ConectGene TESTES GENÉTICOS

Laudo de Exame Farmacogenômico

Médico Responsável: Dr. Paulo Magno do Bem Filho
CRM ES 13785

Rua Equador, 43 – Bloco 3 - Sala 1011
Porto Atlântico Square Business
20220-410 – Rio de Janeiro (RJ)
+55 21 2135 8716

PACIENTE: Jane Doe
DT. NASC.: 01/01/1985
REF.: LCG-1111113

COLETADO: 15/10/2018
RECEBIDO: 06/11/2018
REPORTADO: 20/11/2018

AMOSTRA: Bucal
MÉDICO: Não informado
PRÁTICA: Não informado

SUMÁRIO RÁPIDO

QUIMIOTERÁPICOS

Capecitabina (XELODA®)	⚠ Maior risco de toxidade.
Ciclofosfamida (CYTOXAN®) **Cisplatina** (C-PLATIN®, PLATINOL®) **Fluorouracil** (EFUDEX®, CARAC®, FLUOROPLEX®, ADRUCIL®) **Leucovorina** (FUSILEV®) **Mercaptopurina** (PURINETHOL®, PURIXAN®) **Oxaliplatina** (ELOXATIN®) **Paclitaxel** (TAXOL®, ABRAXANE®) **Tegafur** **Tioguanina** (TABLOID®)	✓ Considere a dosagem da bula se não houverem contraindicações.
Metotrexato (RASUVO®, OTREXUP ™, TREXALL ™)	⚠ Maior risco de doença do enxerto contra o hospedeiro.
Tamoxifeno (NOLVADEX®, SOLTAMOX®)	⊘ Maior risco de recaída. Considere um inibidor de aromatase.

TROMBOFILIA

Trombofilia	✓ Paciente não possui as variantes do Fator V de Leinden nem do Fator II (Protombina).

IMPORTANTE

Este Sumário Rápido fornece uma visão geral da previsão de resposta do paciente. Estas informações estão baseadas somente nas informações do genótipo e não compõe o perfil completo do paciente. A detecção ou ausência de variantes genéticas não substitui a necessidade de monitoramento terapêutico. Antes de tomar decisões clínicas ou terapêuticas, médicos devem considerar a informação contida na seção Detalhada (disponível apenas em inglês), assim como prescrições atuais, histórico familiar, sintomas apresentados e outros fatores.

✓ Nenhuma observação negativa baseada no genótipo.

⚠ Genótipo pode apresentar maior risco ou menor efetividade. Prescreva com precaução.

⊘ Genótipo pode apresentar maior risco ou menor efetividade. Considere outro medicamento.

ConectGene TESTES GENÉTICOS

Pharmacogenetic Test Results

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55 21 21358716 (Ph)

PATIENT: Doe, Jane (F)
DOB: 1985-01-01
PATIENT ID:

COLLECTED: 10/15/2018
RECEIVED: 11/06/2018
REPORTED: 11/30/2018

SAMPLE TYPE: Buccal
PHYSICIAN: Not Provided
PRACTICE: Not Provided

ACCESSION: LGE-9290880938

QUICK SUMMARY

CHEMOTHERAPEUTICS	RESULTS
Capecitabine (XELODA®)	⚠ Increased risk of toxicity.
Cisplatin (PLATINOL®) Cyclophosphamide (CYTOXAN®) Fluorouracil (EFUDEX®, CARAC®, FLUOROPLEX®, ADRUCIL®) Leucovorin (FUSILEV®) Mercaptopurine (PURINETHOL®, PURIXAN®) Oxaliplatin (ELOXATIN®) Paclitaxel (ABRAXANE®) Tegafur Thioguanine (TABLOID®)	✓ Consider label recommended dosage if no contraindication.
Methotrexate (RASUVO®, OTREXUP™, TREXALL™)	⚠ Increased risk of Graft vs Host Disease.
Tamoxifen (NOLVADEX®, SOLTAMOX®)	⊘ Increased risk for relapse. Consider aromatase inhibitor.

THROMBOPHILIA	
Thrombophilia	✓ Patient is negative for the Factor V Leiden and Factor II Prothrombin variants.

IMPORTANT

This Quick Summary provides a brief overview of the predicted response of the patient. This information is based solely on the genotype information and is not based on a complete patient profile. Detection or absence of variants does not replace the need for therapeutic monitoring. Physicians should consider the information contained in the Details section, as well as consider current prescriptions, family history, presenting symptoms, and other factors before making any clinical or therapeutic decisions.

✓ No negative assertions based on genotype.

⚠ Genotype may present increased risk or decreased effectiveness; prescribe with caution.

⊘ Genotype may present increased risk or decreased effectiveness; select alternative drug.

GENE SUMMARY

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*3/*4	⊘ Poor Metabolizer
CYP3A4	*1/*1	✓ Extensive (Normal) Metabolizer
TPMT	*1/*1	✓ Extensive (Normal) Metabolizer
DPYD	*1/*1	✓ Extensive (Normal) Metabolizer
F2/F5	Negative	✓ Normal Thrombophilia Risk

DETAILED INFORMATION

Capecitabine	DPYD *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Capecitabine if no contraindication.		
	MTHFR rs1801131 G/G (HOM)		Evidence ★★
	Patient may have an increased risk of drug toxicity and decreased survival times when receiving capecitabine-based chemotherapy as compared to patients with the wild-type genotype.		
	DPYD rs2297595 T/T (WT)	*Extensive (normal) metabolizer.*	Evidence ★★
	Consider label recommended dosage of Capecitabine if no contraindication.		
	DPYD rs67376798 T/T (WT)	*Extensive (normal) metabolizer.*	Evidence ★
	Consider label recommended dosage of Capecitabine if no contraindication.		
Cisplatin	ABCB1 rs1045642 G/G (HOM)		Evidence ★
	Patients with this genotype may have unfavorable prognosis (increased risk of lymph node metastases and decreased survival rate) when treated with cisplatin in people with Esophageal Neoplasms.		
	TPMT *1/*1	*Extensive (normal) metabolizer.*	Evidence ★
	MTHFR rs1801133 G/G (WT)		
	Consider label recommended dosage of Cisplatin if no contraindication.		
Cyclophosphamide	MTHFR rs1801133 G/G (WT)		Evidence ★★
	Consider label recommended dosage of Cyclophosphamide if no contraindication.		
Fluorouracil	MTHFR rs1801131 G/G (HOM)		Evidence ★★
	Consider label recommended dosage if no contraindication.		
	DPYD rs2297595 T/T (WT)	*Extensive (normal) metabolizer.*	Evidence ★★
	DPYD *1/*1	*Extensive (normal) metabolizer.*	
	Consider label recommended dosage of Fluorouracil if no contraindication.		
	ABCB1 rs1045642 G/G (HOM)		Evidence ★
	Patients with this genotype may have unfavorable prognosis (increased risk of lymph node metastases and decreased survival rate) when treated with fluorouracil in people with Esophageal Neoplasms.		
	DPYD rs115232898 T/T (WT)	*Extensive (normal) metabolizer.*	Evidence ★
	DPYD rs17376848 A/A (WT)	*Extensive (normal) metabolizer.*	
	Consider label recommended dosage of Fluorouracil if no contraindication.		
Leucovorin	MTHFR rs1801131 G/G (HOM)		Evidence ★★
	Consider label recommended dosage if no contraindication.		
Mercaptopurine	TPMT *1/*1	*Extensive (normal) metabolizer.*	Evidence ★★★
	Consider label recommended dosage of Mercaptopurine if no contraindication.		
	MTHFR rs1801133 G/G (WT)		Evidence ★
	Consider label recommended dosage of Mercaptopurine if no contraindication.		
Methotrexate	ABCB1 rs1045642 G/G (HOM)		Evidence ★★
	Consider label recommended dosage of Methotrexate if no contraindication.		
	MTHFR rs1801133 G/G (WT)		Evidence ★
	Patients with this genotype who undergo hematopoietic cell transplant and are treated with methotrexate may have an increased risk of Graft vs Host disease.		

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55 21 21358716 (Ph)

DETAILED INFORMATION

	SLCO1B1 rs4149056 T/T (WT) SLCO1B1 rs2306283 A/G (HET) Consider label recommended dosage of Methotrexate if no contraindication.		Evidence ★
Oxaliplatin	MTHFR rs1801131 G/G (HOM) Consider label recommended dosage if no contraindication.		Evidence ★★
	DPYD rs67376798 T/T (WT) Consider label recommended dosage of Oxaliplatin if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★
Paclitaxel	CYP3A4 rs67666821 G/G (WT) CYP3A4 rs72552799 C/C (WT) ABCB1 rs1045642 G/G (HOM) CYP3A5 rs776746 C/C (WT) Consider label recommended dosage of Paclitaxel if no contraindication.	*Extensive (normal) metabolizer.* *Extensive (normal) metabolizer.*	Evidence ★
Tamoxifen	CYP2D6 *3/*4 Patient is a CYP2D6 Poor Metabolizer. Tamoxifen is a pro-drug requiring metabolic activation by CYP2D6. The DPWG Guidelines warn of an increased risk for relapse of breast cancer. Consider aromatase inhibitor for postmenopausal women.	*Poor metabolizer.*	Evidence ★★★
Tegafur	DPYD *1/*1 Consider label recommended dosage of Tegafur if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★★
Thioguanine	TPMT *1/*1 Consider label recommended dosage of Thioguanine if no contraindication.	*Extensive (normal) metabolizer.*	Evidence ★★★
Thrombophilia	F2 rs1799963 G/G (WT) The patient does not carry the Prothrombin (Factor II: G20210A) Mutation, a common genetic marker associated with inherited thrombophilia.		Evidence ★★★
	F5 rs6025 C/C (HOM) The patient does not carry the Factor V Leiden (G1691A) Mutation, a common genetic marker associated with inherited thrombophilia.		Evidence ★★★

KEY FOR VARIANT-DRUG COMBINATION EVIDENCE

★★★ Replicated in multiple studies with statistical significance and strong effect size.
★★ Replicated in multiple studies with and without statistical significance and effect size may be minimal.
★ Not yet replicated or replicated but lacking clear evidence of an association.
Notable information is available and special considerations may be of interest when prescribing for this genotype.
Literature does not indicate additional risks, benefits, or prescription changes to consider for this genotype.

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REPORTED GENOTYPES

This panel performs genotyping analysis on key genes and variant hot-spot regions, focused on analyzing loci documented as altering the effectiveness of drug metabolism. Key genotyping results include the following:

ABCB1
rs1045642:G/G Hom

CYP2D6
CYP2D6 *3/*4
rs16947:G/G Hom
rs1135840:G/C Het
rs35742686:T/- Het
rs1135824:T/T Wild
rs1065852:G/A Het
rs3892097:C/T Het
rs5030655:A/A Wild
rs5030867:T/T Wild
rs5030865:C/C Wild
rs5030656:CTT/CTT Wild
rs5030863:C/C Wild
rs5030862:C/C Wild
rs72549357:C/C Wild
rs28371706:G/G Wild
rs59421388:C/C Wild
rs769258:C/C Wild
rs28371725:C/C Wild
rs28371696:C/C Wild
rs28371717:C/C Wild

CYP3A4
CYP3A4 *1/*1
rs12721627:G/G Wild
rs12721629:G/G Wild
rs4987161:A/A Wild
rs72552799:C/C Wild
rs67784355:G/G Wild
rs4986909:G/G Wild
rs35599367:G/G Wild
rs67666821:G/G Wild

CYP3A5
CYP3A5 *3/*3
rs776746:C/C Wild

DPYD
DPYD *1/*1
rs67376798:T/T Wild
rs3918290:C/C Wild
rs55886062:A/A Wild
rs2297595:T/T Wild
rs17376848:A/A Wild
rs1801159:T/T Wild
rs1801158:C/C Wild
rs115232898:T/T Wild

F2
rs1799963:G/G Wild

F5
rs6025:C/C Hom

MTHFR
rs1801133:G/G Wild
rs1801131:G/G Hom

SLCO1B1
rs4149056:T/T Wild
rs2306283:A/G Het

TPMT
TPMT *1/*1
rs1142345:T/T Wild
rs1800584:C/C Wild
rs1800460:C/C Wild
rs1800462:C/C Wild

Reported genotype calls are all displayed with respect to the positive DNA strand. Variants indicated as homozygous (Hom) or heterozygous (Het) differ from the GRCh37/hg19 reference sequence (Wild). This report is limited to the following star-alleles: CYP2D6: *1, *2, *3, *3B, *4, *5, *6C, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *29, *33, *35A, *41, *45A & *46. CYP2C19: *1, *2, *3, *4B, *4, *5, *6, *7, *8, *9, *10, *12 & *17. CYP2C9: *1, *2 & *3. CYP3A5: *1 & *3. CYP3A4: *1, *8, *11, *12, *13, *16, *17 & *22. TPMT: *1, *2, *3A, *3C, *3B & *4. DPYD: *1, *2, *4, *5, *13 & rs67376798A. Any genotype identified as a default star-allele (CYP2D6 *2, CYP2C19 *1, CYP2C9 *1, CYP3A5 *3, CYP3A4 *1, TPMT *1, DPYD *1) indicates the absence only of the other alleles listed and does not imply that other variants in the gene are absent. Full allele deletions and duplications are only analyzed for the CYP2D6 gene. This test does not report polymorphisms other than those specifically listed, and mutations in other genes associated with drug metabolism will not be detected. Rare diagnostic errors may occur if variations occur in primer site locations.

DISCLAIMER

The information presented on this report is provided as supplementary health information. The results presented are intended for use by a physician, pharmacist or other healthcare professional to advise a patient on the use of prescribed medications. This test is not a 510k cleared test, but managed by CMS and FDA under the Clinical Laboratory Improvement Amendment (CLIA) as a LDT. The ordering physician is responsible for the diagnosis and management of disease and decisions based on the data provided. Results are dependent on adequate specimen collection and processing.

METHODOLOGY

Genomic DNA is extracted from dry buccal swabs using magnetic particle processing. DNA from patient samples are amplified with primers specific for ABCB1, CYP2D6, CYP3A4, CYP3A5, DPYD, F2, F5, MTHFR, SLCO1B1 & TPMT using Nested Patch PCR (Varley, et. al.). Positive and negative controls are used with each run. Patient samples, positive, and negative controls are sequenced using a MiSeq (Illumina). Sequences are analyzed using alignment and base call algorithms with Kailos Blue Software for the presence or absence of single nucleotide base changes, insertions and deletions. LR-PCR utilized for confirmation of CYP2D6 duplications and deletions. Results and recommendations are compiled as part of a medical report.

Genetic testing was performed in the Kailos Genetics CLIA facility at 601 Genome Way; Huntsville, Al. 35806. CLIA#: 01D2016114. Medical Director: Ronald McGlennen MD, FCAP, FACMG, ABMG.

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55 21 21358716 (Ph)

This report was reviewed and approved for release by CLIA Lab Manager & Supervisor: Michele R. Erickson-Johnson, PhD, MB (ASCP)^{CM}

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