	Rapid cell cycle (THFA)	Normal	LOW RISK
		SHMT	Rapid cell cycle (THFA)	30	HIGH RISK
		GARFT	Rapid cell cycle(THFA)	Normal	LOW RISK
		Ribonucleosider eductase	DNA synthesis	Normal	LOW RISK

DRUG METABOLISMS & TARGETS

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Activation of camptothecin	HIGH RISK	CES1&2 (carboxyesterase)	Resist to camptothecin	-25	HIGH RISK
Xenobiotic	HIGH RISK	CypB1	Xenobiotic metabolism	15	HIGH RISK
DNA repair related gene	HIGH RISK	ERCC1	DNA repair mechanism	10	HIGH RISK
		RRM1	Nucleotide polymerizations	Normal	LOW RISK

MARKERS

CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
LOW RISK	CD33	Myeloid cellorigin	Normal	LOW RISK
LOW RISK	CD52	Leukaemia marker	Normal	LOW RISK
LOW RISK	CD20	Lymphoma related antigen	Normal	LOW RISK
HIGH RISK	EpCAM (EpCAm+ve)	Epithelial marker	15 (3.9 cells/7.5 ml)	HIGH RISK
LOW RISK	PD-L1	Immunoregulatory factor	Normal	LOW RISK
LOW RISK	PD 1	Immunoregulatory factor	Normal	LOW RISK
LOW RISK	PD-L2	Immunoregulatory factor	Normal	LOW RISK

From the investigation above the following were concluded

From the whole neoplastic population we have an expression of MRP in a percentage of 55% over control sample (positive in the check of resistance)

There is great overexpression of EGF, TGF- β
There is normal expression of I κ B(a,b,c), NF κ B

The concentration of p180 is in high range.

It appears to have partial sensitivity in the inhibitors of topoisomerase II a and II b.

Decreased sensitivity in alkylating factors.

There is no sensitivity in the inhibitors of Topoisomerase I

There is great sensitivity in taxanes.

We notice great neoangiogenetic ability (overexpression of VEGF-R 20% over control sample).

There is great sensitivity in alkaloids of vinca.

We noticed down regulation of Heat Shock Protein HSP90 (-20%), HSP72 (-10%), HSP27 (-

There is no sensitivity in Eribulin.

There is partial sensitivity in Etoposides.

There is no sensitivity in Pemetrexed, Cytarabine, Fludarabine

There is great over-expression of COX2 (30%), C-erb-B1 (45%), Estrogen-Receptor (15%)

There is partial sensitivity in 5FU, MTX, Capecitabine, Fudr, UFT, Raltitrexed

There is great sensitivity in Gemcitabine

There is normal expression of 5-LOX, SS-r, C-erb-B2

There is over-expression of ANG 1 (25%), ANG 2 (15%), IGF-r 1 (15%)

We noticed no down-regulation of ALK, EML-4-ALK, C-MET, NPM-ALK, CD 117 (ckit), IGF-r 2, HDAC, HAT, NR3C4-A, NR3C4-B

Conclusion

The neoplastic cells have the greatest sensitivity in Docetaxel, Vinorelbine, Gemcitabine

Also can be used Anastrozol, Everolimus/Temsirolimus, Exemestane, Palbociclib, fulvestrant

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

Sincerely,

