

# Onconomics RGCC™

Results



## Results Analysis Report on a patient test patient 1 suffering from Breast stage II.



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 3.3 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.

Ioannis Papatiriou M.D., PhD Head of molecular medicine dpt of R.G.C.C -Research Genetic Cancer Centre International GmbH Baarerstr 95, 6300, Zug, Switzerland

Tel: +41-41-7250560 Website: [www.rgcc-group.com](http://www.rgcc-group.com) E-mail: [medical@rgcc-genlab.com](mailto:medical@rgcc-genlab.com)

Patient Name: test patient 1 - Date: 21 Feb 2022

## 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 &amp; 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

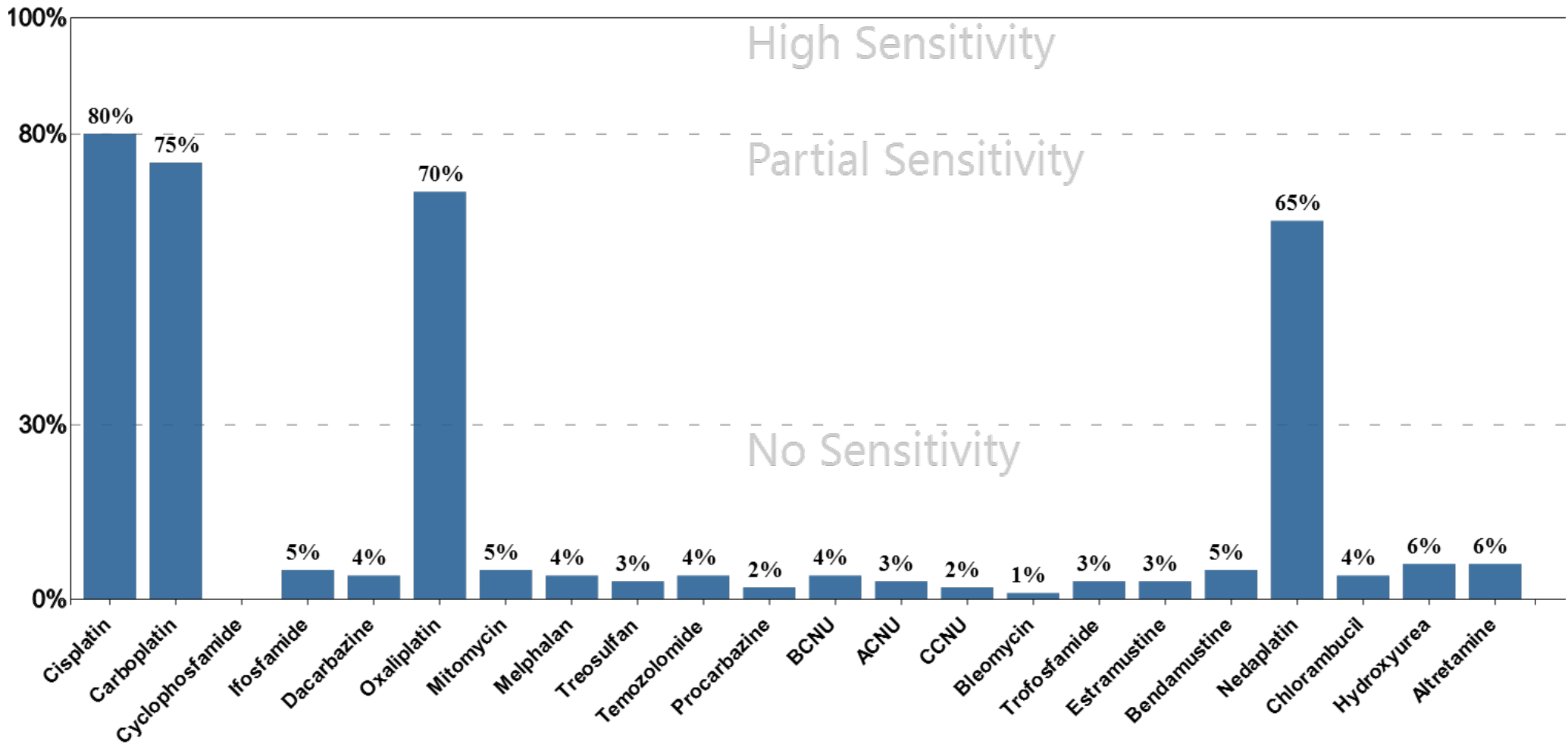
Related with growth signal

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

Related with repair after physical application (radiation, hyperthermia)

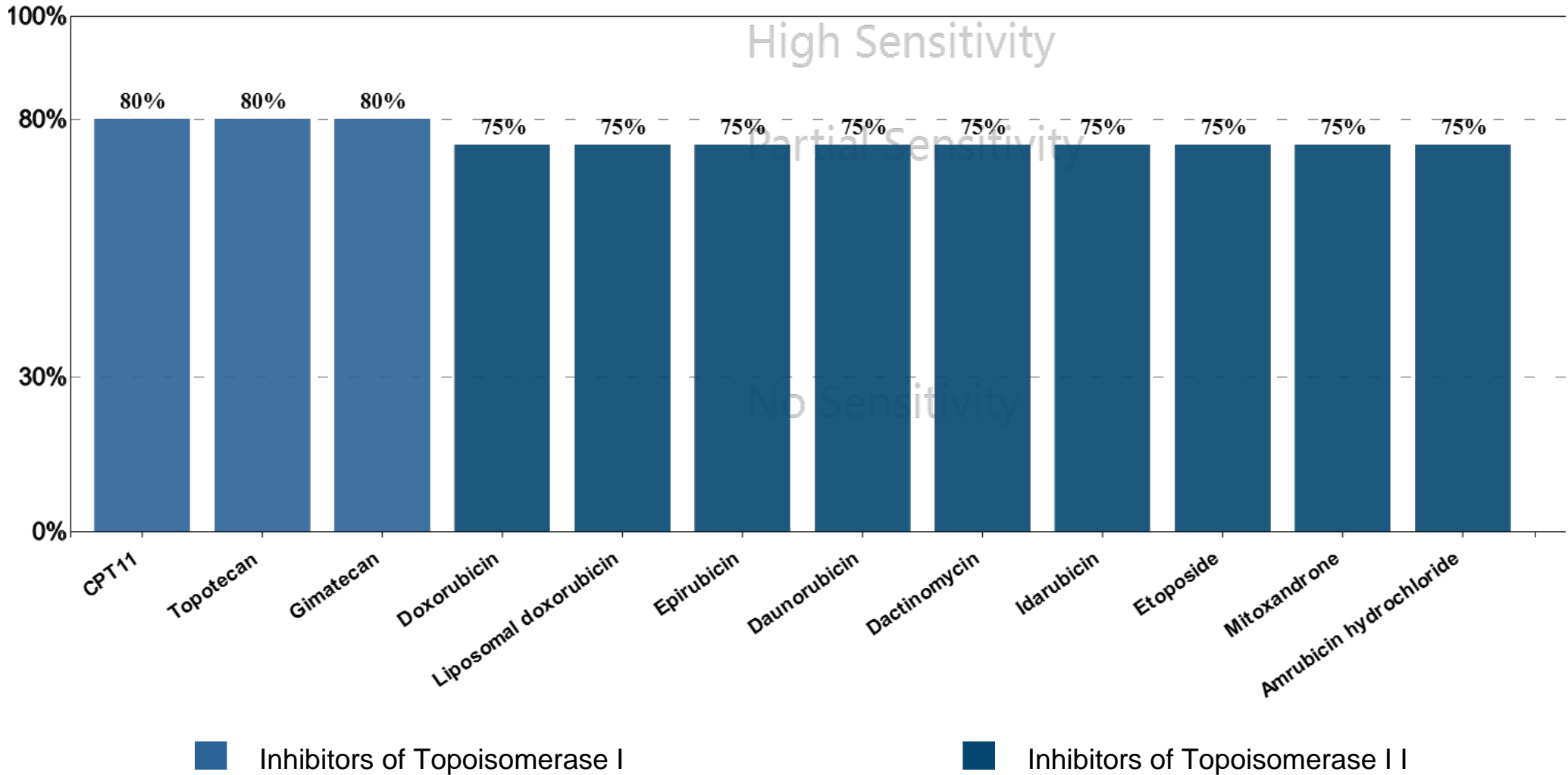
HSP27, HSP70, HSP90, HIF1a, etc.

# Alkylating Agents



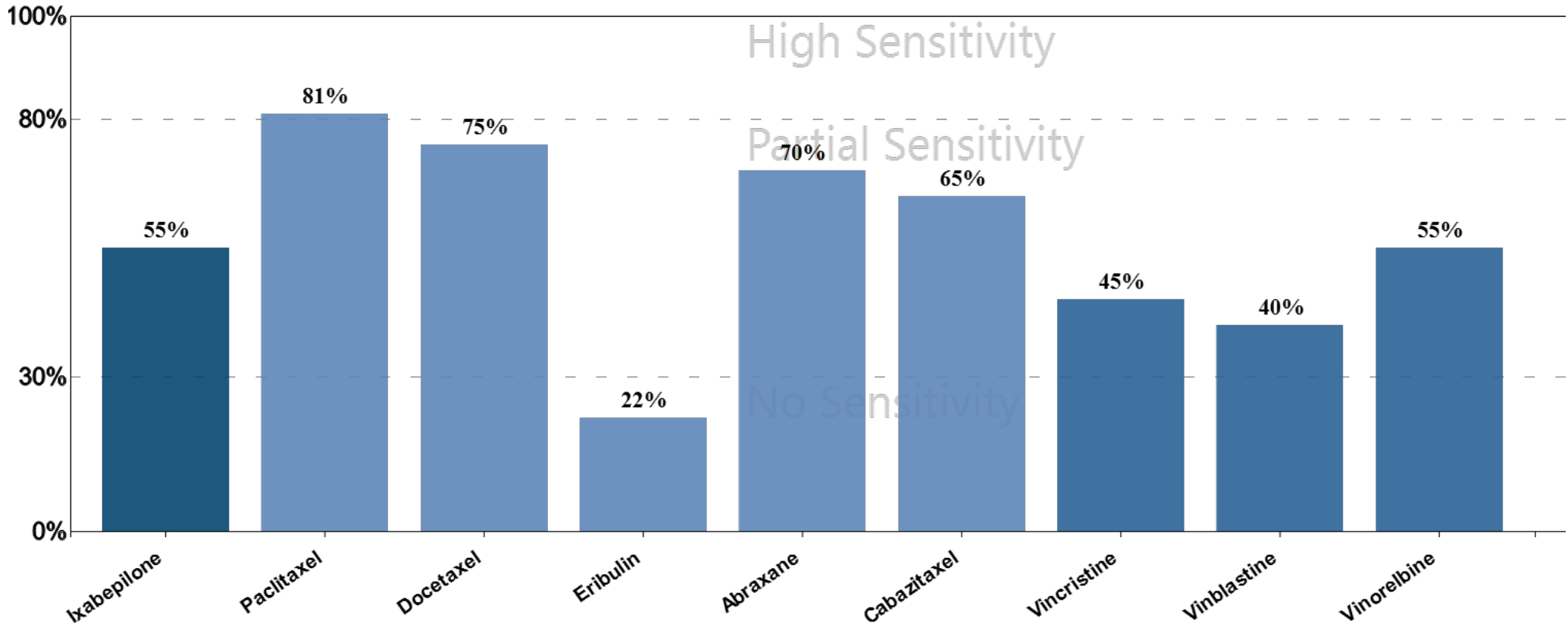
High Sensitivity: Cisplatin

## Inhibitors of Topoisomerase I & II



High Sensitivity: CPT11, Topotecan, Gimatecan

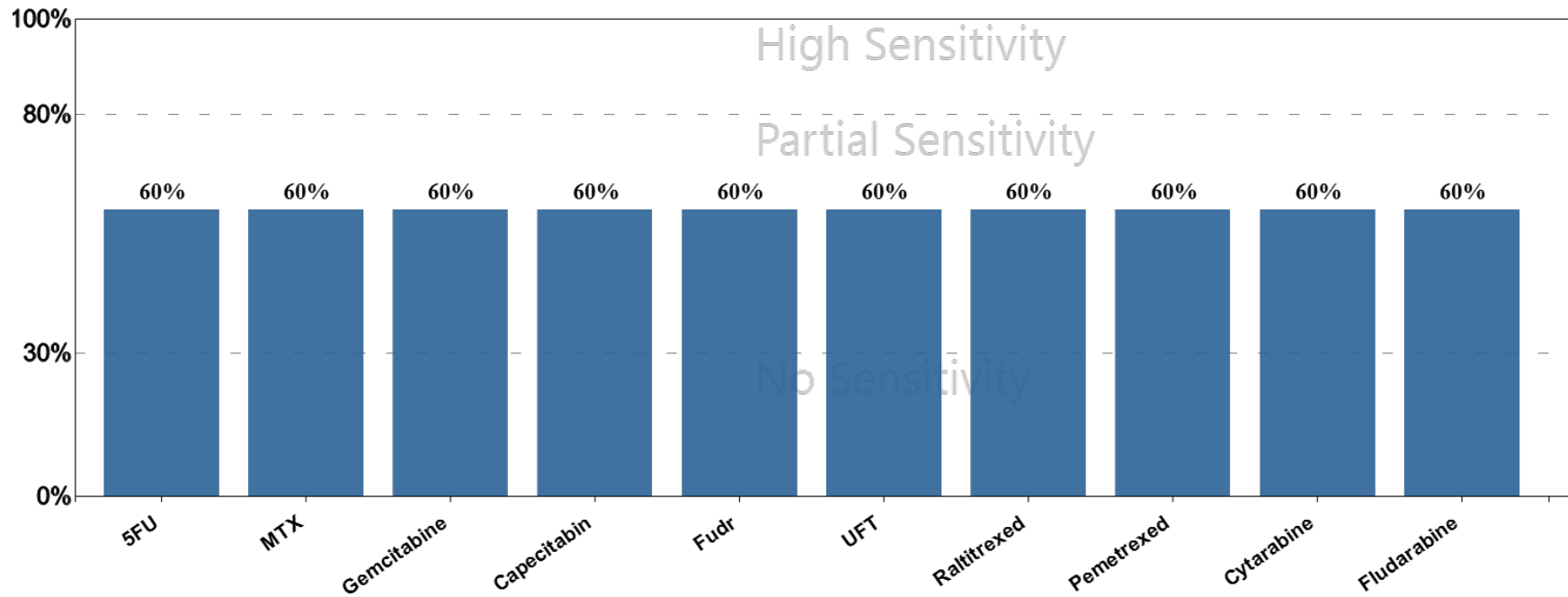
## Epothilones & Nucleus Spindle Stabilizer I & II



Epothilones
  Nucleus Spindle Stabilizer I
  Nucleus Spindle Stabilizer II

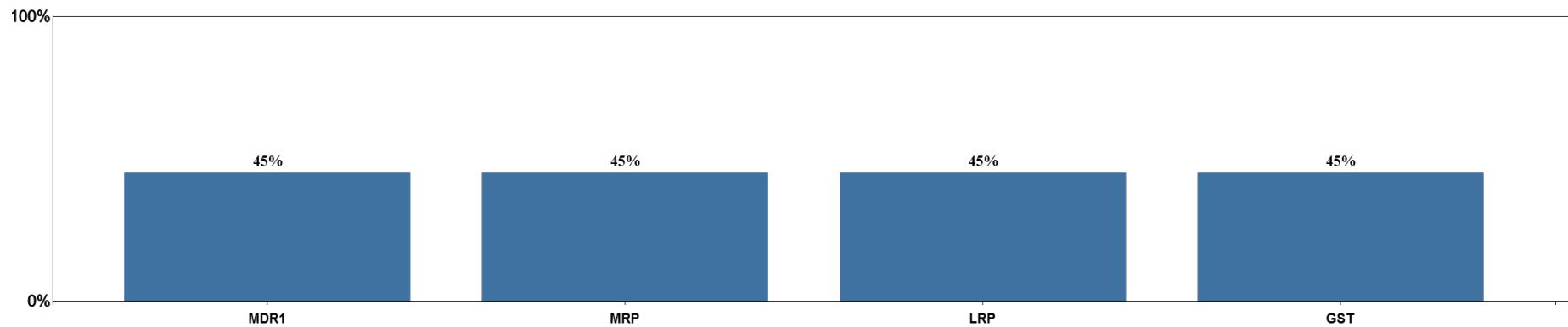
High Sensitivity: Paclitaxel

### Nucleoside Analogues

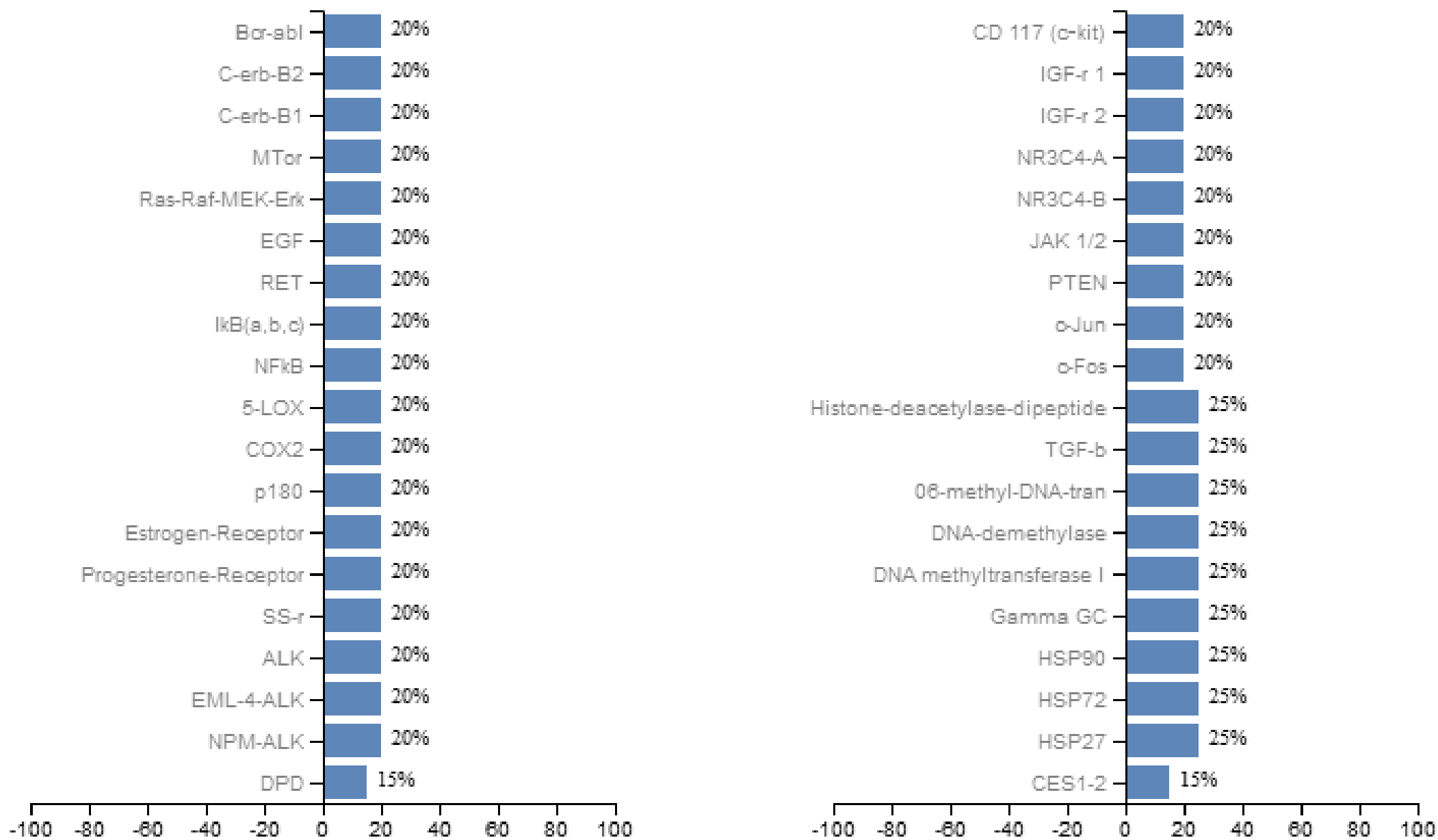


High Sensitivity:

### Resistance Factors

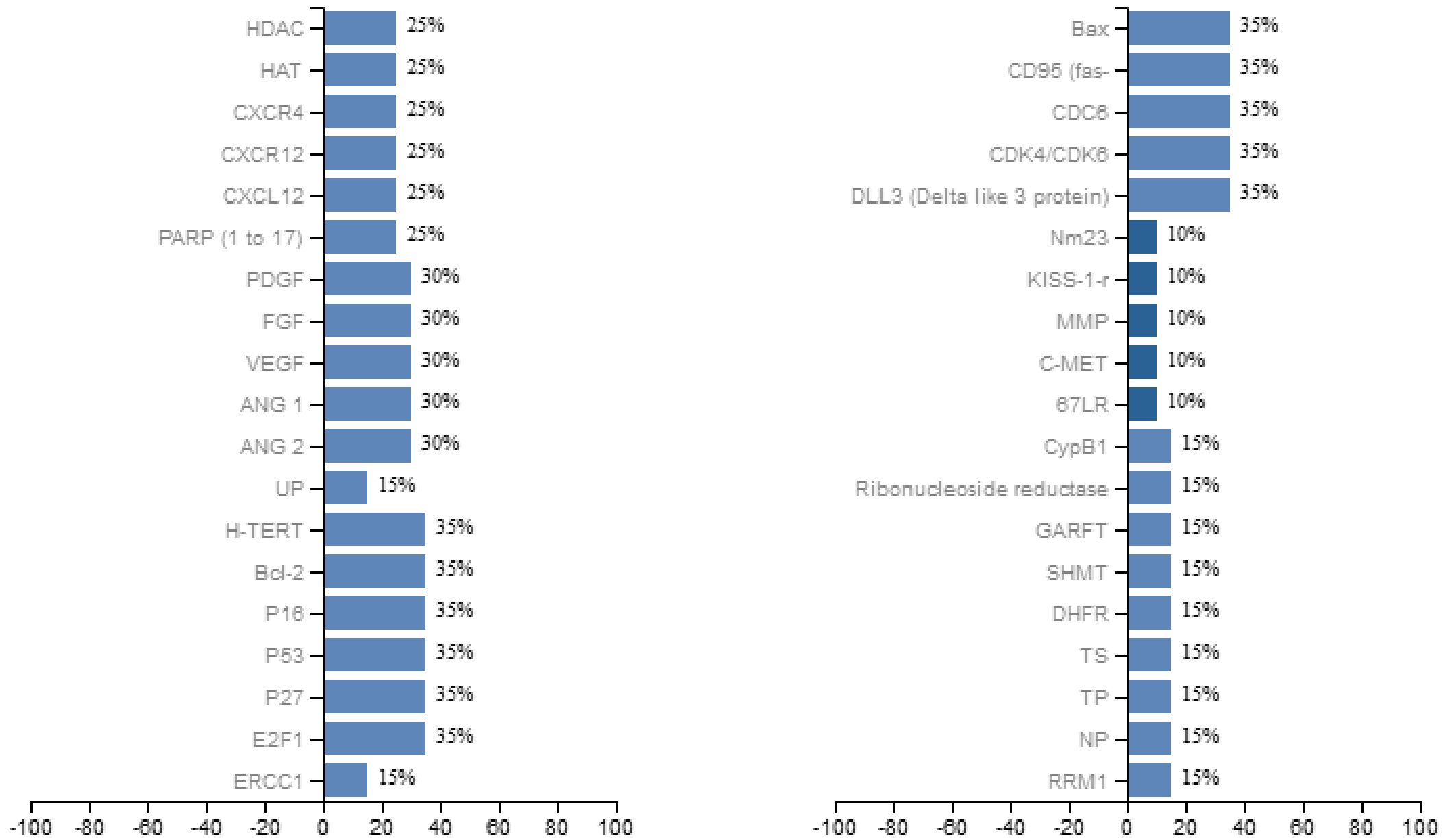


### Tumor Related Genes I

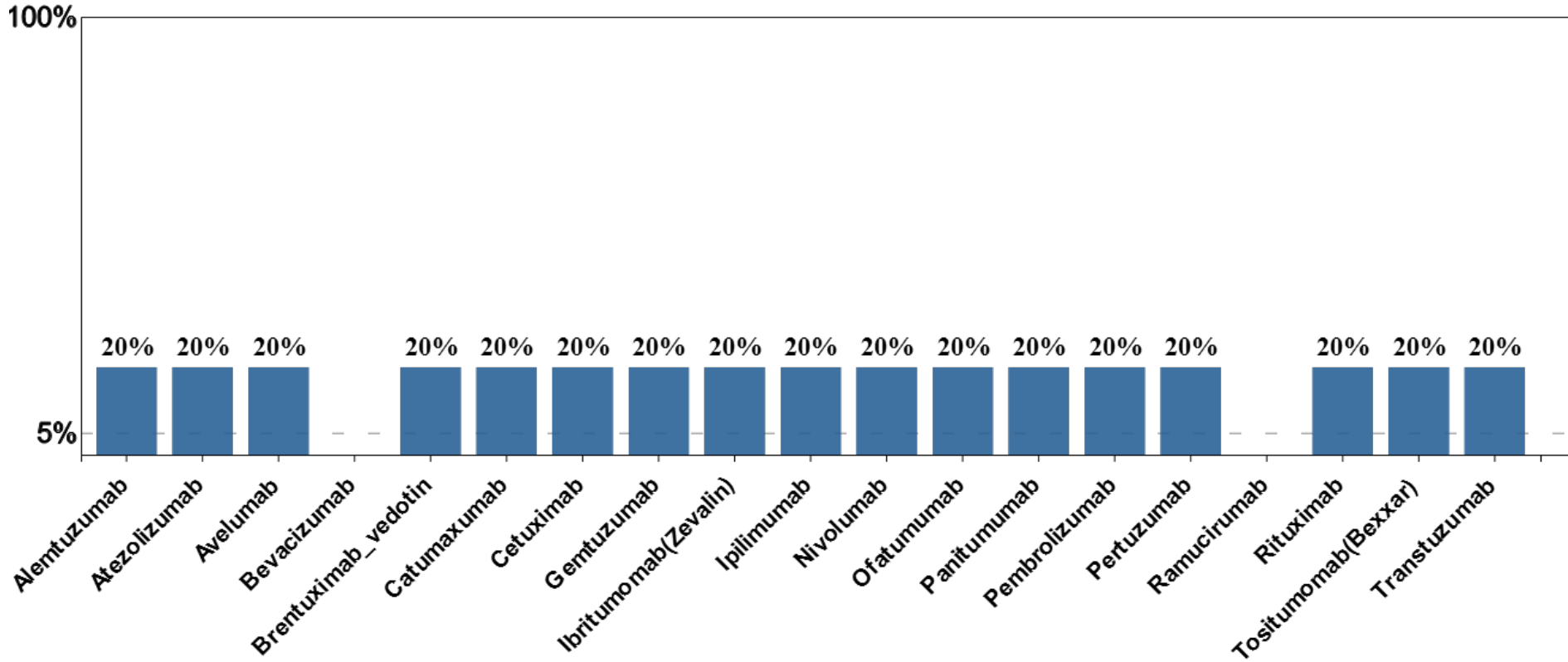




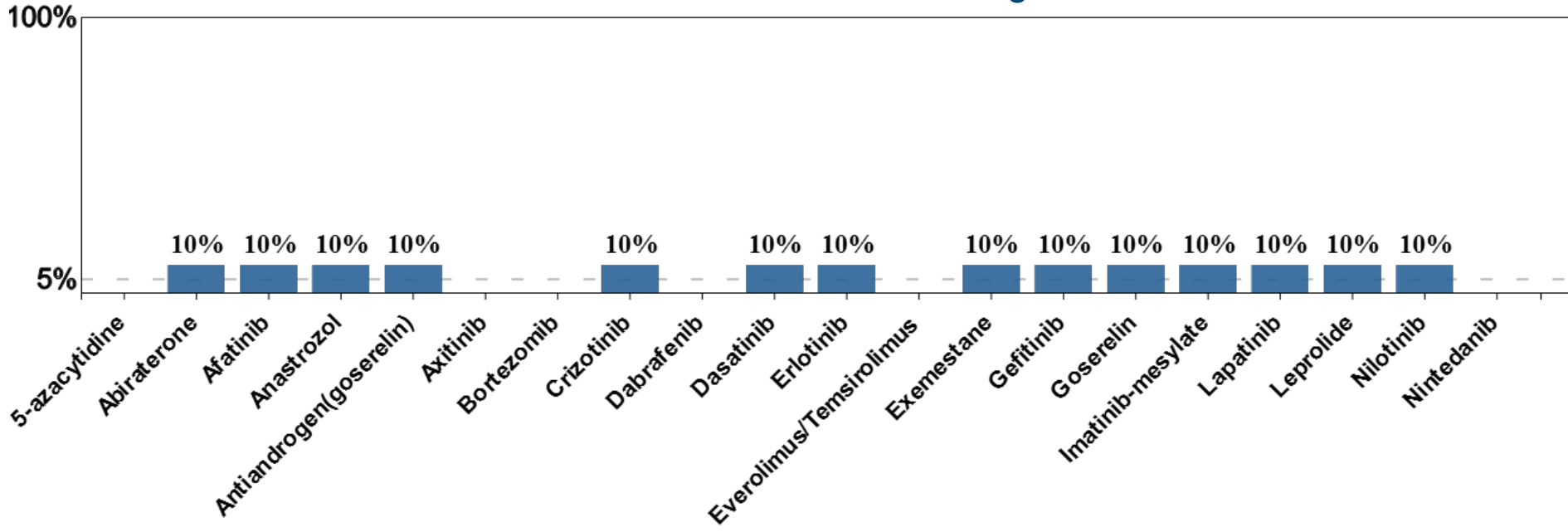
### Tumor Related Genes II



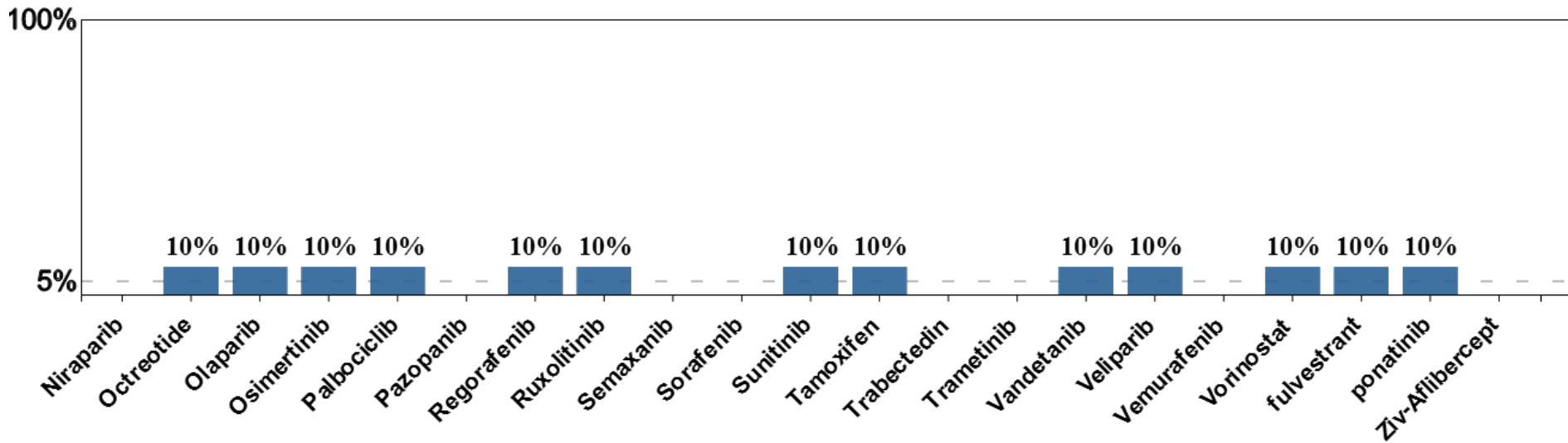
### Moab -Monoclonal Antibodies



### 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.	20	HIGH RISK
Fusion Protein	HIGH RISK	Bcr-abl	Resist phenotype	20	HIGH RISK
Repair Related Gene	HIGH RISK	PTEN	Tumor Suppressor Gene	20	HIGH RISK
Eicosanoid related protein	HIGH RISK	COX2	Tumour Growth	20	HIGH RISK
		5-LOX	Tumour Growth	20	HIGH RISK
Proteasome inhibitors	HIGH RISK	NFkB	Transcription fact	20	HIGH RISK
		IkB(a,b,c)	Inhibitor of NFkB	20	HIGH RISK
Proto-Oncogene	HIGH RISK	ALK	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

## GROWTH FACTORS PROLIFERATION STIMULI

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Growth Factor Receptor	HIGH RISK	SS-r	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
Signal transduction pathway	HIGH RISK	JAK 1/2	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
Hormone Receptors	HIGH RISK	Progesterone Receptor	Growth Factor receptor	20	HIGH RISK
		Estrogene Receptor	Growth Factor receptor	20	HIGH RISK
		NR3C4-A	Nucleous receptor group III Class 4 (androgen receptor A)	20	HIGH RISK
		NR3C4-B	Nucleous receptor group III Class 4 (androgen receptor B)	20	HIGH RISK

## SELF REPAIR - RESISTANCE

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

## ANGIOGENESIS

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Angiogenesis	HIGH RISK	VEGF	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

## CELL CYCLE REGULATION & IMMORTALIZATION / APOPTOSIS

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

## ANGIOGENESIS - METASTASES

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Migration invasion	HIGH RISK	c-MET	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

## DRUG METABOLISMS & TARGETS

FUNCTION	CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
Nucleoside Import transformation	HIGH RISK	DPD	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



## DRUG METABOLISMS & TARGETS

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

## MARKERS

CLINICAL RISK	NAME	RELATED	RESULTS	OUTCOME
HIGH RISK	CD33	Myeloid cellorigin	20	HIGH RISK
HIGH RISK	CD52	Leukaemia marker	20	HIGH RISK
HIGH RISK	CD20	Lymphoma related antigen	20	HIGH RISK
HIGH RISK	EpCAM (EpCAm+ve)	Epithelial marker	20 (2.7 cells/7.5 ml)	HIGH RISK
HIGH RISK	PD-L1	Immunoregulatory factor	20	HIGH RISK
HIGH RISK	PD 1	Immunoregulatory factor	20	HIGH RISK
HIGH RISK	PD-L2	Immunoregulatory factor	20	HIGH RISK

## From the investigation above the following were concluded

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

There is great overexpression of EGF, TGF- $\beta$ , I $\kappa$ B(a,b,c), NF $\kappa$ 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.

Increased sensitivity in alkylating factors.

There is great sensitivity in the inhibitors of Topoisomerase I

There is great sensitivity in taxanes.

We notice great neoangiogenetic ability (overexpression of VEGF-R 30% over control sample).

There is partial sensitivity in alkaloids of vinca.

We noticed no down-regulation of Heat Shock Protein HSP90, HSP72, HSP27

There is no sensitivity in Eribulin.

There is partial sensitivity in Etoposides.

There is partial sensitivity in 5FU, MTX, Gemcitabine, Capecitabine, Fudr, UFT, Raltitrexed, Pemetrexed, Cytarabine, Fludarabine

There is great over-expression of COX2 (20%), 5-LOX (20%), SS-r (20%), C-erb-B1 (20%), C-erb-B2 (20%), Estrogen-Receptor (20%), Progesterone-Receptor (20%)

There is over-expression of ANG 1 (30%), ANG 2 (30%), IGF-r 1 (20%), ALK (20%), EML-4-ALK (20%), C-MET (10%), NPM-ALK (20%), CD 117 (ckit) (20%), IGF-r 2 (20%), HDAC (25%), HAT (25%), NR3C4-A (20%), NR3C4-B (20%)

## Conclusion

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), Trastuzumab, Abiraterone, Afatinib, Anastrozol, Antiandrogen(goserelin), Crizotinib, Dasatinib, Erlotinib, Exemestane, Gefitinib, Goserelin, Imatinib-mesylate, Lapatinib, Leprolide, Nilotinib, Octreotide, Olaparib, Osimertinib, Palbociclib,

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,



Ioannis Papasotiriou MD., PhD Head of molecular medicine dpt. of R.G.C.C.-Research Genetic Cancer Centre International GmbH

Patient Name: test patient 1 - Date: 21 Feb 2022