

### **R.G.C.C.- RESEARCH GENETIC CANCER CENTRE LTD**

Florina, \_\_ / \_\_ /2015

Dear Colleague,

We report the allelic discrimination results for patient **Mr/ Ms** \_\_\_\_\_\_ whose sample receipt on \_\_/\_/2015. DNA was extracted from blood sample and was used as template in PCR reactions. Molecular-based assays and spectrophometer analysis were used to verify the DNA. In all reactions genomic DNA was used as a positive control. The reactions were performed in triplicates.

The "green" square represents the normal allele, while the "red" represents the defect allele. The person can either be equipped with two normal alleles, or two defective, or be heterozygous, namely to one normal and one defective allele.



Homozygote for the wild type (normal) allele



Heterozygote



Homozygote for the mutant (defect) allele

## **BASIC**

GenePolymorphismResultOutcomeCYP2D6*2-1Normal MetabolizerCYP2D6*2-2Normal MetabolizerCYP2D6*3-1Normal MetabolizerCYP2D6*3-2Normal MetabolizerCYP2D6*3-2None ActivityCYP2D6*6Poor Metabolizer/None ActivityCYP2D6*10Decrease or None ActivityCYP2D6*10Decrease or None ActivityCYP2C19*2Normal MetabolizerCYP2C19*3Normal MetabolizerCYP2C19*17Ultra Fast MetabolizerCYP1A2CYP1A2*11FCYP1A2*11KNormal MetabolizerCYP1A2CYP2C9*2CYP1A2*11KNormal MetabolizerCYP1A2*11KNormal MetabolizerCYP1A2CYP2C9*2CYP1A2*11KNormal MetabolizerCYP1A1CYP2C9*2CYP2C9*2Normal MetabolizerCYP131Leu432ValCYP3A4*11BPoor MetabolizerCYP3A4*11BPoor MetabolizerCYP3A4*11BPoor MetabolizerCYP3A4*11BNormal MetabolizerGSTP1His139ArgHis139ArgPoor MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerABCB1Ile1451leSer893AlaPossible Slow MetabolizerABCG2Gin141LvsCYP3Normal Metabolizer	DASIC			
CYP2D6CYP2D6*2-2Normal MetabolizerCYP2D6CYP2D6*3-1Normal MetabolizerCYP2D6*3-2Normal MetabolizerCYP2D6*6Poor Metabolizer/None ActivityCYP2D6*10Decrease or None ActivityCYP2C19*2Normal MetabolizerCYP2C19*3Normal MetabolizerCYP1A2CYP2C19*17CYP1A2CYP1A2*1FCYP1A1CYP2C9*2CYP2C9*2Normal MetabolizerCYP2C9CYP2C9*3CYP2C9*3Poor MetabolizerCYP1B1Leu432ValCYP3A4Possible Slow MetabolizerCYP3A4CYP3A4*1BCYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*20CSTP1His139ArgHis139ArgPoor MetabolizerFPHX1His139ArgNAT2*5DPossible Slow MetabolizerNAT2*6ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*13Normal MetabolizerTPMTTPMT*3ANAT2*14ANormal MetabolizerABCB1Ile145lePossible Slow MetabolizerSer893AlaPossible Slow Metabolizer	Gene	Polymorphism	Resul	t Outcome
CYP2D6*3-1Normal MetabolizerCYP2D6*3-2Normal MetabolizerCYP2D6*3-2Poor Metabolizer/None ActivityCYP2D6*9Normal MetabolizerCYP2D6*10Decrease or None ActivityCYP2C19*2Normal MetabolizerCYP2C19*3Normal MetabolizerCYP2C19*17Ultra Fast MetabolizerCYP1A2CYP1A2*1FCYP1A2*1FNormal MetabolizerCYP1A1CYP1A2*1FCYP2C9*2Normal MetabolizerCYP2C9CYP2C9*2CYP2C9*3Poor MetabolizerCYP3A4CYP3A4*1BCYP3A4*1BPorshibe Slow MetabolizerCYP3A4CYP3A4*1BCYP3A4*1BPoor MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4*1BNormal MetabolizerCYP3A4*1BNormal MetabolizerCYP3A4*1BNormal MetabolizerMAT2*5DPossible Slow MetabolizerNAT2*5DNormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal Metabolizer <t< td=""><td></td><td>CYP2D6*2-1</td><td></td><td>Normal Metabolizer</td></t<>		CYP2D6*2-1		Normal Metabolizer
CYP2D6CYP2D6*3-2None ActivityCYP2D6*6Poor Metabolizer/None ActivityCYP2D6*10Decrease or None ActivityCYP2C19*17Operase or None ActivityCYP2C19*2Normal MetabolizerCYP2C19CYP2C19*3CYP2C19*17Ultra Fast MetabolizerCYP1A2CYP1A2*1FCYP1A1CYP1A2*1KCYP1A2Normal MetabolizerCYP2C9CYP2C9*2CYP2C9CYP2C9*3CYP3A4Possible Slow MetabolizerCYP3A4CYP3A4*1BCYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*1BCYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*1BCYP3A4Normal MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerCYP3A4Normal MetabolizerMAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*1ANormal Metabolizer		CYP2D6*2-2		Normal Metabolizer
CYP2D6*6Poor Metabolizer/None ActivityCYP2D6*9Normal MetabolizerCYP2D6*10Decrease or None ActivityCYP2C19*2Normal MetabolizerCYP2C19*3Normal MetabolizerCYP2C19*3Ormal MetabolizerCYP1A2CYP2C19*3CYP1A2CYP1A2*1FCYP1A1CYP1A2*1FCYP2C9CYP2C9*2CYP2C9CYP2C9*2CYP2C9CYP2C9*2CYP3A4Poor MetabolizerCYP3A4CYP3A4*1BCYP3A4*20Normal MetabolizerCYP3A4CYP3A4*20CSTP1Ile105ValHis139ArgPoor MetabolizerFBHX1His139ArgNAT2*5DPossible Slow MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerTPMTTPMT*3CABCB1Ile1145lleBCR14Normal MetabolizerABCB1Ile1145lleBCR25Ser893AlaSer893AlaSosible Slow Metabolizer		CYP2D6*3-1		Normal Metabolizer
CYP2D6*9Normal MetabolizerCYP2C19*2Normal MetabolizerCYP2C19*2Normal MetabolizerCYP2C19*3Normal MetabolizerCYP2C19*17Ultra Fast MetabolizerCYP1A2CYP1A2*1FCYP1A1CYP1A2*1FCYP2C9*2Normal MetabolizerCYP2C9CYP2C9*2CYP2C9*3Poor MetabolizerCYP1B1Leu432ValCYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*1BCYP3A4*20Normal MetabolizerCYP3A4Poor MetabolizerCYP111His139ArgPOOR MetabolizerFPHX1His139ArgNAT2*5DPossible Slow MetabolizerNAT2*11ANormal MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*3ANormal MetabolizerABCB1ILe1145lleBCR14Normal MetabolizerSer893AlaPossible Slow MetabolizerSer893AlaPossible Slow Metabolizer	CYP2D6	CYP2D6*3-2		None Activity
CYP2D6*10Decrease or None ActivityCYP2C19*2Normal MetabolizerCYP2C19*3Normal MetabolizerCYP2C19*3Ultra Fast MetabolizerCYP1A2CYP1A2*1FCYP1A2CYP1A2*1FCYP1A1CYP1A2*1FCYP1A2*1FNormal MetabolizerCYP1A2CYP1A2*1FCYP1A2*1FNormal MetabolizerCYP1A2CYP1A2*1FCYP1A2CYP1A2*1FCYP1A2Ormal MetabolizerCYP2C9CYP2C9*2CYP2C9*3Poor MetabolizerCYP3A4Poor MetabolizerCYP3A4CYP3A4*1BCYP3A4*20Normal MetabolizerCYP3A4CYP3A4*20CYP3A4*20Normal MetabolizerGSTP1Ile105ValIle105ValNormal MetabolizerHis139ArgPoor MetabolizerFPHX1His139ArgPOOr MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*11ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*14ANormal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleABCB1Ser893AlaCYP3AlaPossible Slow Metabolizer		CYP2D6*6		Poor Metabolizer/None Activity
CYP2C19CYP2C19*2Normal MetabolizerCYP2C19*3Normal MetabolizerCYP2C19*17Ultra Fast MetabolizerCYP1A2CYP1A2*1FNormal MetabolizerCYP1A1CYP1A2*1KNormal MetabolizerCYP1A2CYP1A2*1KNormal MetabolizerCYP1A1CYP1A1*2CNormal MetabolizerCYP2C9CYP2C9*2Normal MetabolizerCYP1B1Leu432ValPoor MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerFPHX1Tyr113HisNormal MetabolizerNAT2*5DPoosible Slow MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerTPMTTPMT*3AABCB1Ile1145IleABCB1Ser893AlaOSer893AlaOSer893AlaOSer893AlaOSer893AlaONorsible Slow Metabolizer		CYP2D6*9		Normal Metabolizer
CYP2C19CYP2C19*3Normal MetabolizerCYP1A2CYP1A2*1FUltra Fast MetabolizerCYP1A2CYP1A2*1FNormal MetabolizerCYP1A1CYP1A1*2CNormal MetabolizerCYP209CYP2C9*2Normal MetabolizerCYP1B1Leu432ValPoor MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerHis139ArgPoor MetabolizerFPHX1His139ArgPoor MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*3ANormal MetabolizerABCB1Ile11451leABCB1Ser893AlaOrdSer893AlaOrdSer893AlaCYP3APossible Slow Metabolizer		CYP2D6*10		Decrease or None Activity
CYP2C19*17Ultra Fast MetabolizerCYP1A2CYP1A2*1FNormal MetabolizerCYP1A1CYP1A2*1KNormal MetabolizerCYP1A1CYP1A1*2CNormal MetabolizerCYP2C9CYP2C9*2Normal MetabolizerCYP1B1Leu432ValPossible Slow MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerGSTP1Ile105ValNormal MetabolizerIle105ValNormal MetabolizerFPHX1His139ArgPoor MetabolizerNAT2*5DPossible Slow MetabolizerNAT2NAT2*5DPossible Slow MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3AABCB1Ile11451leABCB1Ser893AlaOrmal ActabolizerPossible Slow Metabolizer		CYP2C19*2		Normal Metabolizer
CYP1A2CYP1A2*1FNormal MetabolizerCYP1A1CYP1A2*1KNormal MetabolizerCYP1A1CYP1A1*2CNormal MetabolizerCYP2C9CYP2C9*2Normal MetabolizerCYP2C9CYP2C9*3Poor MetabolizerCYP1B1Leu432ValPossible Slow MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerGSTP1Ile105ValNormal MetabolizerIle105ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*13Normal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerABCB1Ile11451lePossible Slow MetabolizerSer893AlaPossible Slow Metabolizer	CYP2C19	CYP2C19*3		Normal Metabolizer
CYP1A2CYP1A2*1KNormal MetabolizerCYP1A1CYP1A1*2CNormal MetabolizerCYP2C9CYP2C9*2Normal MetabolizerCYP2C9CYP2C9*3Poor MetabolizerCYP1B1Leu432ValPossible Slow MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerBEPHX1His139ArgPoor MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*13Normal MetabolizerTPMTTPMT*3AABCB1Ile11451leABCB1Ser893AlaOrmal ActabolizerPossible Slow Metabolizer		CYP2C19*17		Ultra Fast Metabolizer
CYP1A2*1kNormal MetabolizerCYP1A1CYP1A1*2CNormal MetabolizerCYP2C9CYP2C9*2Normal MetabolizerCYP1B1Leu432ValPossible Slow MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*20Normal MetabolizerCYP3A4CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerFPHX1His139ArgPoor MetabolizerMAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*13Normal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerABCB1Ile1145IleABCB1Ser893AlaOrmal MetabolizerSer893AlaCYP3A4Possible Slow Metabolizer	CVD1 A 2	CYP1A2*1F		Normal Metabolizer
CYP2C9CYP2C9*2Normal MetabolizerCYP1B1Leu432ValPoor MetabolizerCYP3A4Poor MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerTyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerABCB1Ile11451leABCB1Ser893AlaOrman AlexabolizerPossible Slow Metabolizer	CIPIA2	CYP1A2*1K		Normal Metabolizer
CYP2C9CYP2C9*3Poor MetabolizerCYP1B1Leu432ValPossible Slow MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerTyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerABCB1Ile11451lePossible Slow MetabolizerSer893AlaPossible Slow Metabolizer	CYP1A1	CYP1A1*2C		Normal Metabolizer
CYP1B1Leu432ValPoor MetabolizerCYP3A4CYP3A4*1BPoor MetabolizerCYP3A4CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerTyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*13Normal MetabolizerNAT2*13Normal MetabolizerTPMTTPMT*3CTPMT*2Normal MetabolizerABCB1Ile1145IlePossible Slow MetabolizerPossible Slow MetabolizerABCB1Ile1145IlePossible Slow MetabolizerPossible Slow MetabolizerABCB1Ile1145IlePossible Slow Metabolizer	CVD2C0	CYP2C9*2		Normal Metabolizer
CYP3A4CYP3A4*1BPoor MetabolizerCYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerTyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*1ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3CABCB1Ile1145IleABCB1Ile1145IlePossible Slow MetabolizerPossible Slow Metabolizer	CYP2C9	CYP2C9*3		Poor Metabolizer
CYP3A4CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerTyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*7ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer	CYP1B1	Leu432Val		Possible Slow Metabolizer
CYP3A4*20Normal MetabolizerGSTP1Ala114ValNormal MetabolizerIle105ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerTyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*7ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer		CYP3A4*1B		Poor Metabolizer
GSTP1Ile105ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerTyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*7ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer	CYP3A4	CYP3A4*20		Normal Metabolizer
Ile105 ValNormal MetabolizerEPHX1His139ArgPoor MetabolizerTyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*7ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile11451leSer893AlaPossible Slow Metabolizer		Ala114Val		Normal Metabolizer
EPHX1Tyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*7ANormal MetabolizerNAT2*1ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer	GSIPI	Ile105Val		Normal Metabolizer
Tyr113HisNormal MetabolizerNAT2*5DPossible Slow MetabolizerNAT2*6BNormal MetabolizerNAT2*7ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3CTPMT*4ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer	EPHX1	His139Arg		Poor Metabolizer
NAT2*6BNormal MetabolizerNAT2*7ANormal MetabolizerNAT2*7ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerNAT2*14ANormal MetabolizerTPMTTPMT*3CTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer		Tyr113His		Normal Metabolizer
NAT2NAT2*7ANormal MetabolizerNAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*4ANormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer		NAT2*5D		Possible Slow Metabolizer
NAT2NAT2*11ANormal MetabolizerNAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*4ANormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer		NAT2*6B		Normal Metabolizer
NAT2*12APossible Slow MetabolizerNAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*4ANormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer		NAT2*7A		Normal Metabolizer
NAT2*13Normal MetabolizerNAT2*14ANormal MetabolizerNAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*4ANormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer	NAT2	NAT2*11A		Normal Metabolizer
NAT2*14ANormal MetabolizerTPMT*3CNormal MetabolizerTPMT*4ANormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer		NAT2*12A		Possible Slow Metabolizer
TPMT*3CNormal MetabolizerTPMT*4ANormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IleSer893AlaPossible Slow Metabolizer		NAT2*13		Normal Metabolizer
TPMTTPMT*4ANormal MetabolizerTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IlePossible Slow MetabolizerSer893AlaPossible Slow Metabolizer		NAT2*14A		Normal Metabolizer
TPMTTPMT*3ANormal MetabolizerTPMT*2Normal MetabolizerABCB1Ile1145IlePossible Slow MetabolizerSer893AlaPossible Slow Metabolizer	TPMT	TPMT*3C		Normal Metabolizer
TPMT*3A Normal Metabolizer   TPMT*2 Normal Metabolizer   ABCB1 Ile1145Ile Possible Slow Metabolizer   Ser893Ala Possible Slow Metabolizer		TPMT*4A		Normal Metabolizer
ABCB1Ile1145IlePossible Slow MetabolizerSer893AlaPossible Slow Metabolizer		TPMT*3A		Normal Metabolizer
ABCB1 Ser893Ala Possible Slow Metabolizer		TPMT*2		Normal Metabolizer
Ser893Ala Possible Slow Metabolizer		Ile1145Ile		Possible Slow Metabolizer
ABCG2 Gln141Lvs Normal Metabolizer	ABCR1	Ser893Ala		Possible Slow Metabolizer
	ABCG2	Gln141Lys		Normal Metabolizer

# ALKYLATING AGENTS

NQ01Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (Cisplatin XPCXPCGln902LysPossible decreased risk for toxicityXRCC1Gln399ArgPossible decreased risk for neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible decreased risk for hearing loss (Cisplatin UBE2IUBE2I157C>GPossible decreased response to cisplatin and irinotecan							
1F33F1033AlgsurvivalABCB1Ile1145IlePossible decreased risk of lymph node metastasi increased survivalTPMTTPMT*3CPossible decreased risk for hearing loss (Cisplati Possible increased risk for toxicity/ decreased survivalERCC1Asn118AsnPossible increased risk for toxicity/ decreased survivalERC2Lys751GlnPossible increased risk for toxicityGSTP1Ile105ValPossible increased risk for toxicityGSTM3110280254delCPossible increased risk of side effectsERCC2Asp288AsnPossible increased overall survival (Cisplatin)TPMTTPMT*3APossible decreased risk for hearing loss (Cisplati NQO1NQO1Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible decreased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased risk for hearing loss (Cisplati XPCKRCC1Gln309ArgPossible decreased risk for hearing loss (Cisplati CD3EAPSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased risk for hearing loss (Cisplati irinotecanUBE21157C>GPossible decreased response to cisplati and irinotecan	Gene	Polymorphism	Resu	ult			
ABCB1Ile1145IlePossible decreased risk of lymph node metastasi increased survivalTPMTTPMT*3CPossible decreased risk for hearing loss (Cisplati ERCC1ERCC1Asn118AsnPossible increased survivalERCC2Lys751GlnPossible increased survivalGSTP1Ile105ValPossible increased risk for toxicity/ decreased survivalGSTM3110280254delCPossible increased risk for toxicityGSTM3110280254delCPossible increased risk for toxicityGSTM3110280254delCPossible increased risk for hearing loss (Cisplatin)TPMTTPMT*3APossible decreased risk for hearing loss (Cisplatin)TPMTTPMT*3APossible better outcome (overall survival and progression-free survival)MQ01Pro149SerPossible increased likelihood of response to chemotherapy and drug toxicityMTHFRAla222ValPossible decreased likelihood of drug toxicityMTRAsp919GlyPossible decreased survival and progression free survivalXPCGln902LysPossible increased likelihood of drug toxicityXRCC1Gln399ArgPossible increased risk for hearing loss (Cisplati neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCOMT19955692C>TPossible increased risk of nephrotoxicityUBE21157C>GPossible decreased response to cisplatin and irinotecan	TP53	Pro33Arg					
ABCB1Itel 1431eincreased survivalTPMTTPMT*3CPossible decreased risk for hearing loss (CisplatinERCC1Asn118AsnPossible increased risk for toxicity/ decreasedERCC2Lys751GlnPossible increased risk for toxicityGSTP1Ile105ValPossible increased risk for toxicityGSTM3110280254delCPossible increased risk for toxicityERCC2Asp288AsnPossible increased overall survival (Cisplatin)TPMTTPMT*3APossible decreased risk for hearing loss (Cisplatin)NQ01Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased risk for hearing loss (Cisplatin)MTRAsp919GlyPossible decreased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased risk for hearing loss (Cisplatin)XPCGln902LysPossible increased risk for toxicityXRCC1Gln399ArgPossible decreased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCOMT19955692C>TPossible increased risk for hearing loss (Cisplatin and irinotecan		11000111g					
TPMTTPMT*3CPossible decreased risk for hearing loss (CisplatiERCC1Asn118AsnPossible increased risk for toxicity/ decreased survivalERCC2Lys751GlnPossible increased risk for toxicityGSTP1Ile105ValPossible increased risk for toxicityGSTM3110280254delCPossible increased risk of side effectsERCC2Asp288AsnPossible increased overall survival (Cisplatin)TPMTTPMT*3APossible decreased risk for hearing loss (Cisplatin)NQO1Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible decreased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased risk for toxicityXRCC1Gln309ArgPossible decreased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCOMT19955692C>TPossible increased risk of nephrotoxicityUBE2I157C>GPossible decreased response to cisplatin and irinotecan	ABCB1	Ile1145Ile			• •		
ERCC1Asn118AsnPossible increased risk for toxicity/ decreased survivalERCC2Lys751GlnPossible increased risk for toxicityGSTP1Ile105ValPossible increased risk for toxicityGSTM3110280254delCPossible increased risk for toxicityGSTM3110280254delCPossible increased risk for toxicityGSTM3110280254delCPossible increased risk for toxicityGSTM3110280254delCPossible increased risk for toxicityImportTPMT*3APossible decreased risk for hearing loss (Cisplatin)TPMTTPMT*3APossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased risk for hearing loss (Cisplati XPCMRCC1Gln902LysPossible increased risk for toxicityXRCC1Gln399ArgPossible increased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk for nephrotoxicityCOMT19955692C>TPossible increased risk for hearing loss (Cisplatin untotecanUBE21157C>GPossible decreased response to cisplatin and irinotecan	трмт	TDMT*2C					
ERCC1Ash118AshsurvivalERCC2Lys751GlnPossible increased survivalGSTP1Ile105ValPossible increased risk for toxicityGSTM3110280254delCPossible increased risk of side effectsERCC2Asp288AsnPossible increased overall survival (Cisplatin)TPMTTPMT*3APossible decreased risk for hearing loss (Cisplatin)NQ01Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression-free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased risk for hearing loss (CisplatiXPCGln902LysPossible decreased risk for toxicityXRCC1Gin399ArgPossible increased risk for toxicitySLC22A2Ser270AlaPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased risk for hearing loss (Cisplatin and irinotecan		IFMI <sup>+</sup> 5C					
GSTP1Ile105ValPossible increased risk for toxicityGSTM3110280254delCPossible increased risk of side effectsERCC2Asp288AsnPossible increased overall survival (Cisplatin)TPMTTPMT*3APossible decreased risk for hearing loss (Cisplatin)NQ01Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased risk for hearing loss (Cisplatin)XPCGln902LysPossible decreased risk for toxicityXRCC1Gln399ArgPossible increased risk for toxicitySLC22A2Ser270AlaPossible increased risk of nephrotoxicityCOMT19955692C>TPossible increased risk for hearing loss (Cisplatin and irinotecanUBE21157C>GPossible decreased response to cisplatin and irinotecan	ERCC1	Asn118Asn					
GSTM3110280254delCPossible increased risk of side effectsERCC2Asp288AsnPossible increased overall survival (Cisplatin)TPMTTPMT*3APossible decreased risk for hearing loss (Cisplatin)NQO1Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (Cisplatin)XPCGln902LysPossible increased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk for nephrotoxicityCOMT19955692C>TPossible increased risk of nephrotoxicityUBE21157C>GPossible decreased response to cisplatin and irinotecan	ERCC2	Lys751Gln			Possible increased survival		
ERCC2Asp288AsnPossible increased overall survival (Cisplatin)TPMTTPMT*3APossible decreased risk for hearing loss (Cisplatin)NQO1Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (Cisplatin XPCXPCGln902LysPossible decreased risk for toxicityXRCC1Gln399ArgPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible increased risk of nephrotoxicityUBE21157C>GPossible decreased response to cisplatin and irinotecan	GSTP1	Ile105Val			Possible increased risk for toxicity		
TPMTTPMT*3APossible decreased risk for hearing loss (Cisplating NQO1NQO1Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression-free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased risk for hearing loss (Cisplating toxicity)MTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (Cisplating toxicity)XRCC1Gln309ArgPossible decreased risk for toxicitySLC22A2Ser270AlaPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased risk for hearing loss (Cisplating toxic)UBE21157C>GPossible decreased response to cisplatin and rintotecan	GSTM3	110280254delC			Possible increased risk of side effects		
NQ01Pro149SerPossible better outcome (overall survival and progression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (Cisplatin XPCXPCGln902LysPossible decreased risk for toxicityXRCC1Gln399ArgPossible decreased risk for neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible decreased risk for hearing loss (Cisplatin UBE21UBE21157C>GPossible decreased response to cisplatin and irinotecan	ERCC2	Asp288Asn			Possible increased overall survival (Cisplatin)		
NQO1Pro149Serprogression-free survival)MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (Cisplatin XPCXPCGln902LysPossible decreased risk for toxicityXRCC1Gln399ArgPossible decreased risk of nephrotoxicitySLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible decreased risk for hearing loss (Cisplatin UBE2IUBE2I157C>GPossible decreased response to cisplatin and irinotecan	TPMT	TPMT*3A			Possible decreased risk for hearing loss (Cisplatin)		
MTHFRGlu429AlaAssociated with overall survival and progression free survivalMTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (Cisplatin XPCXPCGln902LysPossible decreased risk for toxicityXRCC1Gln399ArgPossible decreased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible increased risk for hearing loss (Cisplatin Distribution of the survival and risk of neutropeniaUBE2I157C>GPossible decreased response to cisplatin and irinotecan	NQO1	Pro149Ser					
MTHFRAla222ValPossible increased likelihood of response to chemotherapy and drug toxicityMTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (Cisplatin XPCXPCGln902LysPossible increased risk for toxicityXRCC1Gln399ArgPossible decreased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible increased risk of nephrotoxicityUBE2I157C>GPossible decreased response to cisplatin and irinotecan	MTHFR	Glu429Ala			Associated with overall survival and progression		
MTRAsp919GlyPossible decreased likelihood of drug toxicityLRP2Lys4094GluPossible decreased risk for hearing loss (CisplatinXPCGln902LysPossible increased risk for toxicityXRCC1Gln399ArgPossible decreased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased response to cisplatin and irinotecan	MTHFR	Ala222Val			Possible increased likelihood of response to		
LRP2Lys4094GluPossible decreased risk for hearing loss (Cisplatin XPCXPCGln902LysPossible increased risk for toxicityXRCC1Gln399ArgPossible decreased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased risk for hearing loss (Cisplatin Possible decreased response to cisplatin and irinotecan	МТр	A am 0.10C1.					
XPCGln902LysPossible increased risk for toxicityXRCC1Gln399ArgPossible decreased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased risk for hearing loss (Cisplatin urinotecanUBE2I157C>GPossible decreased response to cisplatin and irinotecan							
XRCC1Gln399ArgPossible decreased survival and risk of neutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased risk for hearing loss (Cisplatin UBE2IUBE2I157C>GPossible decreased response to cisplatin and irinotecan							
XRCC1Gln399ArgneutropeniaSLC22A2Ser270AlaPossible increased risk of nephrotoxicityCD3EAPGln504LysPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased risk for hearing loss (Cisplatin UBE2IUBE2I157C>GPossible decreased response to cisplatin and irinotecan	XPC	Gln902Lys					
CD3EAPGln504LysPossible increased risk of nephrotoxicityCOMT19955692C>TPossible decreased risk for hearing loss (Cisplating UBE2IUBE2I157C>GPossible decreased response to cisplating and the interval of the interv	XRCC1	Gln399Arg					
COMT19955692C>TPossible decreased risk for hearing loss (Cisplatin Display 157C>GUBE2I157C>GPossible decreased response to cisplatin and irinotecan	SLC22A2	Ser270Ala			Possible increased risk of nephrotoxicity		
COMT19955692C>TPossible decreased risk for hearing loss (Cisplatin Possible decreased response to cisplatin and irinotecanUBE2I157C>GPossible decreased response to cisplatin and irinotecan	CD3EAP	Gln504Lys			Possible increased risk of nephrotoxicity		
UBE21 13/C>G irinotecan	COMT				Possible decreased risk for hearing loss (Cisplatin)		
	UBE2I	157C>G					
GALNT14 10069401G>T Possible decreased response and survival	GALNT14	10069401G>T					
Possible decreased overall survival					1		
	EGFR	Leu858Arg			time/progression-free survival time (carboplatin-		
erlotinib-paclitaxel)					1		
DSCAM 27076915T>C Possible increased survival (carboplatin-	DSCAM	27076915T>C			-		
paciitaxei)		2,0,0,101/0			I ,		
PTGS2 427T>C Possible increased progression-free survival/ overall survival (capecitabine-oxaliplatin)	PTGS2	427T>C			1 0		
Possible longer disease-free survival							
NOS3 Asp298Glu (cyclophosphamide-doxorubicin-5FU-MTX)	NOS3	Asp298Glu			-		
ABCB1 Ser893Ala Possible decreased survival in		Sar 202 1 1a					
ABCB1 Ser893Ala (cyclophosphamide-doxorubicin, Breast)	ADUDI	SCI093Ala			(cyclophosphamide-doxorubicin, Breast)		

$Pro320\Delta1a$			Possible increased likelihood of cystitis
110 <i>32)</i> Ala			(carboplatin-cyclophosphamide-thiotepa)
CVD1D6*/			Possible decreased risk for oral mucositis
$C1F2D0^{1}4$			(cyclophosphamide)
			Possible shorter period of time before
CYP3A4*1B			chemotherapy-induced ovarian failure
			(cyclophosphamide)
CVD2D6*6			Possible no requirement for dose reduction
CTP2B0*0			(cyclophosphamide)
Val16Ala			Possible decreased survival (cyclophosphamide)
CYP2B6*2			Possible decreased risk for hemorrhagic cystitis
			(cyclophosphamide)
0002201C T			Possible decreased risk of adverse drug reaction
88033910>1			(cyclophosphamide-doxorubicin-5FU)
1017100/T>C			Possible increased overall survival (melphalan-
181/19841>C			multiple myeloma)
101701500 \			Possible increased overall survival (melphalan-
181/8152G>A			multiple myeloma)
36974946G>A			Possible decreased likelihood for breast
			neoplasms/t-ML (dacarbazine-procarbazine)
Ile443Val			Possible increased survival (bleomycin-testicular
			neoplasms)
	CYP2B6*6 Val16Ala CYP2B6*2 8803391G>T 18171984T>C 18178152G>A 36974946G>A	CYP2B6*4 Image: CYP2B6*6   CYP2B6*6 Image: CYP2B6*2   Val16Ala Image: CYP2B6*2   S803391G>T Image: CYP2B6*2   18171984T>C Image: CYP2B6*2   18178152G>A Image: CYP2B6   36974946G>A Image: CYP2B6*2	CYP2B6*4 I   CYP3A4*1B I   CYP2B6*6 I   Val16Ala I   CYP2B6*2 I   8803391G>T I   18171984T>C I   18178152G>A I   36974946G>A I

## **TOPO I Inhibitors**

Gene	Polymorphism	Res	sult	Outcome
ENOSF1	145-370delT			Possible decreased risk of disease progression (5FU-irinotecan-leucovorin)
UGT1A	172270T>G			Possible increased risk of Neutropenia (irinotecan)
UGT1A1	Gly71Arg			Possible decreased risk of Neutropenia (irinotecan)
UBE2I	157C>G			Possible decreased response to cisplatin-irinotecan

Mr/Ms \_\_\_\_\_\_ Industrial Area of Florina, GR 53100 – Florina, Greece Tel.: +30 23850 41950, 41951, 41960, 41961, Fax.: +30 23850 41931 Website: www.rgcc-genlab.com E-mail:papasotiriou.ioannis@rgcc-genlab.com

# **TOPO II Inhibitors**

Gene	Polymorphism	Result	Outcome
ABCB1	Ile1145Ile		Possible decreased response to anthracycline
ADCD1			regimens and doxorubicin metabolites
RAC2	12536A>T		Possible increased risk for cardiotoxicity
IMIC2	1255011/1		(doxorubicin-non Hodgkin lymphoma)
ABCC2	Val1188Glu		Possible decreased risk for cardiotoxicity
	, un roo oru		(doxorubicin-non Hodgkin lymphoma)
NOS3	Asp298Glu		Possible longer disease-free survival
			(cyclophosphamide-doxorubicin-5FU-MTX)
NCF4	-368G>A		Possible decreased risk for cardiotoxicity
			(doxorubicin-non Hodgkin lymphoma) Possible decreased metabolism of doxorubicin
ABCB1	Ser893Ala		(breast)
CDD1	A 1a 200 A 1a		Possible increased clearance of doxorubicin
CBR1	Ala209Ala		
CYB2B6	CYP2B6*6		Possible no requirement for dose reduction
			(cyclophosphamide-doxorubicin) Possible decreased risk for cardiotoxicity
ABCC1	Gly671Val		(doxorubicin-non Hodgkin lymphoma)
			Possible increased risk for cardiotoxicity
CYBA	Tyr72His		(doxorubicin-non Hodgkin lymphoma)
			Possible decreased likelihood of dose delay
SLC22A16	His49Arg		when treated with cyclophosphamide and
	1100128		doxorubicin
	O 1515T		Possible increased risk for cardiotoxicity
ABCC2	Cys1515Tyr		(doxorubicin-non Hodgkin lymphoma)
CBR1	133G>A		Possible increased clearance of doxorubicin
	0002201C T		Possible decreased risk of adverse drug reaction
ABCC4	8803391G>T		(cyclophosphamide-doxorubicin-5FU)
			Possible increased drug response/decreased
GSTP1	Ile105Val		severity of toxicity (cyclophosphamide-
			epirubicin)
NRP2	110077C>G		Possible increased response to daunorubicin
CBR3	Val244Met		Possible increased risk of cardiac damage after
CDKJ			anthracycline exposure
Chromosome	47386987A>G		<b>Describle lower risk of torigity (stoposide)</b>
12	4/30030/A>U		Possible lower risk of toxicity (etoposide)
			Possible decreased likelihood of drug toxicity
MTHFR	Ala222Val		(cisplatin-cyclophosphamide-dactinomycin-
			doxorubicin-MTX-vincristine) in Osteosarcoma
			Possible decreased likelihood of drug toxicity
MTR	Asp919Gly		(cisplatin-cyclophosphamide-dactinomycin-
			doxorubicin-MTX-vincristine) in Osteosarcoma

# **ANTIMETABOLITES**

Gene	Polymorphism	Resu	ılt	Outcome
<b>TP53</b>	Pro33Arg			Possible increased risk for toxicity/
	1100001115			decreased survival
ABCB1	Ile1145Ile			Possible increased risk of Neutropenia and Neurotoxicity syndromes
ERCC2	Lys751Gln			Possible increased risk of drug toxicity (5FU- leucovorin-oxaliplatin)
<u>GSTP1</u>	Ile105Val			Possible poorer treatment outcome (5FU-oxaliplatin in colorectal)
NOS3	Asp298Glu			Possible longer disease-free survival (cyclophosphamide-doxorubicin-5FU-MTX)
MTHFR	Glu429Ala			Possible decreased risk of drug toxicity (capecitabine)
<u>MTHFR</u>	Ala222Val			Possible decreased risk and severity of mucositis (MTX- leukemia or lumphoma)/ Possible increased risk of drug toxicity (5FU- capecitabine)
<u>DPYD</u>	Ile543Val			Possible decreased likelihood of middle-severe nausea/ vomiting/white blood cell decreases (5FU)
DPYD	Cys29Arg			Possible increased likelihood or middle-severe nauseas/vomiting (5FU)
DPYD	Met166Val			Possible decreased risk of drug toxicity (fluoropyrimidines)
XRCC1	Gln399Arg			Possible decreased response to fluorouracil- containing chemotherapy regimens
ENOSF1	145-370delT			Possible decreased risk of disease progression (5FU-irinotecan-leucovorin)
DPYD	1905+1G>A			Possible increased risk of drug toxicity (fluoropyrimidines based chemotherapy)
DPYD	Asp949Val			Possible increased clearance and decreased risk of drug toxicity (fluoropyrimidines)
ABCC4	8803391G>T			Possible decreased risk of adverse drug reaction (cyclophosphamide-doxorubicin-5FU)
GALNT14	10069401G>T			Possible decreased response (cisplatin-5-FU-mitoxantrone)
<u>CDA</u>	20915590delC			Possible increased risk of drug toxicity (cytarabine)
<u>SLC19A1</u>	His27Arg			Possible decreased risk of hepatotoxicity (MTX)
SLCO1B1	103492T>C			Possible increased clearance of methotrexate/Increased risk for GI toxicity
MTRR	Ile22Met			Possible increased likelihood of methotrexate induced toxicity

Mr/Ms\_

		Possible decreased likelihood of drug toxicity/
MTR	Asp919Gly	<b>.</b>
	1 2	increased response to MTX
SHMT1	Leu435Phe	Possible decreased catalytic activity of TYMS/
		Decreased likelihood of toxic liver disease
MTHFD1	Arg653Gln	Possible decreased event free survival
SLCO1B1	Val174Ala	Possible increased clearance of methotrexate
SLCO1B1	14138145G>A	Possible increased clearance of methotrexate/ Increased risk of GI toxicity
<u>CCND1</u>	Pro241Pro	Possible increased time-to-tumor recurrence when treated with 5FU
ABCC3	-260T>A	Possible decreased event-free survival/ Decreased risk of thrombocytopenia when treated with MTX
<u>CDA</u>	Lys27Gln	Possible decreased risk of toxicity when treated with cytarabine/ Possible lower frequency of GI toxicity/ Decreased risk of developing Neutropenia when treated with gemcitabine
<u>CDA</u>	-451C>T	Possible reduced toxicity / Increased survival time when treated with cytarabine
<u>CDA</u>	-92A>G	Possible decreased risk of diarrhea or dehydration when treated with capecitabine
<u>CDA</u>	Ala70Thr	Possible increased clearance of gemcitabine/ Decreased severity of neutropenia
<u>RRM1</u>	Thr741Thr	Possible decreased risk of toxicity (Neutropenia) when treated with gemcitabine

## SPINDLE POISONS

Gene	Polymorphism	Result	Outcome
ABCB1	Ser893Ala		Possible decreased risk for resistance to taxanes
<u>TP53</u>	Pro33Arg		Possible increased risk for toxicity/ decreased survival
<u>ABCB1</u>	Ile1145Ile		Possible increased risk of Neutropenia and Neurotoxicity syndromes (paclitaxel)
<u>CYP1B1</u>	Leu432Val		Possible shorter disease-free progression (docetaxel-paclitaxel-taxanes)
<u>CYP2C8</u>	23210C>G		Possible increased risk of neurotoxicity (paclitaxel)
<u>CYP2C8</u>	Arg69Lys		Possible decreased risk of neurotoxicity (paclitaxel)
<u>CYP3A5</u>	12083G>A		Possible increased risk of neurotoxicity (paclitaxel)
<b>DSCAM</b>	27076915T>C		Possible increased survival (carboplatin-paclitaxel)
NAT2	NAT2*7A		Possible decreased risk of toxicity (docetaxel- thalidomide)
CYP3A4	CYP3A4*1B		Possible decreased clearance of docetaxel

### **Appendix:**

### Drug Metabolism:

#### Phase I:

Phase I enzymes are responsible reactions that convert parent compound into a more polar metabolite by adding or unmasking functional groups. Usually these metabolites are inactive. Phase I reactions include, oxidation, reduction, hydrolytic cleavage, alkylation, methylation, ring cyclization etc. These reactions prepare chemicals for phase II metabolisms and subsequent excretion.

The Cytochrome P450 (CYP) enzyme superfamily is the most important system in the biotransformation of many endogenous and exogenous substances, such as drugs, toxins and carcinogens. For drug metabolism the most important polymorphisms are those of the genes coding for CYP2C9, CYP2C19, CYP2D6 and CYP3A4. CYP1A1 and CYP1A2 are among the most responsible for biotransformation of chemicals, especially for the metabolic activation of precarcinogens. Genetic polymorphism is an important reason for variations in drug response of the human body. There are four distinct phenotypes: poor metaboliser (PM), intermediate metaboliser (IM), extensive metaboliser (EM) and ultrarapid metaboliser (UM). A poor metaboliser lacks active allele and may present adverse effects at usual doses, due to reduced metabolism and increased drug concentration. Individuals with intermediate metabolic phenotype are homozygous for two reduced activity alleles or are heterozygous for an inactive allele. Extensive metabolisers have two fully active allele and show the expected response to a standard dose. Ultra extensive metabolisers are individuals with more than two copies of active gene.

- Cytochrome P450 2D6 is one of the most important enzymes, involved in the metabolisms of xenobiotics in the body, but also in activation of many substances in their active compounds.
- Cytochrome P450 2C19 is responsible for metabolisation or activation of many hormones and drugs (anti-epileptics, anti-depressants, anti-platelet clopidogrel, esomeprazole).
- Cytochrome P450 1A2 is involved in metabolism of xenobiotics substrates such caffeine, aflatoxin B1 and acetaminophen.

- Cytochrome P450 3A4 is one of the most important enzymes involved in xenobiotics metabolism in human body. It metabolizes some steroids and carcinogens. Approximately half of the drugs that are used are metabolized by this protein, such acetaminophen, codeine, cyclosporine, diazepam and erythromycin.
- Cytochrome P450 2C9 is an enzyme with a major role in the oxidation of both xenobiotics and endogenous compounds. Warfarin, phenytoin, acenocoumarol, tolbutamide, losartan glipizide and a few nonsteroidal anti-inflammatory drugs (aspirin, ibuprofen, naproxen) are metabolized by CYP2C9.

#### Phase II:

The Phase II reactions are conjugations with endogenous substrate to further increase aqueous solubility and conjugations with glucoronide, sulfate, acetate, amino acid etc. N-acetyltransferase 2 (NAT2), Epoxide hydrolase 1 (EPHX1), Glutathione S-transferase P (GSTP1) and Thiopurine methyltransferase (TPMT) are the major enzymes involved in phase II drug metabolism.

- N-acetyltransferase 2 (NAT2), is an enzyme that activates and deactivates arylamine and hydrazine drugs and carcinogens. Human populations segregated into rapid, intermediate and slow acetylator phenotypes, according to different polymorphisms combinations.
- Glutathione S-transferases are responsible for the detoxification of a range of drugs and potential carcinogens, through glutathione conjucation. The GSTP1 is associated with xenobiotics metabolism and susceptibility to cancer and other diseases.
- Thiopurine S-methyltransferase (TPMT) is an enzyme that metabolises thiopurine drugs such as azathioprine, 6-mercaptopurine and 6-thioguanine. Individual homozygous for two non-functional TPMT variants are at high risk for toxic side effects, due to decreased methylation and decreased inactivation of 6MP.

#### Pharmacodynamics:

- P-glycoprotein 1, or multidrug resistance protein 1, or ATP-binding cassette sub-family B member 1 (ABCB1), or CD243, is an ATP-dependent drug efflux pump for xenobiotics compounds with broad substrate specificity. ABCB1 regulates the distribution and bioavailability if drugs, removes toxic metabolites and xenobiotics from cells, transports compounds out of brain and protects hematopoietic stem cells from toxins.
- ATP-binding cassette sub-family G member 2 (ABCG2), is a xenobiotic transporter with important role in the multidrug resistance phenotype of several cancer cell lines.

Sincerely,

Panagiotis Apostolou Molecular Biologist Ioannis Papasotiriou MD., PhD Head of molecular medicine dpt. of R.G.C.C.-RESEARCH GENETIC CANCER CENTRE LTD