Luminus Genetic Response Report

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This report combines (i) an analysis of the patient's DNA by Luminus Diagnostics, identifying relevant genetic variants that are informative for medication efficacy, safety, and dosing, with (ii) an interpretation of the identified DNA variants by Coriell Life Sciences to bring you immediately actionable clinical guidance regarding safer and more effective medications and dosages for the patient.

Patient: DOE, JANE	Physician: TEST	Date Collected: Oct 11, 2017
Date of Birth: Aug 26, 1982	Practice: LUMINUS DIAGNOSTICS	Date Accessioned: Oct 11, 2017
Gender: Female		Specimen type: SS
		Sample ID: 1710111111

Luminus Live Gene Rx

Individualized, additional therapeutic decision support information based on JANE DOE's genetics, drug regimen, indications, demographics, and lifestyle indicators are available at Luminus Live Gene Rx via this secured URL:
https://app.luminuslive.com/?token=prompt

Luminus Live Key: AH22WGWMY
Sample ID: 1710111111

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Genetic Summary Information

† When multiple activities are listed, check information in Medication Report Details (Pg. 12) for specific medication of interest.
Uncertain = No known diplotype/result (name) or activity for this combination of genetic variants; Uninterpretable Genotype.

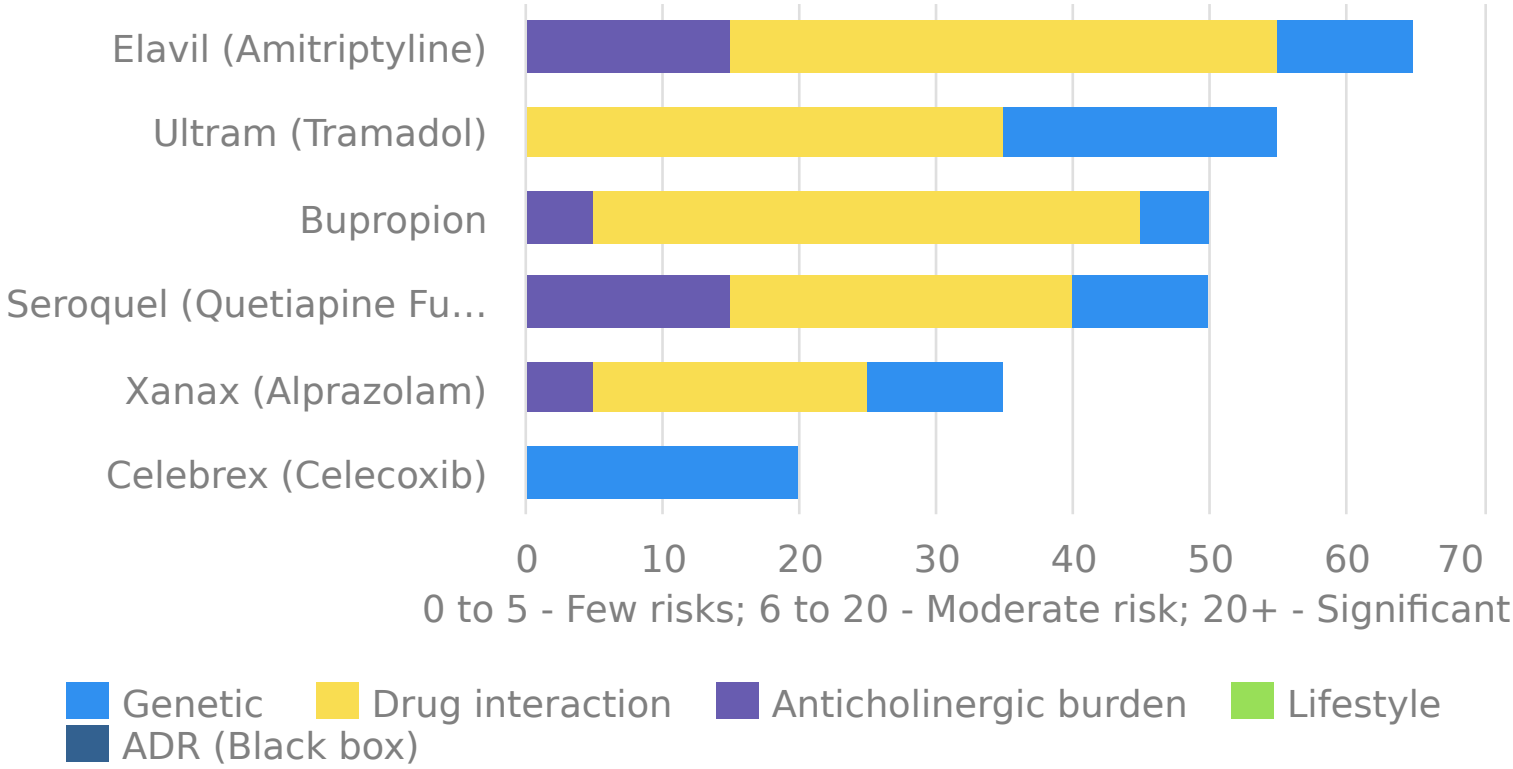
Genetic Summary

Gene	Result	Activity †
ANKK1	G|G	Normal function
BDNF	C|C	Normal function
COMT(Val158Met)	G|A	Uncertain function
CYP1A2	*1F|*1F or *1M|*1M or *1F|*1M	Extensive Metabolizer, Ultrarapid Metabolizer, Unknown Metabolizer
CYP2B6	*1A|*1A	Extensive metabolizer
CYP2C19	*1|*8	Intermediate metabolizer
CYP2C9	*2|*3	Poor metabolizer, Not EM
CYP2D6	*4J|*10	Intermediate metabolizer
CYP3A4	*1A|*1B	Uncertain
CYP3A5	*3A|*3A; or *3C|*3C; or *3A|*3C	Poor metabolizer
Factor V Leiden	Normal	See thrombosis profile
MTHFR (A1298C)	Heterozygous	See thrombosis profile
MTHFR (C677T)	Heterozygous	See thrombosis profile
OPRM1(A118G)	A|A	Normal function
Prothrombin (F2)	Normal	See thrombosis profile
SLCO1B1	*1|*5	Intermediate liver uptake activity

Gene	Result	Activity †
VKORC1	*1|*1	Normal (with respect to Warfarin)

Current Regimen Risk Chart

This chart summarizes the various risk factors associated with each medication entered into Luminus Live Gene Rx for JANE DOE. The length of each colored segment represents the relative contribution of a risk category (detailed in the below legend) to the overall risk associated with the use of a medication. For further information, consult the ***Current Regimen Risk Details*** Pg. 4 section.
For further assistance in choosing alternative medications to reduce this patient's risk, use the modeling tool at https://app.luminuslive.com/?token=prompt.



Current Regimen Risk Detail

Severe Risks

Genetic warning for Ultram (Tramadol)

Individuals with intermediate metabolizer status have decreased metabolism to more active compounds; the resultant decreased plasma concentrations may increase the probability of pharmacotherapy failure. Consider dose increase. If response is still inadequate; select alternative drug (not oxycodone or codeine) or be alert to symptoms of insufficient pain relief.

Genetic warning for Celebrex (Celecoxib)

Individuals with poor metabolizer status are at an increased risk of an adverse drug reaction including serious cardiovascular thrombotic events and should be administered celecoxib with caution as they may have abnormally high plasma levels due to reduced metabolic clearance. Consider a dose reduction by 50%. Consider using alternative management in JRA patients who are poor metabolizers.

Strong regimen anticholinergic burden

The cumulative effect of taking multiple medicines with anticholinergic properties termed as anticholinergic burden can adversely impact cognition, physical function and increase the risk of mortality.

Major Risks

Genetic warning for Seroquel (Quetiapine Fumarate)

Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased clearance of quetiapin; the resultant lower plasma concentrations may increase the probability of pharmacotherapy failure.

Genetic warning for Elavil (Amitriptyline)

Individuals with intermediate metabolizer status have reduced metabolism of amitriptyline to less active compounds; the resultant higher plasma concentrations will increase the probability of side effects. Consider reducing the recommended starting dose by 25% and monitor plasma concentration or select alternative drug (e.g. citalopram, sertraline).

Genetic warning for Xanax (Alprazolam)

Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased metabolism of alprazolam; the resultant lower plasma levels may increase the probability of pharmacotherapy failure.

Ultram (Tramadol) may cause additive sedative, CNS, and/or respiratory-depressant effects with Xanax (Alprazolam)

- consider alternative drug therapy
- decrease drug dosage
- warn against driving or operating machinery or performing other hazardous tasks until drug effects are known
- monitor for an increase in CNS/respiratory depression

Co-use of opiate pain medicines with benzodiazepines may cause profound sedation, respiratory depression, and death. If co-use is needed, use the lowest doses and shortest durations possible.

Bupropion may increase risk for additive serotonin-related side effects with Elavil (Amitriptyline)

- avoid combination unless benefit outweighs potential risk
- monitor for signs or symptoms of serotonin syndrome

The concomitant use of tryptophan with tricyclic antidepressants should be avoided. Since tryptophan is converted to serotonin, the use of tryptophan in patients receiving drugs with serotonergic activity could lead to serotonin syndrome.

Ultram (Tramadol) may increase risk for additive serotonin-related side effects with Elavil (Amitriptyline)

- monitor for signs of drug toxicity
- warn against driving or operating machinery or performing other hazardous tasks until drug effects are known
- monitor for signs or symptoms of serotonin syndrome
- monitor for seizure activity

Coadministration should be done so with caution because of an increased risk of serotonin syndrome and seizures.

Bupropion causes synergistic or additive toxicity with Seroquel (Quetiapine Fumarate)

- dosage reduction may be required
- monitor for seizure activity

Coadministration may increase the risk of seizures. The manufacturer of bupropion recommends low initial dosing and slow dosage titration with coadministration.

Bupropion increases potential side effects of Elavil (Amitriptyline)

- monitor for signs of drug toxicity
- monitor for increased anticholinergic effects
- monitor for seizure activity

Coadministration may result in increased risk of seizures, reduced clearance of TCAs, and additive anticholinergic effects.

Bupropion may increase or decrease the effect of Ultram (Tramadol)

- monitor for signs of drug toxicity
- monitor for altered clinical response to drug therapy
- monitor for seizure activity

Coadministration may enhance the seizure risk. In addition, increased serum concentrations of tramadol and reduced

analgesic effects are possible.

Moderate Risks

Genetic warning for Bupropion

Individuals with the A2|A2 diplotype are expected to respond well to therapy.

Seroquel (Quetiapine Fumarate) may cause additive sedative, CNS, and/or respiratory-depressant effects with Xanax (Alprazolam)

- use combination with caution
- monitor patient clinically
- warn against driving or operating machinery or performing other hazardous tasks until drug effects are known
- monitor for an increase in CNS/respiratory depression

Somnolence is a commonly reported adverse effect of quetiapine; coadministration of quetiapine with anxiolytics, sedatives, and hypnotics, or other CNS depressants may result in additive sedative effects.

Elavil (Amitriptyline) may increase the risk of QT prolongation with Seroquel (Quetiapine Fumarate)

- use combination with caution
- avoid combination unless benefit outweighs potential risk
- monitor for fast, irregular heartbeat

Coadministration increases the risk for QT prolongation and torsade de pointes.

Elavil (Amitriptyline) may result in additive sedative, CNS, and/or respiratory-depressant effects with Xanax (Alprazolam)

- monitor for altered clinical response to drug therapy
- warn against driving or operating machinery or performing other hazardous tasks until drug effects are known
- monitor for an increase in CNS depression

Co-use may result in additive CNS depression. The effect of anticonvulsant benzodiazepines (i.e., clobazam, clonazepam, diazepam, and lorazepam) may also be reduced because tricyclics lower seizure threshold.

Seroquel (Quetiapine Fumarate) causes synergistic or additive toxicity with Ultram (Tramadol)

- use combination with extreme caution
- monitor patient clinically
- warn against driving or operating machinery or performing other hazardous tasks until drug effects are known

Due to the primary CNS effects of quetiapine, caution should be used when given with other centrally acting medications, such as tramadol. Both of these medications can lower the seizure threshold as well, which may increase risk for seizure.

Thrombosis Profile

Tested Genes (Alleles)	Genotype	Predicted Phenotype	Clinical Guidance
Prothrombin (F2)	Normal	Normal risk expected based on the patient's genotype.	The absence of these variant alleles of Prothrombin (Factor II) and Factor V Leiden suggests that the patient does not have the elevated risk of thrombosis associated with these genetic markers. MTHFR alleles without the Factor V Leiden 1691A allele do not predict a significant risk for venous thrombosis.
Factor V Leiden	Normal		
MTHFR (A1298C)	Heterozygous		
MTHFR (C677T)	Heterozygous		

General Description

Genetic analyses of three genes (four alleles) considered to increase the risk for venous thrombosis were performed using molecular genetic techniques. The presence of the Prothrombin (Factor 2) gene allele 20210A and Factor V Leiden allele 1691A are risk factors for venous thrombosis. This risk may be further increased by the use of estrogen therapy, oral contraceptives, pregnancy, and surgery.

Patients who are homozygous for MTHFR 677T or MTHFR 1298C may have a further increased risk for venous thrombosis if they also possess the Factor V Leiden 1691A allele. However the MTHFR alleles alone do not predict a significant risk for venous thrombosis.

References and Useful Information:

- Factor V Leiden Working Group; ACMG Laboratory Quality Assurance Molecular Subcommittee of the ACMG Laboratory Quality Assurance Committee AMERICAN COLLEGE OF MEDICAL GENETICS; Standards and Guidelines for Clinical Genetics Laboratories; 2006 Edition
    - Middeldorp S, Henkens CM, Koopman MM, van Pampus ECM,Hamulyák K, van der Meer J, Prins MH, Büller HR. The incidence of venous thromboembolism in family members of patients with factor V Leiden mutation and venous thrombosis. Ann Intern Med 1998;128:15-20.
    - Vandenbroucke JP, Koster T, Briet E, Reitsma PH, Bertina RM, Rosendaal FR. Increased risk of venous thrombosis in oral contraceptive users who are carriers of factor V Leiden mutation. Lancet 1994;344:1453-1457.
    - Rosendaal FR, Koster T, Vandenbroucke JP, Reitsma PH. High risk of thrombosis in patients homozygous for factor V Leiden (activated protein C resistance). Blood 1995;85(6):1504-1508.
    - Reich LM, Bower M, Key NS. Role of the geneticist in testing and counseling for inherited thrombophilia. Genet Med 2003;5:133-143.
    - Tosetto A, Rodeghiero F, Martinelli I, De Stefano V, Missiaglia E, Chiusolo P, Mannucci PM. Additional genetic risk factors for venous thromboembolism in carriers of the factor V Leiden mutation. Br J Haematol 1998;103:871-876.
    - De Stefano V, Martinelli I, Mannucci PM, Paciaroni K, Chiusolo P, Casorelli I, Rossi E, Leone G. The risk of recurrent deep venous thrombosis among heterozygous carriers of both factor V Leiden and the G20210A prothrombin mutation. N Engl J Med 1999;341:801-806.
- M. Adams, P.D. Smith, D. Martin, J.R. Thompson, D. Lodwick, N.J. Samani. Genetic analysis of thermolabile methylenetetrahydrofolate reductase as a risk factor for myocardial infarction. QJM. 1996 Jun;89(6):437-44.

Medication Summary (more alternatives discoverable at Luminus Live Gene Rx)

Secured URL: https://app.luminuslive.com/?token=AH22WGWMY

Cardiac

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antiarrhythmics		Flecainide Propafenone	
Anticoagulants	Warfarin	Acenocoumarol	
Antiplatelet Agents	Prasugrel	Ticagrelor	Clopidogrel
Beta Blockers	Carvedilol Nebivolol Propranolol Timolol		Metoprolol
Statins		Atorvastatin Simvastatin	

Gastroenterology

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antidepressants	Mirtazapine	Amitriptyline Clomipramine Desipramine Doxepin Nortriptyline Trazodone	
Antiemetics	Ondansetron Tropisetron		
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)			Celecoxib
Proton Pump Inhibitors (PPIs)		Dexlansoprazole Esomeprazole Lansoprazole Omeprazole Pantoprazole Rabeprazole	
Selective Serotonin Reuptake Inhibitors (SSRIs)	Citalopram	Paroxetine	

Infectious Disease

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antifungals		Voriconazole	Ketoconazole

Pain

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antidepressants	Duloxetine Flupenthixol Mirtazapine Moclobemide	Amitriptyline Clomipramine Desipramine Doxepin Nortriptyline Protriptyline Trazodone Venlafaxine Vortioxetine	
Antipsychotics	Olanzapine		
Beta Blockers	Nebivolol Propranolol Timolol		
Muscle Relaxants			Carisoprodol
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)		Diclofenac Flurbiprofen Meloxicam	Celecoxib
Opioids		Buprenorphine Codeine Fentanyl (OPRM1) Oxycodone Oxycodone (CYP3A5)	Tramadol
Selective Serotonin Reuptake Inhibitors (SSRIs)	Citalopram Escitalopram	Fluvoxamine Paroxetine Sertraline	

Psychotropic

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Anti-ADHD Agents	Atomoxetine		
Antidementia Agents	Donepezil		

Psychotropic

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antidepressants	Duloxetine Flupenthixol Mirtazapine Moclobemide	Amitriptyline Bupropion Clomipramine Desipramine Doxepin Nortriptyline Protriptyline Trazodone Venlafaxine Vortioxetine	
Antipsychotics	Brexpiprazole Clozapine Haloperidol Iloperidone Olanzapine	Aripiprazole Perphenazine Pimozide Quetiapine Risperidone Zuclopenthixol	Thioridazine
Anxiolytics		Alprazolam Buspirone Clonazepam Diazepam	
Beta Blockers	Propranolol		
Central Monoamine-Depleting Agents		Tetrabenazine	
Central Nervous System Agents		Dextromethorphan-Quinidine	
Cholinesterase Inhibitors		Galantamine	
Hypnotics		Eszopiclone	
Selective Serotonin Reuptake Inhibitors (SSRIs)	Citalopram Escitalopram	Fluvoxamine Paroxetine Sertraline	

Surgery

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antiemetics	Ondansetron Tropisetron		
Opioids		Fentanyl (OPRM1)	

Other Drugs

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antidiabetics	Glibenclamide Gliclazide Glimepiride Tolbutamide	Saxagliptin	
EGFR Inhibitors	Gefitinib		

Legend

- Typical response is expected
- Change recommended
- Consider alternative therapy
- Additional information available
- Response is uncertain

Clinical Evidence Level

- Strong
- Moderate
- Emerging

Medication Report Details (by therapeutic class)

Drug	Finding	Recommendation	Concern	Evidence
Anti-ADHD Agents				
Atomoxetine (Strattera)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		Moderate
Antiarrhythmics				
Flecainide (Tambocor)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have the potential for decreased elimination. Consider reducing dose by 25%; record ECG; monitor plasma concentration.	ADR	Strong
Propafenone (Rythmol)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased plasma concentrations may increase the risk proarrhythmia, exaggerated beta-adrenergic blocking activity, and other adverse events. Adjust dose in response to plasma concentration and record ECG or select alternative drug (e.g. sotalol, disopyramide, quinidine, amiodarone).	ADR	Strong

Drug	Finding	Recommendation	Concern	Evidence
Anticoagulants				
Acenocoumarol (Sintrom, Acitrom)	CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Individuals with variant CYP2C9 genotype (i.e., other than *1|*1) have increased risk of adverse drug reactions after initiating or discontinuing NSAIDs. Checking INR more frequently is recommended.	ADR	
Warfarin (Coumadin)	Multigenic: VKORC1, CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Individuals with this combination of alleles may benefit from the standard dose of Warfarin. The FDA table recommends a therapeutic dose of 3-4 mg/day.		
Antidementia Agents				
Donepezil	CYP2D6: *4J|*10	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Antidepressants				
Amitriptyline (Elavil)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have reduced metabolism of amitriptyline to less active compounds; the resultant higher plasma concentrations will increase the probability of side effects. Consider reducing the recommended starting dose by 25% and monitor plasma concentration or select alternative drug (e.g. citalopram, sertraline).	ADR	
Bupropion (Wellbutrin)	ANKK1: Normal function. Two alleles with normal activity.	Individuals with the A2|A2 diplotype are expected to respond well to therapy.	Efficacy	
Clomipramine (Anafranil)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have reduced metabolism to less active compounds; the resultant higher plasma concentrations may increase the probability of side effects. Insufficient evidence to allow calculation of dose adjustment. Monitor (desmethyl) clomipramine plasma concentration.	ADR	
Desipramine (Norpramin)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have reduced metabolism of tricyclic antidepressants; the resultant higher plasma concentrations may increase the probability of side effects. Monitor plasma concentration or select alternative drug.	ADR	
Doxepin (Deptran)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have reduced metabolism to less active compounds. Higher plasma concentrations will increase the probability of side effects. Reduce dose by 20%. Adjust maintenance dose in response to (nor)doxepin plasma concentration.	ADR	
Duloxetine (Cymbalta)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		
Flupenthixol	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Imipramine (Tofranil)	Multigenic: CYP2C19, CYP2D6: Intermediate metabolizer. One allele showing normal activity and one likely showing reduced activity. Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Multiple results from uncorrelated genes. CYP2C19: Potentially consider alternative therapy CYP2D6: Recommended dosage adjustment and additional monitoring suggested		
Mirtazapine	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		
Moclobemide	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one likely showing reduced activity.	Typical response is expected; no additional therapeutic recommendations.		
Nortriptyline (Pamelor)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers; the resultant higher plasma concentrations will increase the probability of side effects. Consider reducing the dose by 40% and monitor nortriptyline 10-hydroxynortriptyline plasma concentrations.	ADR	
Protriptyline (Vivactil)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have reduced metabolism of tricyclic antidepressants; the resultant higher plasma concentrations may increase the probability of side effects. Monitor plasma concentration or select alternative drug.	ADR	
Trazodone (Oleptro, Desyrel)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased metabolism of trazodone; the resultant lower plasma concentrations may increase the probability of pharmacotherapy failure.	Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Venlafaxine (Effexor)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Insufficient evidence to allow calculation of dose adjustment. Consider selecting alternative drug (e.g. citalopram, sertraline) or adjust dose to clinical response and monitor (O-desmethyl) venlafaxine plasma concentration.		
Vortioxetine (Brintellix)	CYP2D6: *4J|*10	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced metabolic clearance and high plasma concentrations of the active compound. Consider reducing the dose.	ADR	
Antidiabetics				
Glibenclamide (Glyburide)	CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Typical response is expected; no additional therapeutic recommendations.		
Gliclazide	CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Typical response is expected; no additional therapeutic recommendations.		
Glimepiride	CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Typical response is expected; no additional therapeutic recommendations.		
Saxagliptin (Onglyza)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased metabolism of saxagliptin; the resultant lower plasma concentrations may increase the probability of pharmacotherapy failure.	Efficacy	
Tolbutamide (Orinase)	CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Typical response is expected; no additional therapeutic recommendations.		
Antiemetics				
Ondansetron (Zofran)	CYP2D6: *4J|*10	Typical response is expected; no additional therapeutic recommendations.		
Tropisetron	CYP2D6: *4J|*10	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Antifungals				
Ketoconazole (Nizoral)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased metabolism of ketoconazole; the resultant lower plasma concentrations may increase the probability of pharmacotherapy failure. Ketoconazole is not recommended.	Efficacy	
Voriconazole	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one likely showing reduced activity.	Individuals with intermediate metabolizer status may have higher voriconazole exposure. Adjust the dose and monitor for adverse events or lack of efficacy.	ADR & Efficacy	
Antiplatelet Agents				
Clopidogrel (Plavix)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Individuals with intermediate metabolizer status are at an increased risk therapeutic failure due to reduced activation of the prodrug and low plasma concentrations of the active compound. Clopidogrel is not recommended.	Efficacy	
Prasugrel (Effient)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Typical response is expected; no additional therapeutic recommendations.		
Ticagrelor (Brilinta)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may be at an increased risk of adverse drug reactions and decreased efficacy due to reduced metabolism of the prodrug to the active metabolite.	ADR & Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Antipsychotics				
Aripiprazole (Abilify)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Intermediate metabolizers are at uncertain risk of adverse drug reaction. However, note that for individuals with poor metabolizer status it is recommended to reduce the maximum dose to 10 mg/day (67% of the maximum recommended daily dose).	ADR	
Brexpiprazole (Rexulti)	CYP2D6: *4J|*10	Typical response is expected; no additional therapeutic recommendations.		
Clozapine	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		
Haloperidol (Haldol)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		
Iloperidone (Fanapt)	CYP2D6: *4J|*10	Individuals with poor metabolizer status may be at increased risk of adverse events due to increased Iloperidone concentrations. Consider dose reduction based upon assessment of clinical benefit and tolerability.		
Olanzapine (Zalasta, Zyprexa)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		
Perphenazine (Trilafon, Etrafon)	CYP2D6: *4J|*10	Individuals with intermediate metabolizer status may be at increased risk of adverse effects due to increased plasma concentrations of perphenazine. Insufficient evidence to allow calculation of dose adjustment. Be alert to adverse reactions.	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Pimozide (Orap)	CYP2D6: *4J|*10	Typical response is expected. For children, the drug label recommends an initial dose of 0.05 mg/kg followed by titration to response up to a maximum of 0.2 mg/kg and not to exceed 10 mg/day. In adults the drug label recommends an intial dose of 1 to 2 mg a day in divided doses followed by titration to response up to a maximum of 0.2 mg/kg/day or 10 mg/day.	ADR	
Quetiapine (Seroquel)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased clearance of quetiapin; the resultant lower plasma concentrations may increase the probability of pharmacotherapy failure.	Efficacy	
Risperidone (Risperdal)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Insufficient evidence to allow calculation of dose adjustment. Consider selecting alternative drug (e.g. quetiapine, olanzapine, clozapine) or being extra alert to adverse drug events and adjusting dose to clinical response.	ADR	
Thioridazine	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status are at an increased risk of serious adverse drug reactions due to elevated levels of thioridazine. Select alternative drug.	ADR	
Zuclopenthixol	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with poor metabolizer status have decreased metabolism to less active compounds; the resultant increased plasma concentrations may increase the risk of adverse drug reactions. Reduce the standard dose by 25% or select an alternative drug (flupenthixol, quetiapine, olanzapine, clozapine).	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Anxiolytics				
Alprazolam (Xanax, Niravam)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased metabolism of alprazolam; the resultant lower plasma levels may increase the probability of pharmacotherapy failure.	Efficacy	
Buspirone (Buspar)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased metabolism of buspirone; the resultant lower plasma levels may increase the probability of pharmacotherapy failure.	Efficacy	
Clonazepam (Klonopin)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased metabolism of clonazepam; the resultant lower plasma concentrations may increase the probability of pharmacotherapy failure.	Efficacy	
Diazepam (Diastat, Valium)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Individuals with intermediate metabolizer status may emerge from anesthesia less rapidly due to decreased metabolic clearance. Insufficient evidence to allow calculation of dose adjustment. Be alert to symptoms of excessive drug exposure.	ADR & Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Beta Blockers				
Carvedilol (Coreg)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		
Metoprolol (Lopressor)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have increased risk of adverse drug reactions. For heart failure (indication): select alternative drug (e.g. bisoprolol, carvedilol) or reduce dose by 50%. For other indications: be alert to adverse drug events (e.g. bradycardia, cold extremities) or select alternative drug (e.g. atenolol, bisoprolol).	ADR	
Nebivolol (Bystolic)	CYP2D6: *4J|*10	Typical response is expected; no additional therapeutic recommendations.		
Propranolol (Inderal)	CYP2D6: *4J|*10	Typical response is expected; no additional therapeutic recommendations.		
Timolol (Blocadren)	CYP2D6: *4J|*10	Typical response is expected; no additional therapeutic recommendations.		
Central Monoamine-Depleting Agents				
Tetrabenazine (Xenazine)	CYP2D6: *4J|*10	Typical response is expected. The drug label recommends a maximum daily dose of 100 mg and a maximum single dose of 37.5 mg.		
Central Nervous System Agents				
Dextromethorphan-Quinidine (Nuedexta)	CYP2D6: *4J|*10	Individuals with intermediate metabolizer status may be at an increased risk of adverse events and therapeutic failure. Consider alternative therapy.		
Cholinesterase Inhibitors				
Galantamine (Razadyne)	CYP2D6: *4J|*10	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions and/or therapeutic failure. Insufficient evidence to allow calculation of dose adjustment. Be alert to adverse reactions and/or symptoms of insufficient therapy.	ADR & Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
EGFR Inhibitors				
Gefitinib (Iressa)	CYP2D6: *4J|*10	Typical response is expected; no additional therapeutic recommendations.		
Hypnotics				
Eszopiclone (Lunesta)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased metabolism of eszopiclone; the resultant lower blood concentrations may increase the probability of pharmacotherapy failure.	Efficacy	
Muscle Relaxants				
Carisoprodol (Soma)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one likely showing reduced activity.	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced carisoprodol metabolism. Carisoprodol should be administered with caution.	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Non-drug				
ANKK1	ANKK1: Normal function. Two alleles with normal activity.	Normal function. Two alleles with normal activity.		
BDNF	BDNF: C|C	Normal function. Two alleles with normal activity.		
COMT(Val158Met)	COMT(Val158Met): Uncertain function. One allele showing increased activity and one showing decreased activity.	Uncertain function. One allele showing increased activity and one showing decreased activity.		
CYP1A2	CYP1A2: Likely Extensive metabolizer; potentially Ultrarapid metabolizer in Smokers and Heavy Coffee Drinkers. Two alleles showing potentially increased activity via induction; or, two alleles with unknown activity; or, one allele showing potentially increased activity via induction and one with unknown activity.	No additional therapeutic recommendations.		
CYP2B6	CYP2B6: Extensive metabolizer. Two alleles showing normal activity.	No additional therapeutic recommendations.		
OPRM1(A118G)	OPRM1(A118G): Normal function. Two alleles with normal activity.	Normal function. Two alleles with normal activity.		

Drug	Finding	Recommendation	Concern	Evidence
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)				
Celecoxib (Celebrex)	CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Individuals with poor metabolizer status are at an increased risk of an adverse drug reaction including serious cardiovascular thrombotic events and should be administered celecoxib with caution as they may have abnormally high plasma levels due to reduced metabolic clearance. Consider a dose reduction by 50%. Consider using alternative management in JRA patients who are poor metabolizers.	ADR	
Diclofenac (Cataflam)	CYP2C9:rs1057910: Overall metabolizer status uncertain. One allele showing normal activity and one showing reduced activity.	Individuals with the A/C genotype who are treated with the non-steroid antiinflammatory may have an increased risk of gastrointestinal bleeding. Consider alternative therapy.	ADR	
Flurbiprofen (Ocufen)	CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Individuals with poor metabolizer status may be at an increased risk of adverse drug reactions due to reduced metabolic clearance and abnormally high plasma concentrations of the active compound. Insufficient evidence to allow calculation of dose adjustment. Flurbiprofen should be administered with caution.	ADR	
Meloxicam (Mobic)	CYP2C9: Poor metabolizer. Two alleles showing reduced activity.	Individuals with poor metabolizer status may have increased plasma concentrations and decreased clearance of meloxicam. However, there is no current association with treatment response or severity of side effects in the literature.	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Opioids				
Buprenorphine (Butrans, Buprenex)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status may have increased clearance of buprenorphine; the resultant lower plasma concentrations may increase the probability of pharmacotherapy failure.	Efficacy	
Codeine	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	For analgesia, select alternative drug (e.g. acetaminophen, NSAID, morphine; not tramadol or oxycodone) or be alert to symptoms of insufficient pain relief. For cough, there are no data on the effect of CYP2D6 genotype or phenotype on the antitussive effect of codeine.	Efficacy	
Fentanyl (Duragesic, Sublimaze)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.			
Fentanyl (OPRM1) (Duragesic, Sublimaze)	OPRM1(A118G): Normal function. Two alleles with normal activity.	Individuals with A118G A/A genotype are associated with decreased epidural analgesia satisfaction at standard doses. Consider increasing dose based upon assessment of clinical benefit and tolerability.	Efficacy	
Oxycodone (Oxycontin)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status are at risk of potentially reduced efficacy; consider alternative therapy. Insufficient evidence to allow calculation of dose adjustment. Select alternative drug (not tramadol or codeine) or be alert to symptoms of insufficient pain relief.	Efficacy	
Oxycodone (CYP3A5) (Oxycontin)	CYP3A5: Two alleles showing little or no activity.	In a preliminary study, individuals with poor metabolizers status have a significantly higher opioid escalation index compared to normal (extensive) metabolizers. Though the impact of metabolizer status at CYP3A5 on pain relief is currently unknown, consider reducing the initial dose. There does not appear to be an effect of this metabolizer status on the incidence of drowsiness.	ADR & Efficacy	
Tramadol (Ultracet, Ultram)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status have decreased metabolism to more active compounds; the resultant decreased plasma concentrations may increase the probability of pharmacotherapy failure. Consider dose increase. If response is still inadequate; select alternative drug (not oxycodone or codeine) or be alert to symptoms of insufficient pain relief.	Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Proton Pump Inhibitors (PPIs)				
Dexlansoprazole (Kapidex, Dexilant)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Esomeprazole (Nexium)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Lansoprazole (Prevacid)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Omeprazole (Prilosec, Zegerid)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Pantoprazole (Protonix)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Rabeprazole (Aciphex)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing reduced activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Selective Serotonin Reuptake Inhibitors (SSRIs)				
Citalopram (Celexa)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one likely showing reduced activity.	Typical response is expected; no additional therapeutic recommendations.		
Escitalopram (Lexapro)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one likely showing reduced activity.	Typical response is expected; no additional therapeutic recommendations.		
Fluvoxamine (Luvox)	CYP2D6: *4J|*10	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced metabolic clearance. Insufficient evidence to allow calculation of dose adjustment. Be alert to adverse reactions.	ADR	
Paroxetine (Paxil)	CYP2D6: Intermediate metabolizer. One allele showing reduced activity and one showing little or no activity.	Individuals with intermediate metabolizer status may have increased plasma concentrations/ decreased clearance of paroxetine. However, an association with treatment response or severity of side effects is not conclusive.	ADR	
Sertraline (Zoloft)	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one likely showing reduced activity.	Individuals with intermediate metabolizer status may have higher plasma concentrations and decreased clearance. Insufficient evidence to allow calculation of dose adjustment. Be extra alert to adverse drug reactions (e.g. nausea; vomiting; diarrhea).	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Statins				
Atorvastatin (Lipitor, Caduet)	CYP3A4: Uncertain metabolizer status. One allele showing normal activity and one showing increased activity.	Overall metabolizer status and treatment response uncertain for this genetic combination. However, note that individuals with known ultrarapid metabolizer status eliminate atorvastatin more rapidly than extensive/normal metabolizers and may not respond well to a standard dose.		
Simvastatin (Zocor)	SLCO1B1: Intermediate liver uptake activity.	Individuals with intermediate SLCO1B1 liver uptake activity have a moderately increased risk of myopathy when taking a 40 mg/day or higher dose of simvastatin. A reduced dosage or alternate statin drug should be considered.	ADR	

Clinical Evidence Levels

Strong

- Includes gene-drug pairs approved by the Coriell Institute for Medical Research Pharmacogenomics Advisory Group.
- Includes gene-drug pairs supported by multiple studies documenting consistent effects of specific genetic variant(s) on clinical outcomes.
- Includes gene-drug pairs approved by the Dutch Pharmacogenetics Working Group (DPWG) and/or guidelines published in Clinical Pharmacology and Therapeutics by the Clinical Pharmacogenetics Implementation Consortium (CPIC).

Moderate

- Includes gene-drug pairs supported by pharmacokinetic, pharmacodynamic, or molecular/cellular functional studies showing consistent effects of genetic variant(s).
- Includes Drug product information (e.g. This interpretation is based on guidance available in the FDA (Food and Drug Administration) drug label for ABILIFY® (10/2013).
- Includes gene-drug pairs for which potential clinical outcomes are inferred from similar gene-drug interactions approved by the Dutch Pharmacogenetics Working Group (DPWG), and/or guidelines published in Clinical Pharmacology and Therapeutics by the Clinical Pharmacogenetics Implementation Consortium (CPIC), and/or pharmacogenomic reports and submission from the Coriell Institute for Medical Research.

Emerging

- Includes gene-drug pairs supported by published studies of the drug, related drug, or a probing compound of interest involving limited data and/or inconsistent findings.

Patient Information Card

This card contains an abbreviated genetic summary.
It is not intended as a replacement for the complete GeneDose™ report.

Luminus Diagnostics
http://luminusdiagnostics.com

Patient: DOE, JANE
DOB: 1982-08-26
Sample ID: 1710111111
Luminus Live Key: AH22WGWMY

Pharmacogenomic Summary

CYP2C9:rs1057910	A|C	Uncertain
Factor V Leiden	Normal	See full GeneDose report
MTHFR (A1298C)	Heterozygous	See full GeneDose report
MTHFR (C677T)	Heterozygous	See full GeneDose report
Prothrombin (F2)	Normal	See full GeneDose report

This card shows information about your genetics that relate to drug metabolism. Show to your doctors before being prescribed new medications.
For additional support and guidance:
• Physicians can visit
https://app.luminuslive.com/?token=prompt

ANKK1	G|G	Normal function
BDNF	C|C	Normal function
COMT(Val158Met)	G|A	Uncertain function
CYP1A2	*1F|*1F or *1M|*1M or *1F|*1M	Extensive Metabolizer, Ultrarapid Metabolizer, Unknown Metabolizer
CYP2B6	*1A|*1A	Extensive metabolizer
CYP2C19	*1|*8	Intermediate metabolizer
CYP2C9	*2|*3	Poor metabolizer, Not EM
CYP2D6	*4J|*10	Intermediate metabolizer
CYP3A4	*1A|*1B	Uncertain
CYP3A5	*3A|*3A; or *3C|*3C; or *3A|*3C	Poor metabolizer
OPRM1(A118G)	A|A	Normal function
SLCO1B1	*1|*5	Intermediate liver uptake activity
VKORC1	*1|*1	Normal (with respect to Warfarin)

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