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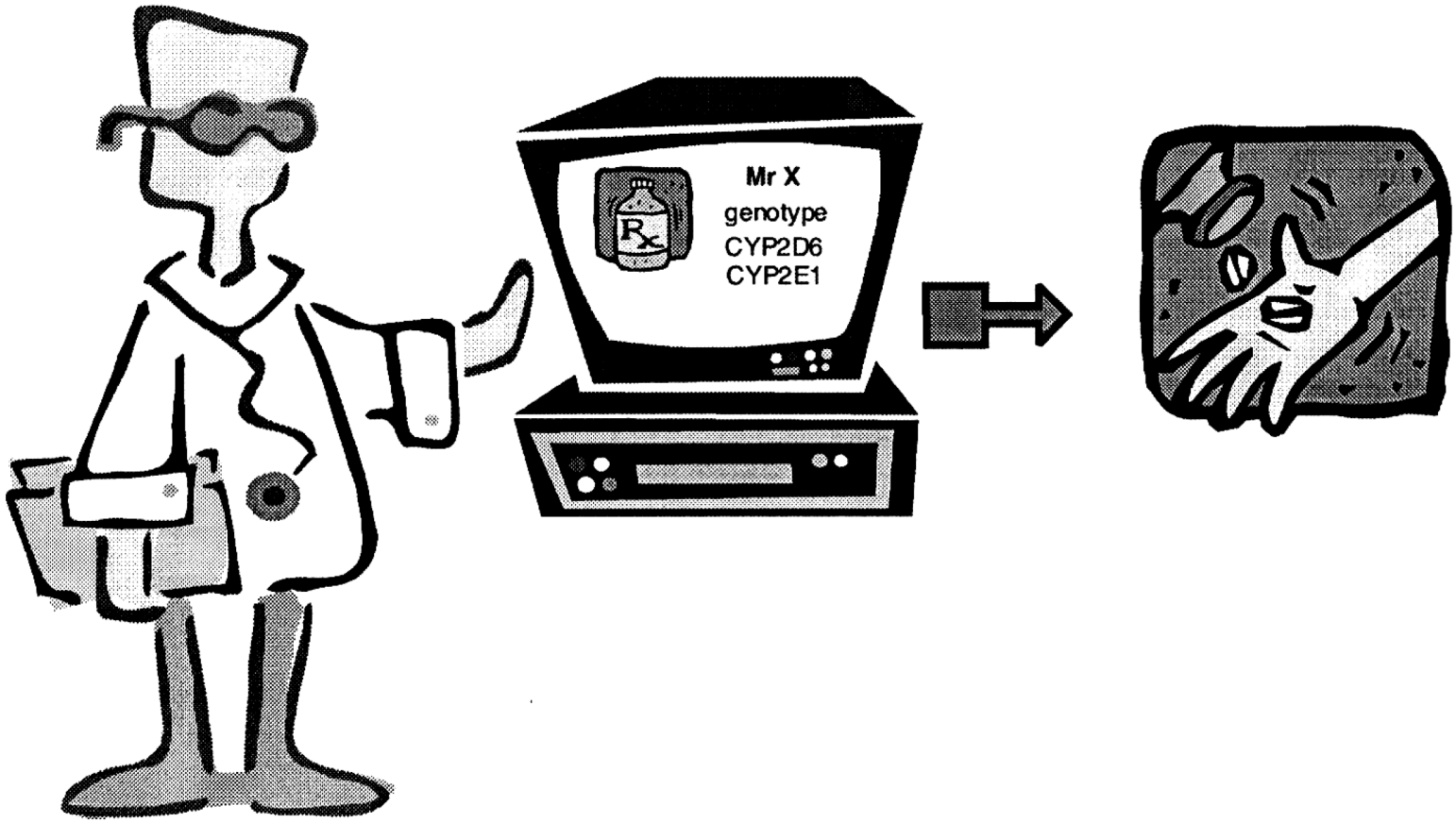
Dose / Concentração Plasmática

- medicamento
- paciente
- fármacos associados

POLYMORPHISMS

Figure 2. The future of prescribing.



Projected future scenario where the patient has been screened for important polymorphisms that are involved in the regulation of a number of drugs. This information will be recorded electronically, (say by a 'smart card') and the information fed into a computer, which has software that advises the doctor about appropriate prescribing.

CYP: Cytochrome P450.

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REFARGEN

REDE NACIONAL DE FARMACOGENÉTICA

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CPIC®
Clinical Pharmacogenetics Implementation Consortium

- CPIC guidelines are designed to help clinicians understand HOW available genetic test results should be used to optimize drug therapy.

Varfarina: CYP2C9 e VKORC1

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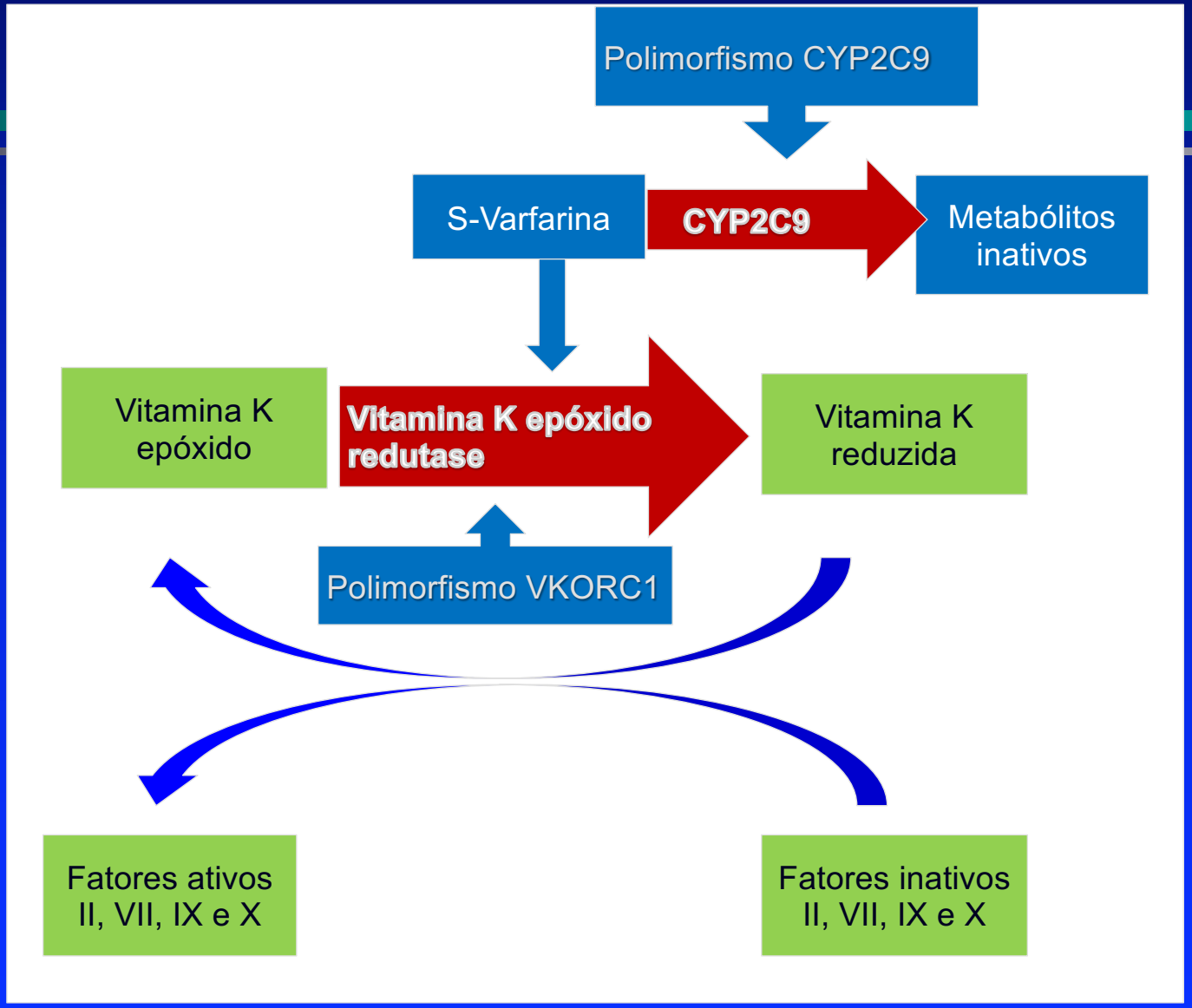

INR=2-3
(doses de 1-20mg/dia)

$INR = T_{teste} / T_{pool\ normal}$

Kim et al., 2009

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CYP2C9

CYP2C9 PHENOTYPES BASED ON GENOTYPES

Table 1 Assignment of likely phenotype based on genotypes

Assignment of likely CYP2C9 phenotype based on genotype

Likely phenotype[a]	Genotype	Examples of diplotypes
Extensive metabolizer (normal activity) (constitutes ~91% of patients)	An individual carrying two normal-function alleles	*1/*1
Intermediate metabolizer (heterozygote or intermediate activity) (constitutes ~8% of patients)[c]	An individual carrying one normal-function allele plus one decreased-function allele	*1/*3, *1/*2
Poor metabolizer (homozygous variant, low or deficient activity) (constitutes ~1% of patients)	An individual carrying two decreased-function alleles	*2/*2, *3/*3, *2/*3

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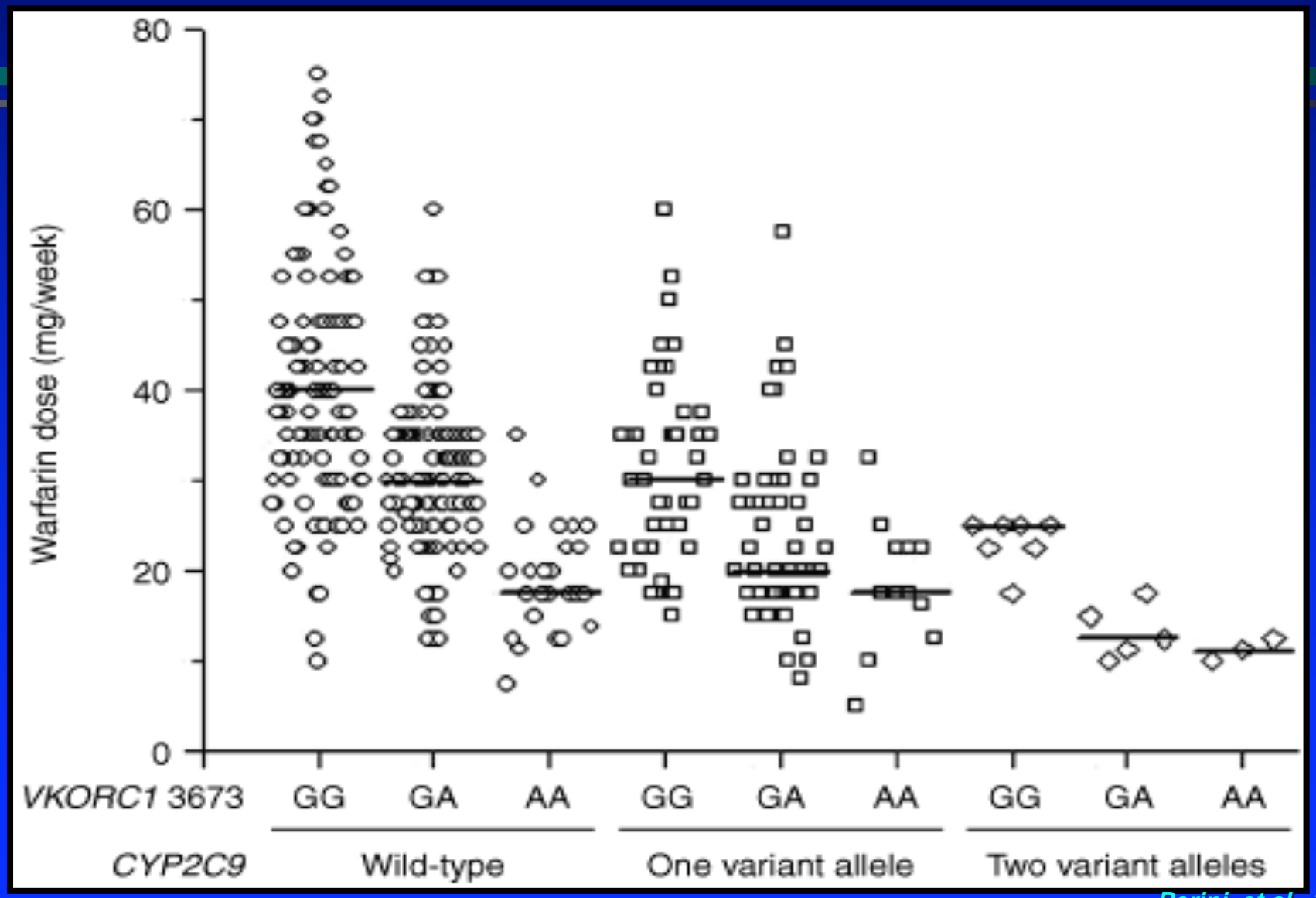
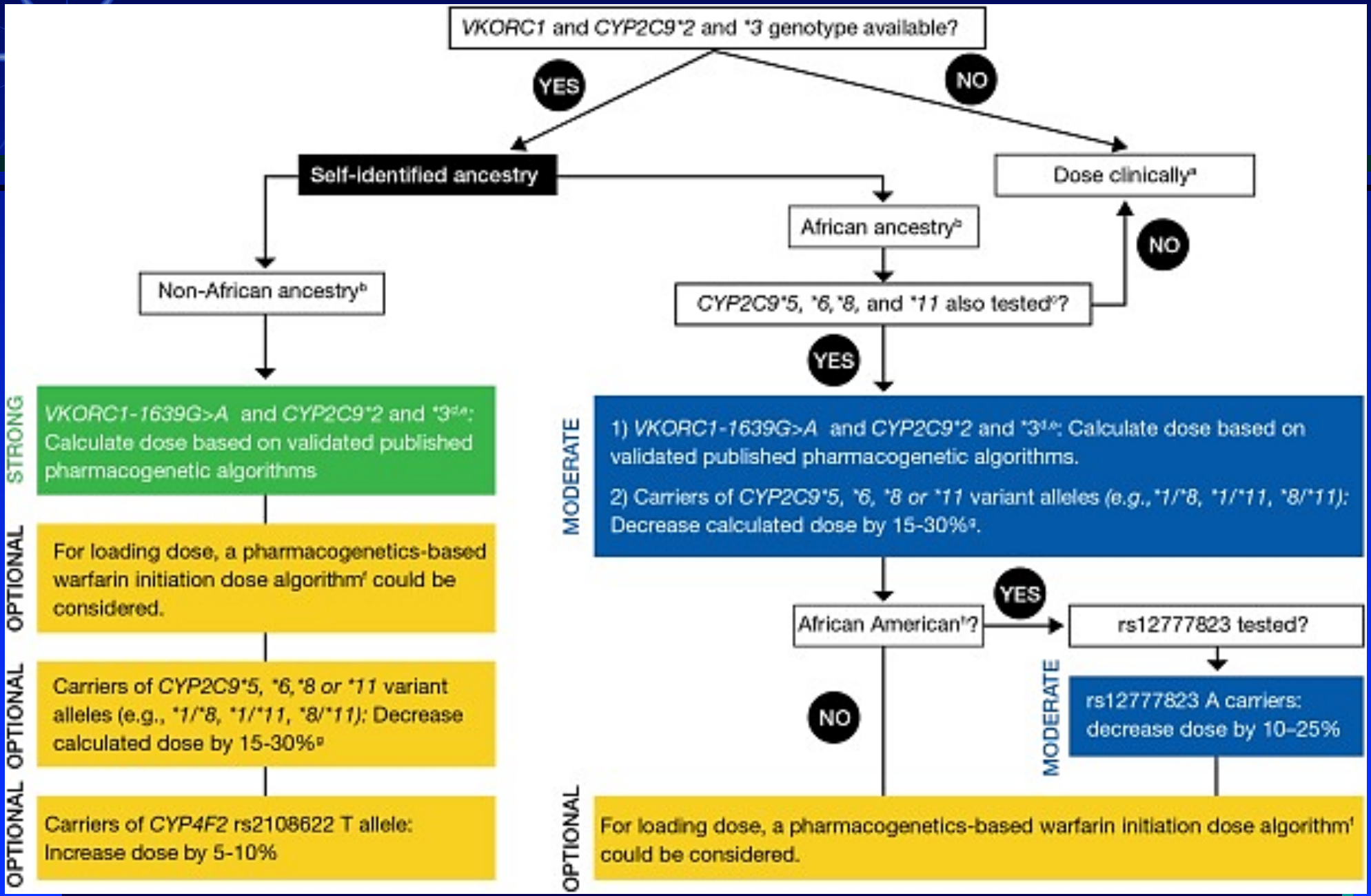
Warfarin Therapy



Perini et al., 2008

CPIC GUIDELINE FOR PHARMACOGENETICS-GUIDED WARFARING DOSING: 2017 UPDATE



Dosing Recommendations with Consideration of Genotype

Table 1: Three Ranges of Expected Maintenance COUMADIN Daily Doses Based on CYP2C9 and VKORC1 Genotypes†

VKORC1	CYP2C9					
	*1/*1	*1/*2	*1/*3	*2/*2	*2/*3	*3/*3
GG	5-7 mg	5-7 mg	3-4 mg	3-4 mg	3-4 mg	0.5-2 mg
AG	5-7 mg	3-4 mg	3-4 mg	3-4 mg	0.5-2 mg	0.5-2 mg
AA	3-4 mg	3-4 mg	0.5-2 mg	0.5-2 mg	0.5-2 mg	0.5-2 mg

†Ranges are derived from multiple published clinical studies. VKORC1 –1639G>A (rs9923231) variant is used in this table. Other co-inherited VKORC1 variants may also be important determinants of warfarin dose.

Table 1 displays three ranges of expected maintenance COUMADIN doses observed in subgroups of patients having different combinations of CYP2C9 and VKORC1 gene variants [see *Clinical Pharmacology (12.5)*]. If the patient's CYP2C9 and/or VKORC1 genotype are known, consider these ranges in choosing the initial dose. Patients with CYP2C9 *1/*3, *2/*2, *2/*3, and *3/*3 may require more prolonged time (>2 to 4 weeks) to achieve maximum INR effect for a given dosage regimen than patients without these CYP variants.

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Bula Varfarina Brasil Coumadin®

A Varfarina Sódica é estereosseletivamente metabolizada por enzimas microssômicas hepáticas do citocromo P-450 (CYP450) em metabólitos hidroxilados inativos (via predominante), e por redutases em metabólitos reduzidos (álcoois de Varfarina Sódica), com atividade anticoagulante mínima. Os metabólitos da Varfarina Sódica identificados incluem a d-hidrovarfarina, dois álcoois diastereoisômeros e 4-, 6-, 7-, 8- e 10-hidroxivarfarina. As isoenzimas do citocromo P-450 envolvidas no metabolismo da Varfarina Sódica incluem a 2C9, 2C19, 2C8, 2C18, 1A2 e 3A4. O CYP2C9, uma enzima polimórfica, é provavelmente a principal forma do P-450 hepático humano que modula a atividade anticoagulante *in vivo* da Varfarina Sódica. Pacientes com uma ou mais variações dos alelos da isoenzima 2C9 apresentam um *clearance* da S-varfarina diminuído.

CYP2D6 phenotypes based on genotype

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LIKELY PHENOTYPE	ACTIVITY SCORE	GENOTYPES	EXAMPLE OF DIPLOTYPES
Ultrarapid metabolizer (~1-2% of patients)	> 2.0	An individual carrying duplications of functional alleles	(*1/*1)xN (*1/*2)xN (*2/*2)xN
Extensive metabolizer (~77-92% of patients)	1.0 – 2.0	An individual carrying two functional alleles or two reduced function alleles or one functional and non functional allele or one functional and reduced function allele	*1/*1, *1/*2, *2,*2, *1/*9, *1/*41, *41/*41, *1/*5, *1/*4
Intermediate metabolizer (~2-11% of patients)	0.5	An individual carrying one reduced function and one nonfunctional allele	*4/*41, *5/*9, *4/*10
Poor metabolizer (~5-10% of patients)	0	An individual carrying only nonfunctional alleles	*4/*4, *3/*4, *5/*5, *5/*6

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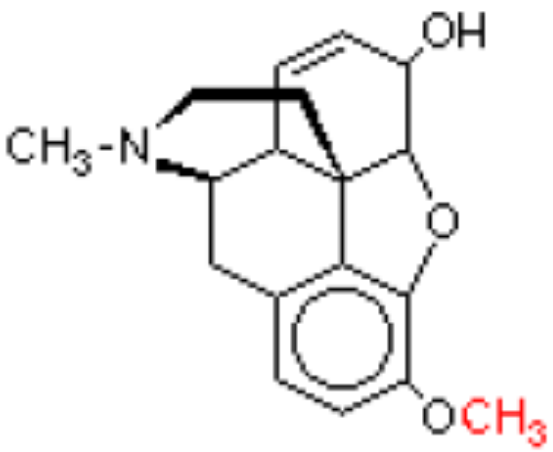
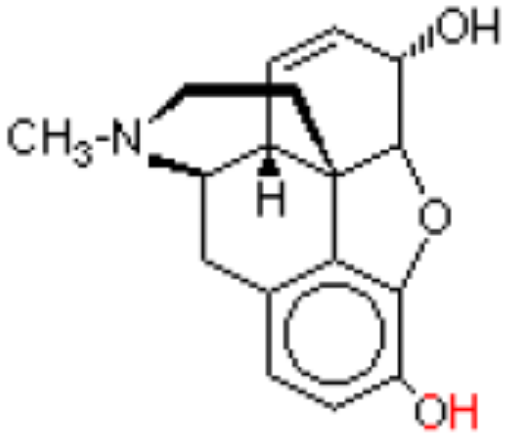
Codeine



5-10%

CYP2D6



$C_{18}H_{21}NO_3$

$C_{17}H_{19}NO_3$

codeine

morphine

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Codeine therapy recommendations based on CYP2D6 phenotype

Codeine therapy recommendations based on cytochrome P450 2D6 (CYP2D6) phenotype

Phenotype	Implications for codeine metabolism	Recommendations for codeine therapy	Classification of recommendation for codeine therapy[a]	Considerations for alternative opioids
Ultrarapid metabolizer	Increased formation of morphine following codeine administration, leading to higher risk of toxicity	Avoid codeine use due to potential for toxicity.	Strong	Alternatives that are not affected by this CYP2D6 phenotype include morphine and nonopioid analgesics. Tramadol and, to a lesser extent, hydrocodone and oxycodone are not good alternatives because their metabolism is affected by CYP2D6 activity.[b,c]
Extensive metabolizer	Normal morphine formation	Use label-recommended age- or weight-specific dosing.	Strong	—
Intermediate metabolizer	Reduced morphine formation	Use label-recommended age- or weight-specific dosing. If no response, consider alternative analgesics such as morphine or a nonopioid.	Moderate	Monitor tramadol use for response.
Poor metabolizer	Greatly reduced morphine formation following codeine administration, leading to insufficient pain relief	Avoid codeine use due to lack of efficacy.	Strong	Alternatives that are not affected by this CYP2D6 phenotype include morphine and nonopioid analgesics. Tramadol and, to a lesser extent, hydrocodone and oxycodone are not good alternatives because their metabolism is affected by CYP2D6 activity; these agents should be avoided.[b,c]

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Exercício 1

A tabela abaixo mostra os valores de clearance total, clearance renal e a correlação entre o clearance total e o fenótipo para o CYP2D6 para diferentes β-bloqueadores:

Fármaco	clearance total (L/h)	clearance renal (L/h)	Correlação entre o clearance total e o fenótipo para o CYP2D6
atenolol	5,0	4,3	Fraca
metoprolol	63,0	6,0	Forte
propranolol	50,0	<0,3	Fraca
timolol	31,0	4,7	Forte

a) Discutir as possíveis razões para as correlações observadas.

b) Qual o impacto dos dados no regime de dosagem dos referidos fármacos?

CYP2C19 phenotypes based on genotypes

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LIKELY PHENOTYPE	GENOTYPES	EXAMPLE OF DIPLOTYPES
PHENOTYPE		
Ultrarapid metabolizer : normal or increased activity (~5-30% of patients)	An individual carrying two increased activity alleles (*17) or one functional allele (*1) plus one increased-activity allele (*17)	*1/*17, *17/*17
Extensive metabolizer : homozygous wild-type or normal activy (~35-50% of patients)	An individual carrying two functional (*1) alleles	*1/*1
Intermediate metabolizer : heterozygote or intermediate activity (~18-45% of patients)	An individual carrying one functional allele (*1) plus one loss-of-function allele (*2-*8) or one loss-of-function allele (*2-*8) plus one increased-activity allele (*17)	*1/*2, *1/*3, *2/*17
Poor metabolizer: homozygous variant, mutant, low, or deficient activity (~2-15% of patients)	An individual carrying two loss-of-function alleles	*2/*2, *2/*3, *3/*3

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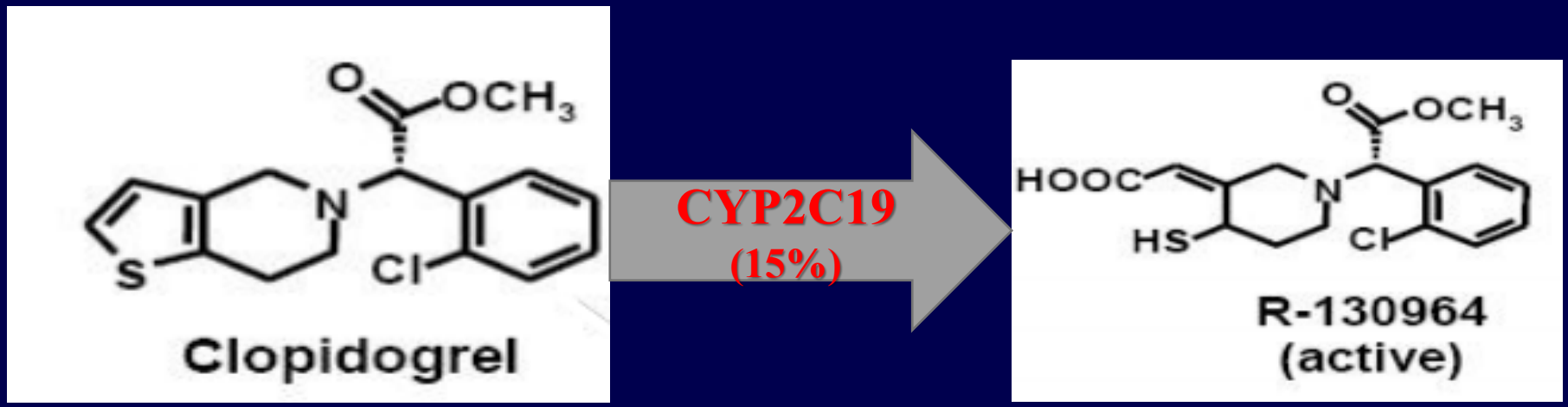
CYP2C19



Pró-fármaco

Metabólito ativo

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Antiplatelet therapy recommendations based on CYP2C19: clopidogrel

PHENOTYPE (GENOTYPE)	IMPLICATIONS FOR CLOPIDOGREL	THERAPEUTIC RECOMMENDATIONS	CLASSIFICATION OF RECOMMENDATIONS
Ultrarapid metabolizer (*1/*17, *17/*17,) and extensive metabolizer (*1/*1)	Normal (EM) or increased (UM) platelet inhibition	Clopidogrel: label-recommended dosage and administration	Strong
Intermediate metabolizer (*1/*2, *1/*3, *2/*17)	Reduced platelet inhibition and increased risk for adverse cardiovascular events	Alternative antiplatelet therapy (if no contraindication), e.g, prasugrel, ticagrelor	Moderate
Poor metabolizer (*2/*2, *2/*3, *3/*3)	Significantly reduced platelet inhibition and increased risk for adverse cardiovascular events	Alternative antiplatelet therapy (if no contraindication), e.g, prasugrel, ticagrelor	Strong

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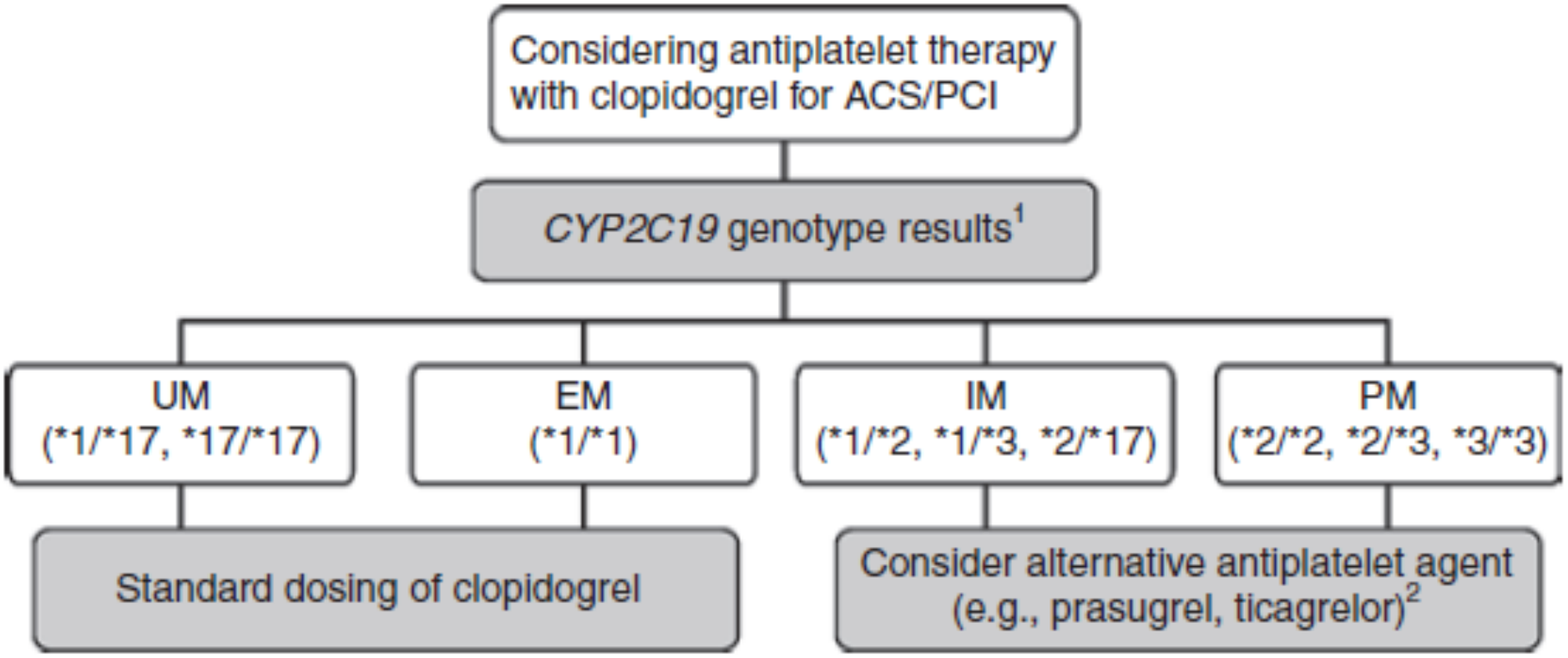
CPIC guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update



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clopidogrel - FDA

WARNING: DIMINISHED ANTIPLATELET EFFECT IN PATIENTS WITH TWO LOSS-OF-FUNCTION ALLELES OF THE CYP2C19 GENE

See full prescribing information for complete boxed warning.

- **Effectiveness of Plavix depends on conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1, 12.3)**
- **Tests are available to identify patients who are CYP2C19 poor metabolizers. (12.5)**
- **Consider use of another platelet P2Y12 inhibitor in patients identified as CYP2C19 poor metabolizers. (5.1)**

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Bula clopidogrel - Brasil

Populações especiais

Farmacogenética: pacientes que apresentam um estado de metabolizador lento da enzima CYP2C19 (enzima localizada no fígado) apresentam uma diminuição da resposta antiplaquetária do clopidogrel. Uma posologia maior para estes pacientes aumenta a resposta antiplaquetária. O uso de doses maiores de clopidogrel deve ser considerado, porém a posologia apropriada para esta população de pacientes não foi estabelecida em ensaios clínicos.

Considerando as recomendações do CPIC, qual o erro dessa bula?

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Exercício 2

- Uma paciente de 74 anos com doença coronária aguda iniciou o tratamento com clopidogrel após uma intervenção coronariana (angioplastia). Após múltiplos episódios de reestenose (estreitamento do vaso com redução do fluxo sanguíneo), a equipe clínica suspeita de resistência ao clopidogrel e solicita o teste de genotipagem para CYP2C19.
- **O exame revelou que a paciente apresenta o genótipo CYP2C19 *2/*2.**
- 1) Qual o fenótipo da paciente?
- 2) Qual o melhor tratamento para esta paciente segundo o CPIC?

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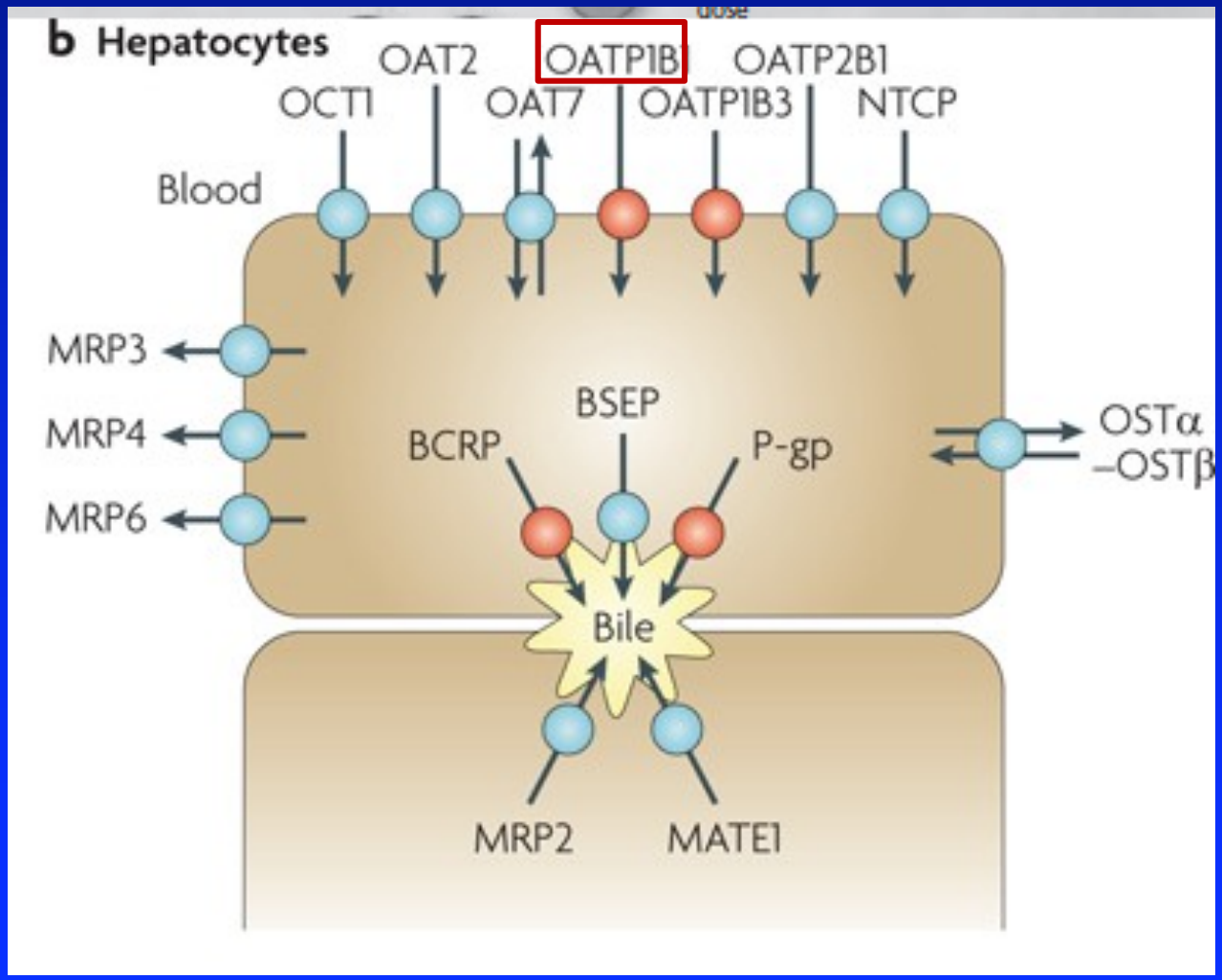
OATP1B1 – gene SLCO1B1



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OATP1B1 phenotypes based on genotypes

Assignment of likely SLCO1B1 phenotype based on genotype

Phenotype	Genotype definition	Examples of diplotypes	Genotype at rs4149056
Normal function; homozygous wild type or normal (55–88% of patients[a])	An individual carrying two normal-function alleles	**1a/*1a, *1a/*1b, *1b/*1b*	TT
Intermediate function; heterozygous (11–36% of patients[a])	An individual carrying one normal-function allele plus one decreased-function allele	**1a/*5, *1a/*15, *1a/*17, *1b/*5, *1b/*15, *1b/*17*	TC
Low function; homozygous variant or mutant (0–6% of patients[a])	An individual carrying two decreased-function alleles	**5/*5, *5/*15, *5/*17, *15/*15, *15/*17, *17/*17*	CC

[a]Frequency of the polymorphism varies by ancestral group (**Supplementary Tables S3** and **S4** online).

Dosing recommendations for simvastatin based on OATP1B1 phenotype

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Dosing recommendations for simvastatin based on SLCO1B1 phenotype

Phenotype	Implications for simvastatin	Dosing recommendations for simvastatin[a,b]	Classification of recommendations[c]
Normal function	Normal myopathy risk	Prescribe desired starting dose[b] and adjust doses of simvastatin based on disease-specific guidelines	Strong
Intermediate function	Intermediate myopathy risk	Prescribe a lower dose or consider an alternative statin (e.g., pravastatin or rosuvastatin); consider routine CK surveillance	Strong
Low function	High myopathy risk	Prescribe a lower dose or consider an alternative statin (e.g., pravastatin or rosuvastatin); consider routine CK surveillance	Strong

CK, creatine kinase.

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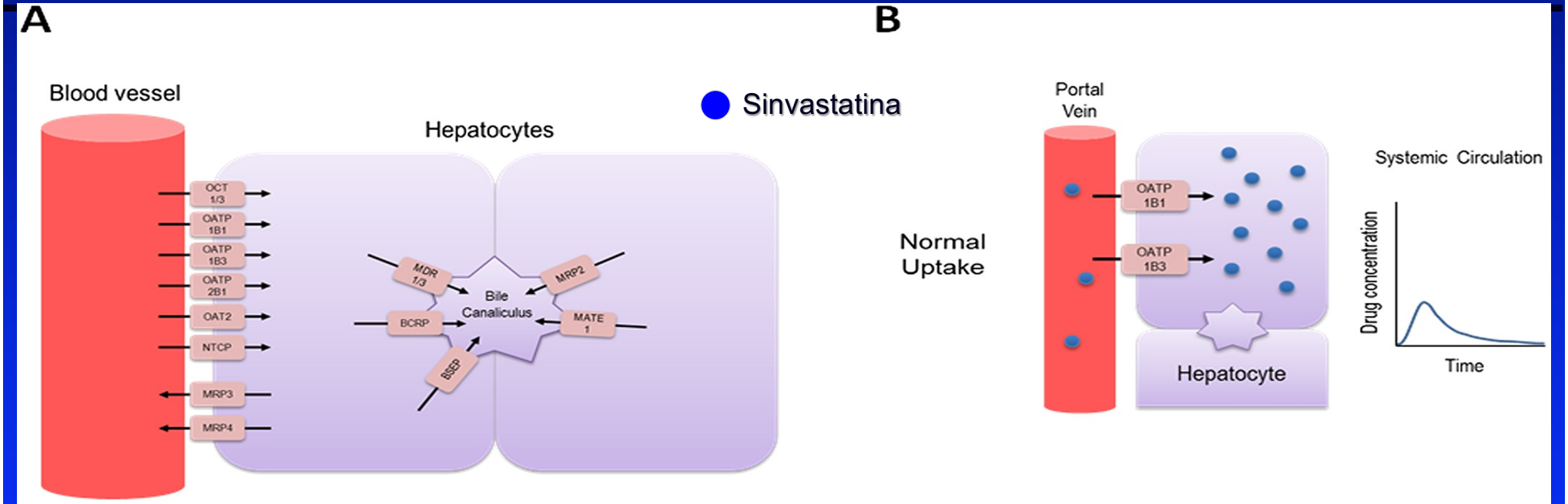
Exercício 3



a) Qual o perfil concentração plasmática versus tempo (em comparação ao gráfico padrão) esperado para a sinvastatina em um paciente que apresenta baixa atividade da OATP1B1?

b) Espera-se maior ou menor risco de miopatia neste paciente? Explique.

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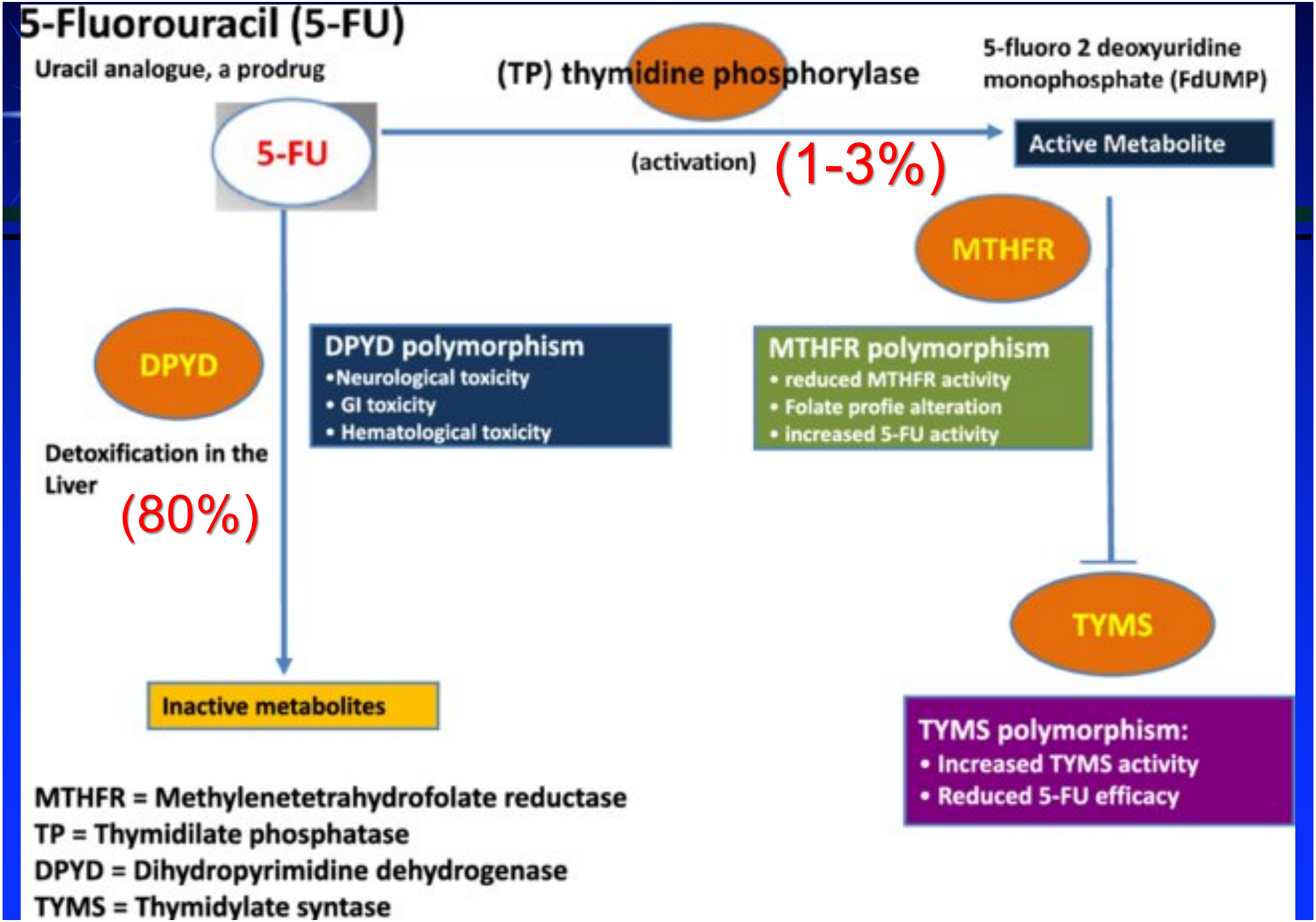
Dihydropyrimidine dehydrogenase genotype

Table 1 Assignment of likely DPD phenotypes based on *DPYD* genotypes

Likely phenotype	Activity score[a]	Genotypes[b]	Examples of genotypes[c]
DPYD normal metabolizer	2	An individual carrying two normal function alleles.	c.[=];[=], c.[85T>C];[=], c.[1627A>G];[=]
DPYD intermediate metabolizer	1 or 1.5	An individual carrying one normal function allele plus one no function allele or one decreased function allele, or an individual carrying two decreased function alleles.	c.[1905+1G>A];[=], c.[1679T>G];[=], c.[2846A>T];[=]; c.[1129–5923C>G];[=][d]; c.[1129–5923C>G];[1129–5923C>G][d]; c.[2846A>T];[2846A>T]
DPYD poor metabolizer	0 or 0.5	An individual carrying two no function alleles or an individual carrying one no function plus one decreased function allele.	c.[1905+1G>A];[1905+1G>A], c.[1679T>G];[1679T>G], c.[1905+1G>A];[2846A>T] c.[1905+1G>A]; [1129-5923C>G]


5-Fluorouracil (5-FU)
Uracil analogue, a prodrug
(TP) thymidine phosphorylase
5-fluoro 2 deoxyuridine monophosphate (FdUMP)
5-FU
(activation)
(1-3%)
Active Metabolite
MTHFR
DPYD
DPYD polymorphism
•Neurological toxicity
• GI toxicity
• Hematological toxicity
MTHFR polymorphism
• reduced MTHFR activity
• Folate profie alteration
• increased 5-FU activity
Detoxification in the Liver
(80%)
TYMS
Inactive metabolites
TYMS polymorphism:
• Increased TYMS activity
• Reduced 5-FU efficacy
MTHFR = Methylenetetrahydrofolate reductase
TP = Thymidilate phosphatase
DPYD = Dihydropyrimidine dehydrogenase
TYMS = Thymidylate syntase

Recommended dosing of fluoropyrimidines by DPYD phenotype

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Table 2 Recommended dosing of fluoropyrimidines[a] by DPD phenotype

Phenotype	Implications for phenotypic measures	Dosing recommendations	Classification of recommendations[b]
DPYD normal metabolizer	Normal DPD activity and "normal" risk for fluoropyrimidine toxicity.	Based on genotype, there is no indication to change dose or therapy. Use label-recommended dosage and administration.	Strong
DPYD intermediate metabolizer	Decreased DPD activity (leukocyte DPD activity at 30% to 70% that of the normal population) and increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidine drugs.	Reduce starting dose based on activity score followed by titration of dose based on toxicity[c] or therapeutic drug monitoring (if available). **Activity score 1:** Reduce dose by 50% **Activity score 1.5:** Reduce dose by 25% to 50%	**Activity score 1:** Strong **Activity score 1.5:** Moderate
DPYD poor metabolizer	Complete DPD deficiency and increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidine drugs.	**Activity score 0.5:** Avoid use of 5-fluorouracil or 5-fluorouracil prodrug-based regimens. In the event, based on clinical advice, alternative agents are not considered a suitable therapeutic option, 5-fluorouracil should be administered at a strongly reduced dose[d] with early therapeutic drug monitoring.[e] **Activity score 0:** Avoid use of 5-fluorouracil or 5-fluorouracil prodrug-based regimens.	Strong

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Fluorouracil (FDA)

- **Increased Risk of Serious or Fatal Adverse Reactions in Patients with Low or Absent Dipyrimidine Dehydrogenase (DPD)**
- Patients with partial DPD activity may have increased risk of severe, or fatal adverse reactions caused by fluorouracil. There is insufficient data to recommend a specific dose in patients with partial DPD activity as measured by any specific test

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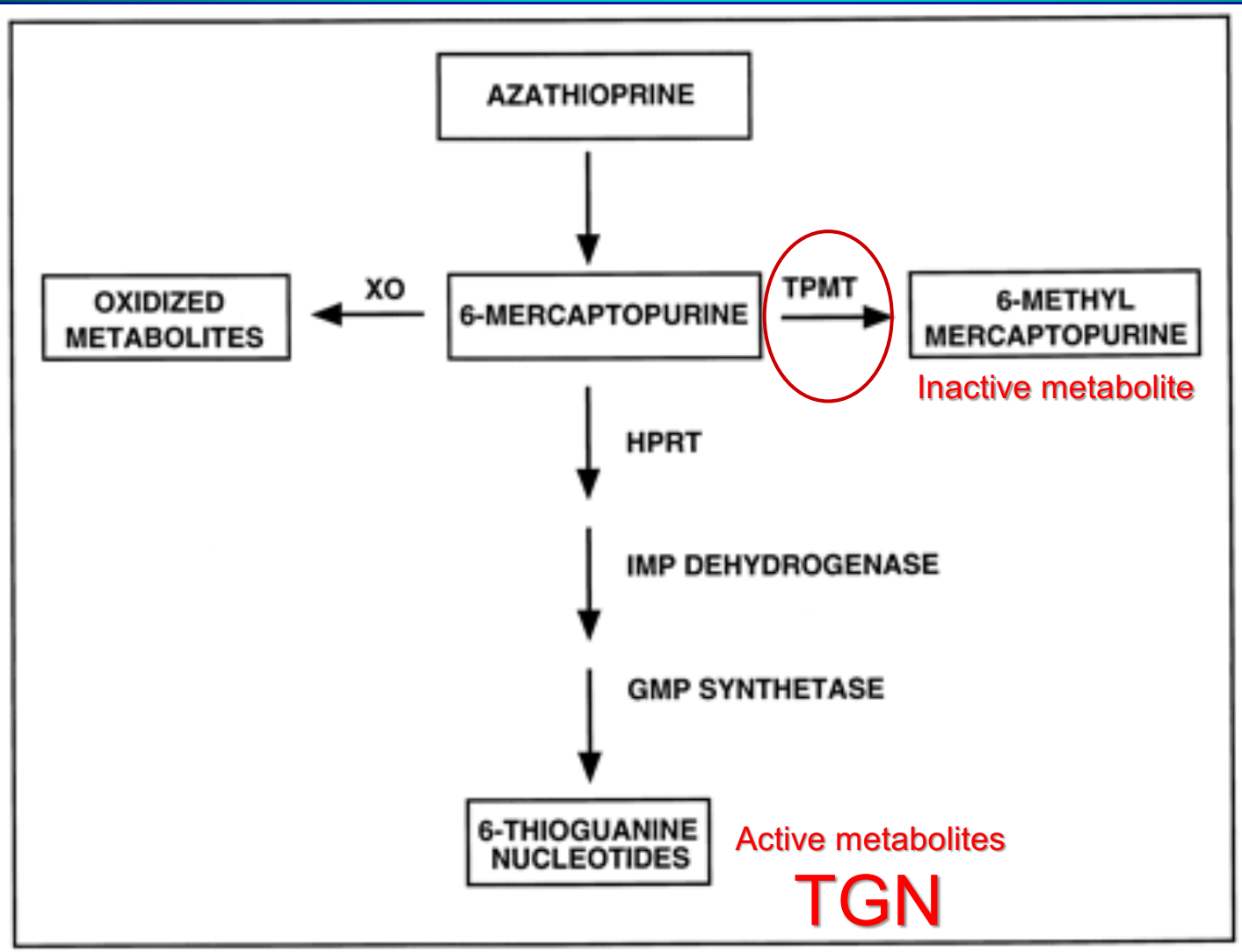
Thiopurine methyltransferase (TPMT)



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Thiopurine methyltransferase (TPMT)

Likely phenotype[a]	Genotypes	Examples of diplotypes
Assignment of likely TPMT phenotypes based on genotypes		
Normal metabolizer	An individual carrying two normal function alleles	*1/*1
Intermediate metabolizer	An individual carrying one normal function allele PLUS one no function allele	*1/*2, *1/*3A, *1/*3B, *1/*3C, *1/*4
Possible intermediate metabolizer	An individual carrying one uncertain/unknown function allele PLUS one no function allele	*2/*8, *3A/*7
Poor metabolizer	An individual carrying two no function alleles	*3A/*3A, *2/*3A, *3A/*3C, *3C/*4, *2/*3C, *3A/*4
Indeterminate	An individual carrying two uncertain/unknown function alleles OR one normal function allele plus one uncertain allele function allele	*6/*8 *1/*8

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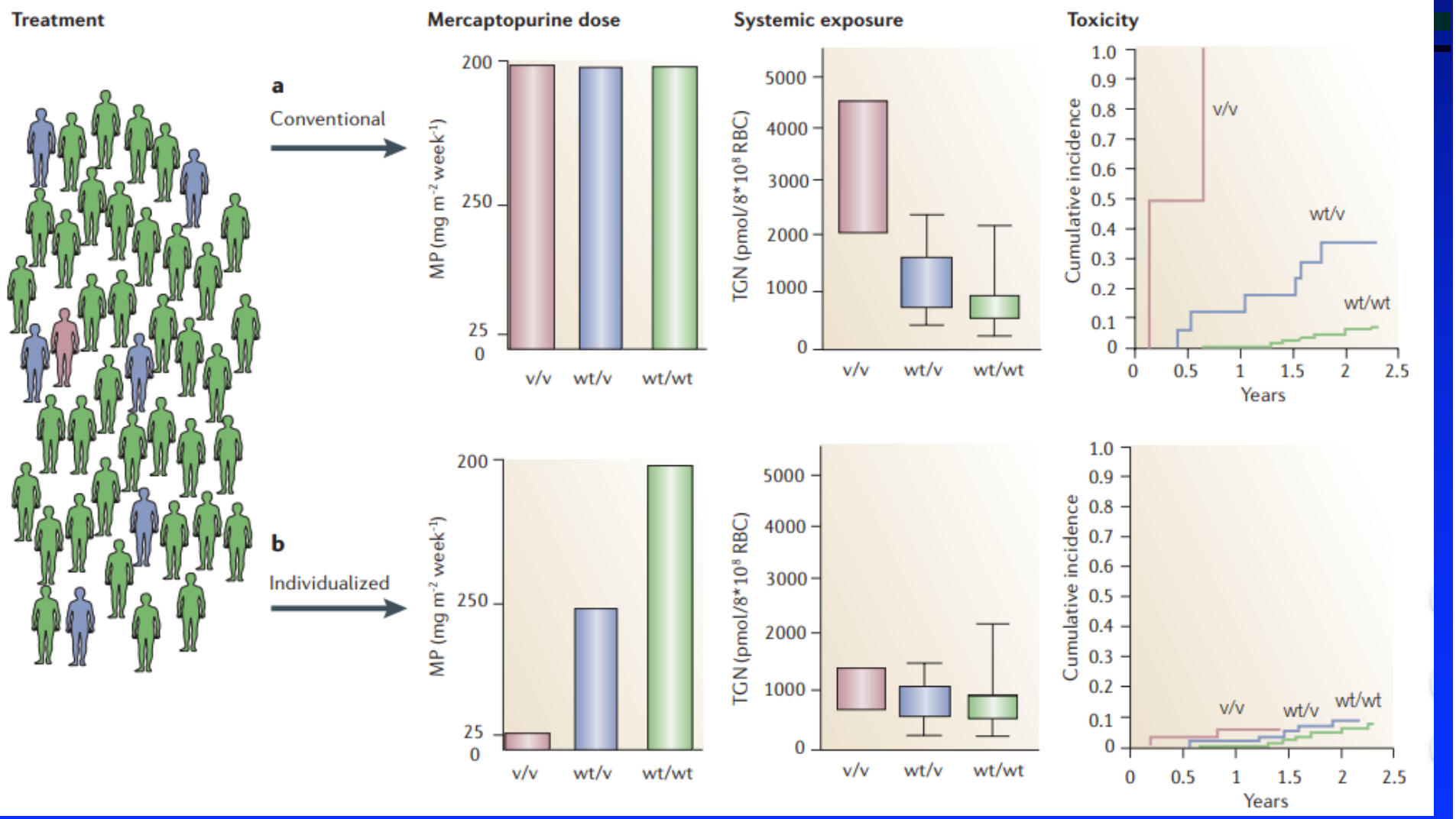
TPMT – Ajuste de dose da mercaptopurina baseado no genótipo



Evans Nature Reviews Cancer 2006

Recommended dosing of Mercaptopurine by TPMT phenotype

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Metabolizer-		Dosing recomendations	Classification recommendation
Normal	Higher MeTIPM Lower TGN metabolites	Start with normal dose 75 mg/m^2/day	Strong
Intermediate	Low methylTIMP Moderate to highTGN metabolites	Start with reduced doses (30-80%)	Strong
Poor	No methylTIMP metabolite Extremely high TGN metabolites	-Reduce daily dose by 10-fold -Reduce frequency to thrice weekly -Alternative drug	Strong

Adjust dose based on myelosuppression and disease-specific guidelines

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Bula da mercaptopurina (ANVISA)

- Pacientes portadores de deficiência hereditária da enzima tiopurina-metiltransferase (TPMT) podem apresentar sensibilidade não usual ao efeito mielossupressivo da Mercaptopurina e podem ser suscetíveis a desenvolver supressão da medula óssea após o início do tratamento com Mercaptopurina.
- Alguns laboratórios realizam testes para detectar a deficiência da TPMT. Entretanto, esses testes não conseguem identificar todos os pacientes com risco de toxicidade

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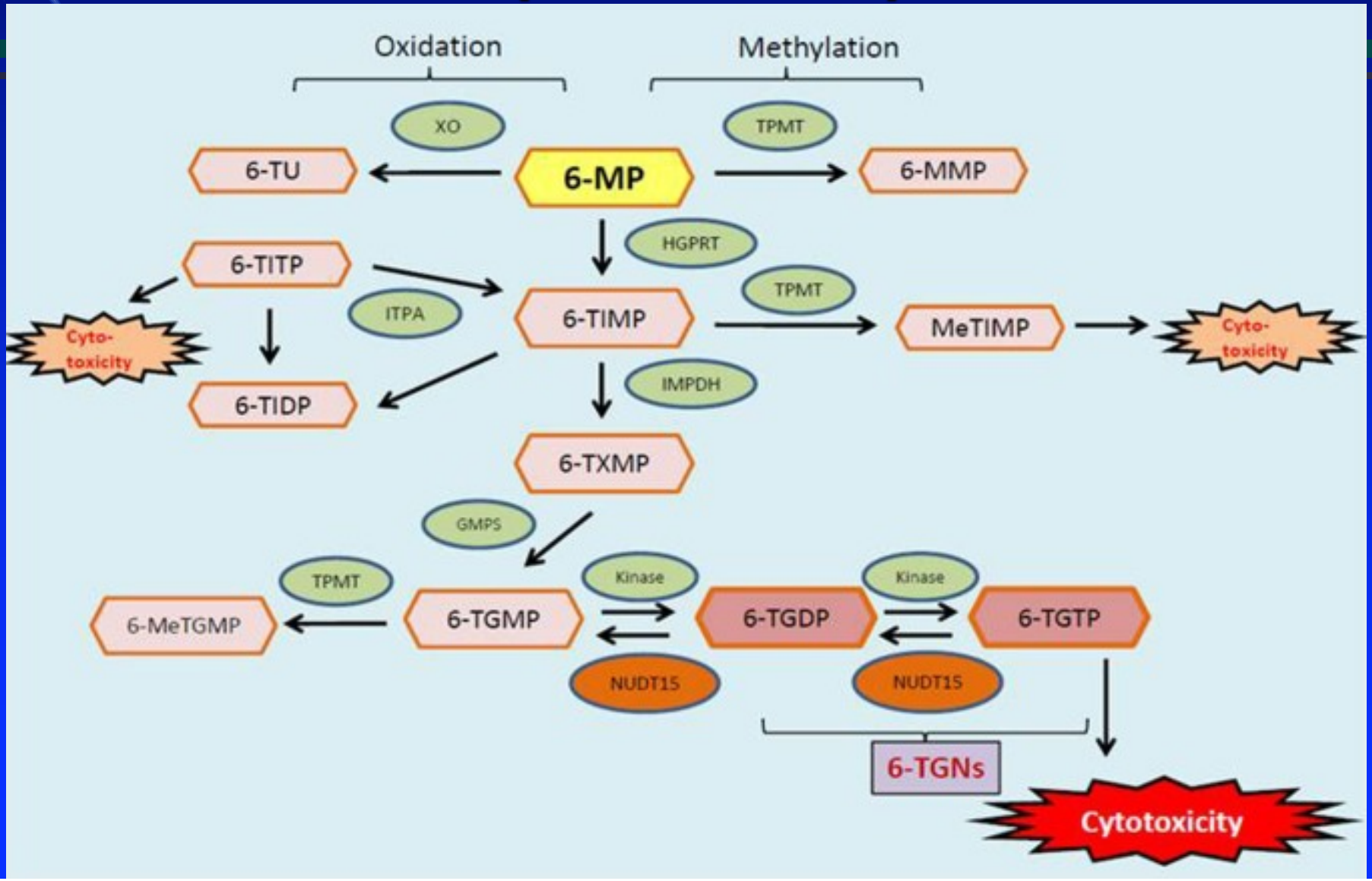
Nucleoside diphosphatase (NUDT15)



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Recommended dosing of Mercaptopurine by NUDT15 phenotype

Metabolyzer		Dosing recomendations	Classification recommendation
Normal	Normal risk of thiopurine-related, myelosuppression	Normal dose	Strong
Intermediate	Increased risk of thiopurine-related, myelosuppression	Reduced dose (30-80%)	Strong
Poor	Greatly increased risk of thiopurine-related, myelosuppression	Reduced dose (by 10-fold)	Strong

Adjust dose based on myelosuppression and disease-specific guidelines

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Nucleoside diphosphatase (NUDT15)

Assignment of likely NUDT15 phenotypes based on genotypes		
Normal metabolizer	An individual carrying two normal function alleles	*1/*1
Intermediate metabolizer	An individual carrying one normal function allele PLUS one no function allele	*1/*2, *1/*3
Possible intermediate metabolizer	An individual carrying one uncertain function allele PLUS one no function allele	*2/*5, *3/*6
Poor metabolizer	An individual carrying two no function alleles	*2/*2, *2/*3, *3/*3
Indeterminate	An individual carrying two uncertain function alleles OR one normal function allele plus one uncertain function allele	*1/*4, *1/*5 *4/*5, *5/*6

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NUDT15 Polymorphism
Native American Populations of Brazil

Table 1 Amerindian groups investigated: location, languages, and distribution of *NUDT15* rs116855232 (c.414C>T)

Population	Localities	Geographical coordinates	Region	Linguistic group	Number of individuals	Genotype frequency (%)			T allele frequency (CI 95%)
						CC	CT	TT	
Guarani	Amambai	23°S, 55°W	Center-West	Tupi	49	67.3	26.5	6.1	19.4 (12.8–28.3)
	Limão Verde	23°S, 55°W	Center-West						
Kaingang-1	Rio das Cobras	25°S, 52°W	South	Gê	60	60.0	28.3	11.7	25.8 (18.9–34.3)
	Ivaí	24°S, 51°W	South						
Kaingang-2	Nonoai	27°S, 52°W	South	Gê	71	54.9	26.8	18.3	31.7 (24.6–39.7)
Xavante	Pimentel Barbosa	13°S, 51°W	Center-West	Gê	87	89.7	10.3	0	5.2 (2.7–9.5)

CI, confidence interval.

FCFRP-USP

Recommended therapeutic use of abacavir in relation to HLA-B genotype

Genotype	Implications for phenotypic measures	Recommendations for abacavir	Classification of recommendations[a]
Noncarrier of *HLA-B*57:01*	Low or reduced risk of abacavir hypersensitivity	Use abacavir per standard dosing guidelines	Strong
Carrier of *HLA-B*57:01*	Significantly increased risk of abacavir hypersensitivity	Abacavir is not recommended	Strong

HLA-B, human leukocyte antigen B.

[a]Rating scheme described in **Supplementary Data** online.

FCFRP-USP

Assignment of likely HLA-B phenotypes based on genotypes

Likely phenotype	Genotypes	Examples of diplotypes
Very low risk of hypersensitivity (constitutes ~94%[a] of patients)	Absence of **57:01* alleles (reported as "negative" on a genotyping test)	*X/*X[b]
High risk of hypersensitivity (~6% of patients)	Presence of at least one **57:01* allele (reported as "positive" on a genotyping test)	*57:01/*X[b] *57:01/*57:01

HLA-B, human leukocyte antigen B.

[a]See **Supplementary Data** online for estimates of genotype frequencies among different ethnic/geographic groups. [b]*X = any *HLA-B* genotype other than **57:01*.

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ZIAGEN (abacavir sulfate) FDA LABEL

- Patients who carry the HLA-B*5701 allele are at high risk for experiencing a hypersensitivity reaction to abacavir. Prior to initiating therapy with abacavir, screening for the HLA-B*5701 allele is recommended; this approach has been found to decrease the risk of hypersensitivity reaction.

FCFRP-USP

Bula do abacavir (ANVISA)

- O *status* relativo ao teste de HLA-B * 5701 deve ser considerado antes de se iniciar o tratamento com Abacavir e também antes de reiniciar o tratamento com este medicamento em pacientes com *status* desconhecido do alelo HLA-B * 5701, ainda que previamente tenham tolerado o Abacavir.

SUS disponibiliza exame antes da prescrição do Abacavir

709 unidades coletoras estão aptas para a coleta do exame desde 12 de março

O SUS passa a oferecer o exame de Tipificação do alelo HLA-B*5701, visando oferecer mais segurança na prescrição do medicamento Abacavir.

Veja aqui os endereços das unidades coletoras

O Departamento de Vigilância, Prevenção e Controle das IST, do HIV/AIDS e das Hepatites Virais (DIAHV/SVS/MS), emitiu Ofício-Circular nº 5/2018/COVIG/CGVP/ reforçando a divulgação deste serviço.

A realização deste exame já está indicado antes de iniciar a terapia com o medicamento Abacavir para compor o esquema antirretroviral (ARV). Para a pessoa que já esteja usando o Abacavir e não apresentou reação de hipersensibilidade ao medicamento não há indicação de realização do referido exame.

Informações mais detalhadas para indicação desse exame podem ser encontradas no Protocolo Clínico e Diretrizes Terapêuticas (PCDT) para Manejo da Infecção pelo HIV em Adultos; no PCDT para Manejo da Infecção pelo HIV em Crianças e Adolescentes; e no PCDT para Prevenção da Transmissão Vertical de HIV, Sífilis e Hepatites Virais, atualizados em 2017.

Pharmacogenetic information in the FDA label

FCFRP-USP

Gene	Drug	*CPIC Guideline	FDA Label
CYP2C19	clopidogrel	✓	✓
TPMT	thiopurines	✓	✓
SLCO1B1	simvastatin	✓	
CYP2C9/VKORC1	warfarin	✓	✓
CYP2D6	codeine	✓	✓
DPYD	fluorouracil, capecitabine	✓	✓
HLAB	abacavir	✓	✓

*CPIC, Clinical Pharmacogenetics Implementation Consortium