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DANTE LABS™ TEST RESULTS

KIT ID:

INTRODUCTION

This document is your genetic report, which is a straightforward and non-technical presentation of the results. It provides clear solutions to optimize your health and longevity. The insights obtained from learning about your genes may enable you, in partnership with your healthcare provider, formulate a plan to outsmart your genes and live a longer, more vibrant life. Our report tells you how your DNA can affect your reaction to certain medications. Genetic variants are differences in DNA between people. Some variants may increase the risk of toxic effects from using some medications or may alter the optimal dosage. However, not everyone with such variants will necessarily experience altered reactions to medications. Also, it is possible for people without a genetic variant to experience them too. Some variants are more common in certain ethnicities. Dante Labs recommends that you discuss your report with a healthcare provider/geneticist or Genetic Counselor in order to correctly interpret the results. As Science progresses, variants may be subject to score changes or reclassification.

QUICK SUMMARY

MEDICATIONS

CONDITION NAME	RESULTS	MAIN MESSAGE
Acenocoumarol	⛔	We found a variant related to your reaction to Acenocoumarol
Adalimumab	✅	No variants detected
Allopurinol	✅	No variants detected
Amisulpride	✅	No variants detected
Amitriptyline	⚠	We found a variant related to your reaction to Amitriptyline
Anastrozole	⚠	We found a variant related to your reaction to Anastrozole
Aripiprazole	✅	No variants detected
Asparaginase	⛔	We found a variant related to your reaction to Asparaginase
Aspirin	✅	No variants detected
Ataluren	✅	No variants detected
Atazanavir	✅	No variants detected
Atorvastatin	⚠	We found a variant related to your reaction to Atorvastatin
Azathioprine	✅	No variants detected
Boceprevir	⚠	We found a variant related to your reaction to Boceprevir
Budesonide	✅	No variants detected
Buprenorphine	✅	No variants detected
Caffeine	✅	No variants detected
Carbamazepine	⚠	We found a variant related to your reaction to Carbamazepine
Carboplatin	⚠	We found a variant related to your reaction to Carboplatin
Celecoxib	✅	No variants detected
Cerivastatin	✅	No variants detected

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MEDICATIONS

CONDITION NAME	RESULTS	MAIN MESSAGE
Cetuximab	⚠	We found a variant related to your reaction to Cetuximab
Chlorproguanil	✓	No variants detected
Cisplatin	⚠	We found a variant related to your reaction to Cisplatin
Citalopram	⚠	We found a variant related to your reaction to Citalopram
Clomipramine	✓	No variants detected
Clozapine	✓	No variants detected
Cocaine	✓	No variants detected
Cyclosporine	✓	No variants detected
Dapsone	✓	No variants detected
Daunorubicin	⛔	We found a variant related to your reaction to Daunorubicin
Desipramine	✓	No variants detected
Diclofenac	✓	No variants detected
Digoxin	⚠	We found a variant related to your reaction to Digoxin
Docetaxel	⚠	We found a variant related to your reaction to Docetaxel
Doxepin	✓	No variants detected
Doxorubicin	⚠	We found a variant related to your reaction to Doxorubicin
Efavirenz	⚠	We found a variant related to your reaction to Efavirenz
Epirubicin	⚠	We found a variant related to your reaction to Epirubicin
Erlotinib	✓	No variants detected
Escitalopram	✓	No variants detected
Etanercept	✓	No variants detected
Ethambutol	⛔	We found a variant related to your reaction to Ethambutol
Ethanol	✓	No variants detected
Etoposide	⛔	We found a variant related to your reaction to Etoposide
Exemestane	⚠	We found a variant related to your reaction to Exemestane
Fentanyl	⚠	We found a variant related to your reaction to Fentanyl
Fluorouracil	⚠	We found a variant related to your reaction to Fluorouracil
Fluoxetine	⚠	We found a variant related to your reaction to Fluoxetine
Fluticasone propionate	✓	No variants detected
Fluticasone-salmeterol	✓	No variants detected
Furosemide	✓	No variants detected
Gefitinib	✓	No variants detected
Glibenclamide	✓	No variants detected
Gliclazide	✓	No variants detected

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CONDITION NAME	RESULTS	MAIN MESSAGE
Glimepiride	✓	No variants detected
Glipizide	✓	No variants detected
Haloperidol	✓	No variants detected
Heroin	✓	No variants detected
Hydrochlorothiazide	⚠	We found a variant related to your reaction to Hydrochlorothiazide
Imipramine	✓	No variants detected
Infliximab	✓	No variants detected
Interferon alfa-2b	✓	No variants detected
Isoniazid	⛔	We found a variant related to your reaction to Isoniazid
Ivacaftor	✓	No variants detected
Lamotrigine	✓	No variants detected
Latanoprost	✓	No variants detected
Leucovorin	✓	No variants detected
Lorazepam	✓	No variants detected
Lovastatin	⚠	We found a variant related to your reaction to Lovastatin
Mercaptopurine	✓	No variants detected
Metformin	✓	No variants detected
Methadone	⚠	We found a variant related to your reaction to Methadone
Methotrexate	✓	No variants detected
Mirtazapine	⚠	We found a variant related to your reaction to Mirtazapine
Morphine	⚠	We found a variant related to your reaction to Morphine
Naloxone	✓	No variants detected
Nevirapine	⛔	We found a variant related to your reaction to Nevirapine
Nicotine	✓	No variants detected
Nortriptyline	✓	No variants detected
Olanzapine	✓	No variants detected
Ondansetron	⚠	We found a variant related to your reaction to Ondansetron
Oxaliplatin	⚠	We found a variant related to your reaction to Oxaliplatin
Oxazepam	✓	No variants detected
Oxycodone	⚠	We found a variant related to your reaction to Oxycodone
Paclitaxel	⚠	We found a variant related to your reaction to Paclitaxel
Paliperidone	✓	No variants detected
Panitumumab	✓	No variants detected
Paroxetine	⚠	We found a variant related to your reaction to Paroxetine

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MEDICATIONS

CONDITION NAME	RESULTS	MAIN MESSAGE
Peginterferon alfa-2a	⚠	We found a variant related to your reaction to Peginterferon alfa-2a
Peginterferon alfa-2b	⚠	We found a variant related to your reaction to Peginterferon alfa-2b
Phenprocoumon	⛔	We found a variant related to your reaction to Phenprocoumon
Phenytoin	✓	No variants detected
Platinum based therapies	⚠	We found a variant related to your reaction to Platinum based therapies
Pravastatin	⚠	We found a variant related to your reaction to Pravastatin
Prednisolone	⛔	We found a variant related to your reaction to Prednisolone
Pyrazinamide	⛔	We found a variant related to your reaction to Pyrazinamide
Quetiapine	✓	No variants detected
Radiotherapy	⚠	We found a variant related to your reaction to Radiotherapy
Ribavirin	⚠	We found a variant related to your reaction to Ribavirin
Rifampin	⛔	We found a variant related to your reaction to Rifampin
Risperidone	✓	No variants detected
Rituximab	✓	No variants detected
Rosiglitazone	✓	No variants detected
Rosuvastatin	✓	No variants detected
Salbutamol	⚠	We found a variant related to your reaction to Salbutamol
Salmeterol	⚠	We found a variant related to your reaction to Salmeterol
Sildenafil	⚠	We found a variant related to your reaction to Sildenafil
Simvastatin	⚠	We found a variant related to your reaction to Simvastatin
Sirolimus	✓	No variants detected
Spironolactone	✓	No variants detected
Streptomycin	✓	No variants detected
Sunitinib	✓	No variants detected
Tacrolimus	⚠	We found a variant related to your reaction to Tacrolimus
Tamoxifen	⚠	We found a variant related to your reaction to Tamoxifen
Telaprevir	⚠	We found a variant related to your reaction to Telaprevir
Tramadol	⚠	We found a variant related to your reaction to Tramadol
Trastuzumab	⚠	We found a variant related to your reaction to Trastuzumab
Triamcinolone	✓	No variants detected
Trimipramine	✓	No variants detected
Venlafaxine	⚠	We found a variant related to your reaction to Venlafaxine
Vincristine	⛔	We found a variant related to your reaction to Vincristine
Warfarin	⛔	We found a variant related to your reaction to Warfarin

MEDICATIONS

CONDITION NAME	RESULTS	MAIN MESSAGE
Ziprasidone	✓	No variants detected

KEY SUMMARY

The above Summary provides an overview of the predicted risks for the patient. This information is based solely on genotype information and does not replace a doctor visit or a complete patient profile. Healthcare providers should consider also family history, presenting symptoms, current prescriptions, and other factors before making any clinical or therapeutic decisions.

No negative assertion based on your genotype.

We have found one or more variants associated with alterations in your reaction to the medication.

We have found one or more variants potentially associated with an increased risk for side effects.

DETAILED INFORMATION

ACENOCOUMAROL

Variant found:

- Gene: VKORC1
- Marker: rs9923231
- Position: chr16:31107689
- Genotype: CT

Individuals with the CT genotype who are treated with warfarin or acenocoumarol may have an increased risk of Hemorrhage as compared to the CC genotypes, however this is contradicted in nearly half the studies. Other clinical and genetic factors may also influence risk of hemorrhage in patients administered warfarin or acenocoumarol.

Variant found:

- Gene: VKORC1
- Marker: rs9923231
- Position: chr16:31107689
- Genotype: CT

Individuals with the CT genotype who are treated with acenocoumarol or phenprocoumon may require a lower dose as compared to patients with the CC genotype, although some suggest that the CT genotype may also require a higher dose as compared to patients with the TT genotype. Other genetic and clinical factors may also influence a patient's acenocoumarol or phenprocoumon dose.

Description

Acenocoumarol is an anticoagulant that functions as a vitamin K antagonist (like warfarin). It is a derivative of coumarin and is generic, so is marketed under many brand names worldwide.

AMITRIPTYLINE

Variant found:

- Gene: CYP2C19
- Marker: rs4244285
- Position: chr10:96541616
- Genotype: GA

Individuals with the AG genotype who are treated with amitriptyline may have decreased metabolism of amitriptyline (increased amitriptyline plasma concentrations and decreased nortriptyline plasma concentrations) as compared to patients with the GG genotype. Other genetic factors, including other CYP2C19 alleles *17 rs12248560 and *3 rs4986893, along with clinical factors, may also influence a patient's required dose and should be taken into consideration.

Description

Amitriptyline, sold under the brand name Elavil among others, is a medicine primarily used to treat a number of mental illnesses. These include major depressive disorder and anxiety disorders, and less commonly attention deficit hyperactivity disorder and bipolar disorder. Other uses include prevention of migraines, treatment of neuropathic pain such as fibromyalgia and postherpetic neuralgia, and less commonly insomnia. It is in the tricyclic antidepressant (TCA) class and its exact mechanism of action is unclear. Amitriptyline is taken by mouth. Common side effects include blurred vision, dry mouth, low blood pressure on standing, sleepiness, and constipation. Serious side effects may include seizures, an increased risk of suicide in those less than 25 years of age, urinary retention, glaucoma, and a number of heart issues. It should not be taken with MAO inhibitors or the medication cisapride. Amitriptyline may cause problems if taken during pregnancy. Use during breastfeeding appears to be relatively safe.

ANASTROZOLE

Variant found:

- Gene: CYP19A1
- Marker: rs4646
- Position: chr15:51502844
- Genotype: AC

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Anastrozole, sold under the brand name Arimidex among others, is a medication used in addition to other treatments for breast cancer. Specifically it is used for hormone receptor-positive breast cancer. It has also been used to prevent breast cancer in those at high risk. It is taken by mouth. Common side effects include hot flushes, altered mood, joint pain, and nausea. Severe side effects include an increased risk of heart disease and osteoporosis. Use during pregnancy is known to harm the baby. Anastrozole is in the aromatase-inhibiting family of medications. It works by blocking the creation of estrogen.

ASPARAGINASE

Variant found:

- Gene: PNPLA3
- Marker: rs738409
- Position: chr22:44324727
- Genotype: CG

Individuals with the CG genotype may have increased risk of hepatotoxicity when treated with remission induction therapy (including asparaginase) in children with acute lymphoblastic leukemia (ALL) as compared to patients with genotype CC. Other genetic and clinical factors may also influence the risk of toxicity to remission induction therapy.

Description

Asparaginase is an enzyme that is used as a medication and in food manufacturing. As a medication, L-asparaginase is used to treat acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and non-Hodgkin's lymphoma. It is given by injection into a vein, muscle, or under the skin. A pegylated version is also available. In food manufacturing it is used to decrease acrylamide. Common side effects when used by injection include allergic reactions, pancreatitis, blood clotting problems, high blood sugar, kidney problems, and liver dysfunction. Use in pregnancy may harm the baby. As a food it is generally recognized as safe. Asparaginase works by breaking down the amino acid known as asparagine without which the cancer cells cannot make protein.

ATORVASTATIN

Variant found:

- Gene: APOA5
- Marker: rs662799
- Position: chr11:116663707
- Genotype: AA

Individuals with the AA genotype and Hyperlipidemia who are treated with atorvastatin, lovastatin or simvastatin may have a higher reduction in LDL-cholesterol as compared to patients with the AG or GG genotype. Other genetic and clinical factors may also influence a patient's response to statin treatment.

Variant found:

- Gene: KIF6
- Marker: rs20455
- Position: chr6:39325078
- Genotype: AG

Individuals with the AG genotype may have a higher risk of coronary disease and may be more likely to benefit from atorvastatin treatment as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to atorvastatin treatment.

Description

Atorvastatin, sold under the trade name Lipitor among others, is a statin medication used to prevent cardiovascular disease in those at high risk and treat abnormal lipid levels. For the prevention of cardiovascular disease, statins are a first-line treatment. It is taken by mouth. Common side effects include joint pain, diarrhea, heart burn, nausea, and muscle pains. Serious side effects may include rhabdomyolysis, liver problems, and diabetes. Use during pregnancy

may harm the baby. Like all statins, atorvastatin works by inhibiting HMG-CoA reductase, an enzyme found in the liver that plays a role in producing cholesterol.

BOCEPREVIR

Variant found:

- **Gene: IFNL3, IFNL4**
- **Marker: rs12979860**
- **Position: chr19:39738787**
- **Genotype: CT**

Individuals with the CT genotype may have poorer response to triple therapy (boceprevir, peginterferon alfa-2b and ribavirin) in people with Hepatitis C as compared to patients with the CC genotype. Other genetic and clinical factors may also influence a patient's response.

Description

Boceprevir (INN, trade name Victrelis) is a protease inhibitor used to treat hepatitis caused by hepatitis C virus (HCV) genotype 1. It binds to the HCV nonstructural protein 3 active site. It was initially developed by Schering-Plough, then by Merck after it acquired Schering in 2009. It was approved by the FDA in May 2011. In January 2015, Merck announced that they would be voluntarily withdrawing Victrelis from the market due to the overwhelming superiority of newer direct-acting antiviral agents, such as ledipasvir/sofosbuvir.

CARBAMAZEPINE

Variant found:

- **Gene: EPHX1**
- **Marker: rs2234922**
- **Position: chr1:226026406**
- **Genotype: AG**

Individuals with the AG genotype may require an increased dose of carbamazepine as compared to patients with the AA genotype, although this is contradicted in one study. Other genetic and clinical factors may also influence dose of carbamazepine.

Description

Carbamazepine (CBZ), sold under the trade name Tegretol, among others, is a anticonvulsant medication used primarily in the treatment of epilepsy and neuropathic pain. It is not effective for absence or myoclonic seizures. It is used in schizophrenia along with other medications and as a second-line agent in bipolar disorder. Carbamazepine appears to work as well as phenytoin and valproate. Common side effects include nausea and drowsiness. Serious side effects may include skin rashes, decreased bone marrow function, suicidal thoughts, or confusion. It should not be used in those with a history of bone marrow problems. Use during pregnancy may cause harm to the baby; however, stopping the medication in pregnant women with seizures is not recommended. Its use during breastfeeding is not recommended. Care should be taken in those with either kidney or liver problems.

CARBOPLATIN

Variant found:

- **Gene: XRCC1**
- **Marker: rs25487**
- **Position: chr19:44055726**
- **Genotype: CC**

Individuals with cancer and the CC genotype may have increased response (in the form of longer progression-free or overall survival) when treated with platinum-based therapies as compared to patients with the CT or TT genotype. However, a few studies report no association or decreased survival and response for patients with the CC as compared to the TT genotype only. Other genetic and clinical factors may also influence response to platinum-based regimens.

Description

Carboplatin, sold under the trade name Paraplatin among others, is a chemotherapy medication used to treat a number of forms of cancer. This includes ovarian cancer, lung cancer, head and neck cancer, brain cancer, and neuroblastoma. It is used by injection into a vein. Side effects generally occur. Common side effects include low blood cell levels, nausea, and electrolyte problems. Other serious side effects include allergic reactions and increased future risk of another cancer. Use during pregnancy may result in harm to the baby. Carboplatin is in the platinum-based antineoplastic family of medications and works by interfering with duplication of DNA.

CETUXIMAB

Variant found:

- **Gene: EGF**
- **Marker: rs4444903**
- **Position: chr4:110834110**
- **Genotype: AG**

Individuals with the AG genotype who are treated with cetuximab may have a poorer response as compared to patients with the GG genotype or may have a better response as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to cetuximab treatment.

Description

Cetuximab is an epidermal growth factor receptor (EGFR) inhibitor used for the treatment of metastatic colorectal cancer, metastatic non-small cell lung cancer and head and neck cancer. Cetuximab is a chimeric (mouse/human) monoclonal antibody given by intravenous infusion that is distributed under the trade name Erbitux in the U.S. and Canada by the drug company Bristol-Myers Squibb and outside those countries by the drug company Merck KGaA. In Japan, Merck KGaA, Bristol-Myers Squibb and Eli Lilly have a co-distribution. In July 2009, the FDA approved cetuximab (Erbitux) for treatment of colon cancer with wild-type KRAS, since it had little or no effect in colorectal tumors harboring a KRAS mutation (this also applied to the EGFR antibody panitumumab). This was the first genetic test to guide treatment of cancer. In July 2012, the FDA approved a real time PCR companion diagnostic test for KRAS, the therascreen KRAS test.

CISPLATIN

Variant found:

- **Gene: XRCC1**
- **Marker: rs25487**
- **Position: chr19:44055726**
- **Genotype: CC**

Individuals with cancer and the CC genotype may have increased response (in the form of longer progression-free or overall survival) when treated with platinum-based therapies as compared to patients with the CT or TT genotype. However, a few studies report no association or decreased survival and response for patients with the CC as compared to the TT genotype only. Other genetic and clinical factors may also influence response to platinum-based regimens.

Description

Cisplatin is a chemotherapy medication used to treat a number of cancers. These include testicular cancer, ovarian cancer, cervical cancer, breast cancer, bladder cancer, head and neck cancer, esophageal cancer, lung cancer, mesothelioma, brain tumors and neuroblastoma. It is given by injection into a vein. Common side effects include bone marrow suppression, hearing problems, kidney problems, and vomiting. Other serious side effects include numbness, trouble walking, allergic reactions, electrolyte problems, and heart disease. Use during pregnancy is known to harm the baby. Cisplatin is in the platinum-based antineoplastic family of medications. It works in part by binding to DNA and inhibiting its replication.

CITALOPRAM

Variant found:

- **Gene: FKBP5**
- **Marker: rs4713916**
- **Position: chr6:35669983**
- **Genotype: GG**

Individuals with the GG genotype may have a reduced response to antidepressants as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to antidepressant treatment.

Variant found:

- **Gene: HTR2A**
- **Marker: rs7997012**
- **Position: chr13:47411985**
- **Genotype: AG**

Individuals with the AG genotype and depression who are treated with citalopram may be more likely to have improvement in symptoms as compared to patients with the GG genotype. However, no association has been reported in studies that determined response to different Selective serotonin reuptake inhibitors (SSRIs) or antidepressants as a drug class. Other genetic and clinical factors may also influence a patient's response to antidepressants.

Description

Citalopram, sold under the brand name Celexa among others, is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. It is used to treat major depressive disorder, obsessive compulsive disorder, panic disorder, and social phobia. Benefits may take one to four weeks to occur. It is taken by

mouth. Common side effects include nausea, trouble sleeping, sexual problems, shakiness, feeling tired, and sweating. Serious side effects include an increased risk of suicide in those under the age of 25, serotonin syndrome, glaucoma, and QT prolongation. It should not be used in someone on a MAO inhibitor. Antidepressant discontinuation syndrome may occur when stopped. There are concerns that use during pregnancy may harm the baby.

DAUNORUBICIN

Variant found:

- **Gene: PNPLA3**
- **Marker: rs738409**
- **Position: chr22:44324727**
- **Genotype: CG**

Individuals with the CG genotype may have increased risk of hepatotoxicity when treated with remission induction therapy (including asparaginase) in children with acute lymphoblastic leukemia (ALL) as compared to patients with genotype CC. Other genetic and clinical factors may also influence the risk of toxicity to remission induction therapy.

Description

Daunorubicin, also known as daunomycin, is a chemotherapy medication used to treat cancer. Specifically it is used for acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (CML), and Kaposi's sarcoma. It is used by injection into a vein. A liposomal formulation known as liposomal daunorubicin also exists. Common side effects include hair loss, vomiting, bone marrow suppression, and inflammation of the inside of the mouth. Other severe side effects include heart disease and tissue death at the site of injection. Use in pregnancy may harm the baby. Daunorubicin is in the anthracycline family of medication. It works in part by blocking the function of topoisomerase II.

DIGOXIN

Variant found:

- **Gene: ABCB1**
- **Marker: rs1045642**
- **Position: chr7:87138645**
- **Genotype: GG**

Individuals with GG genotype may have increased metabolism and decreased serum concentration of digoxin as compared to patients with the AA genotype. Other genetic and clinical factors may also impact the metabolism of digoxin.

Description

Digoxin, sold under the brand name Lanoxin among others, is a medication used to treat various heart conditions. Most frequently it is used for atrial fibrillation, atrial flutter, and heart failure. Digoxin is taken by mouth or by injection into a vein. Common side effects include breast enlargement with other side effects generally due to an excessive dose. These side effects may include loss of appetite, nausea, trouble seeing, confusion, and an irregular heartbeat. Greater care is required in older people and those with poor kidney function. It is unclear whether use during pregnancy is safe. Digoxin is in the cardiac glycoside family of medications.

DOCETAXEL

Variant found:

- **Gene: CYP19A1**
- **Marker: rs4646**
- **Position: chr15:51502844**
- **Genotype: AC**

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Docetaxel (DTX or DXL), sold under the brand name Taxotere among others, is a chemotherapy medication used to treat a number of types of cancer. This includes breast cancer, head and neck cancer, stomach cancer, prostate cancer and non-small-cell lung cancer. It may be used by itself or along with other chemotherapy medication. It is given by slow injection into a vein. Common side effects include hair loss, low blood cell counts, numbness, shortness of breath, vomiting, and muscle pains. Other severe side effects include allergic reactions and future cancers. Side effects are more common in people with liver problems. Use during pregnancy may harm the baby. Docetaxel is in the taxane family of medications. It works by disrupting the normal function of microtubules and thereby stopping cell division.

DOXORUBICIN

Variant found:

- **Gene: CYP19A1**
- **Marker: rs4646**
- **Position: chr15:51502844**
- **Genotype: AC**

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Doxorubicin, sold under the trade names Adriamycin among others, is a chemotherapy medication used to treat cancer. This includes breast cancer, bladder cancer, Kaposi's sarcoma, lymphoma, and acute lymphocytic leukemia. It is often used together with other chemotherapy agents. Doxorubicin is given by injection into a vein. Common side effects include hair loss, bone marrow suppression, vomiting, rash, and inflammation of the mouth. Other serious side effects may include allergic reactions such as anaphylaxis, heart damage, tissue damage at the site of injection, radiation recall, and treatment-related leukemia. People often experience red discoloration of the urine for a few days. Doxorubicin is in the anthracycline and antitumor antibiotic family of medications. It works in part by interfering with the function of DNA.

EFAVIRENZ

Variant found:

- Gene: CYP2B6
- Marker: rs3745274
- Position: chr19:41512841
- Genotype: GT

Individuals with the GT genotype and HIV infection may have increased plasma concentrations and decreased clearance of efavirenz as compared to patients with the GG genotype. Other genetic and clinical factors may also influence a patient's exposure to efavirenz.

Variant found:

- Gene: CYP2B6
- Marker: rs4803419
- Position: chr19:41512792
- Genotype: CT

Individuals with HIV and the CT genotype may have higher plasma concentrations of efavirenz as compared to patients with the CC genotype and lower plasma concentrations as compared to patients with the TT genotype. Other clinical and genetic factors may also influence plasma concentrations of efavirenz in patients with HIV.

Variant found:

- Gene: CYP2B6
- Marker: rs2279345
- Position: chr19:41515702
- Genotype: CC

Individuals with the CC genotype and HIV may have increased metabolism of efavirenz resulting in lower efavirenz plasma levels as compared to patients with the TT genotype. Other genetic and clinical factors may also influence metabolism and plasma concentrations of efavirenz.

Description

Efavirenz (EFV), sold under the brand names Sustiva among others, is an antiretroviral medication used to treat and prevent HIV/AIDS. It is generally recommended for use with other antiretrovirals. It may be used for prevention after a needlestick injury or other potential exposure. It is sold both by itself and in combination as efavirenz/emtricitabine/tenofovir. It is taken by mouth once a day. Common side effects include rash, nausea, headache, feeling tired, and trouble sleeping. Some of the rashes may be serious such as Stevens-Johnson syndrome. Other serious side effects include depression, thoughts of suicide, liver problems, and seizures. It is not safe for use during pregnancy. It is a non-nucleoside reverse transcriptase inhibitor (NNRTI) and works by blocking the function of reverse transcriptase.

EPIRUBICIN

Variant found:

- Gene: CYP19A1

- Marker: rs4646
- Position: chr15:51502844
- Genotype: AC

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Epirubicin is an anthracycline drug used for chemotherapy. It can be used in combination with other medications to treat breast cancer in patients who have had surgery to remove the tumor. It is marketed by Pfizer under the trade name Ellence in the US and Pharmorubicin or Epirubicin Ebewe elsewhere. Similarly to other anthracyclines, epirubicin acts by intercalating DNA strands. Intercalation results in complex formation which inhibits DNA and RNA synthesis. It also triggers DNA cleavage by topoisomerase II, resulting in mechanisms that lead to cell death. Binding to cell membranes and plasma proteins may be involved in the compound's cytotoxic effects. Epirubicin also generates free radicals that cause cell and DNA damage. Epirubicin is favoured over doxorubicin, the most popular anthracycline, in some chemotherapy regimens as it appears to cause fewer side-effects. Epirubicin has a different spatial orientation of the hydroxyl group at the 4' carbon of the sugar - it has the opposite chirality - which may account for its faster elimination and reduced toxicity. Epirubicin is primarily used against breast and ovarian cancer, gastric cancer, lung cancer and lymphomas.

ETHAMBUTOL

Variant found:

- Gene: NAT2
- Marker: rs1799930
- Position: chr8:18258103
- Genotype: AA

Individuals with the AA genotype and tuberculosis (TB) may have an increased risk of hepatotoxicity when treated with anti-TB drugs as compared to patients with the GG genotype. They also may have decreased clearance of isoniazid as compared to those with the AG or GG genotype. Other genetic and clinical factors may also influence risk for hepatotoxicity and clearance of isoniazid.

Variant found:

- Gene: NAT2
- Marker: rs1041983
- Position: chr8:18257795
- Genotype: TT

Individuals with the TT genotype and tuberculosis (TB) may have an increased risk for hepatotoxicity when treated with anti-TB drugs as compared to patients with the CC genotype. Other genetic and clinical factors may also influence risk for hepatotoxicity.

Description

Ethambutol (EMB, E) is a medication primarily used to treat tuberculosis. It is usually given in combination with other tuberculosis medications, such as isoniazid, rifampicin and pyrazinamide. It may also be used to treat Mycobacterium avium complex, and Mycobacterium kansasii. It is taken by mouth. Common side effects include problems with vision, joint pain, nausea, headaches, and feeling tired. Other side effects include liver problems and allergic reactions. It is not recommended in people with optic neuritis, significant kidney problems, or under the age of five. Use during pregnancy or breastfeeding has not been found to cause harm. In the United States the FDA has raised concerns about eye issues in the baby if used during pregnancy. Ethambutol is believed to work by interfering with the bacteria's metabolism.

ETOPOSIDE

Variant found:

- **Gene: DYNC2H1**
- **Marker: rs716274**
- **Position: chr11:103418158**
- **Genotype: GG**

Individuals with the GG genotype may have increased risk of Death when treated with etoposide and Platinum compounds in people with Carcinoma, Small Cell as compared to patients with genotype AA. Other genetic and clinical factors may also influence the response to etoposide and Platinum compounds.

Description

Etoposide, sold under the brand name Etopophos among others, is a chemotherapy medication used for the treatments of a number of types of cancer. This includes testicular cancer, lung cancer, lymphoma, leukemia, neuroblastoma, and ovarian cancer. It is used by mouth or injection into a vein. Side effects are very common. They can include low blood cell counts, vomiting, loss of appetite, diarrhea, hair loss, and fever. Other severe side effects include allergic reactions and low blood pressure. Use during pregnancy will likely harm the baby. Etoposide is in the topoisomerase inhibitor family of medication. It is believed to work by damaging DNA.

EXEMESTANE

Variant found:

- **Gene: CYP19A1**
- **Marker: rs4646**
- **Position: chr15:51502844**
- **Genotype: AC**

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Exemestane, sold under the brand name Aromasin among others, is a medication used to treat breast cancer. It is a member of the class of antiestrogens known as aromatase inhibitors. Some breast cancers require estrogen to grow. Those cancers have estrogen receptors (ERs), and are called ER-positive.

They may also be called estrogen-responsive, hormonally-responsive, or hormone-receptor-positive. Aromatase is an enzyme that synthesizes estrogen. Aromatase inhibitors block the synthesis of estrogen. This lowers the estrogen level, and slows the growth of cancers.

FENTANYL

Variant found:

- **Gene: ABCB1**
- **Marker: rs1045642**
- **Position: chr7:87138645**
- **Genotype: GG**

Individuals with the GG genotype may experience decreased efficacy of opioids and may require an increased dose as compared to patients with the AA and possibly AG genotypes, although this is contradicted in most studies, which report no association between the allele with dose or efficacy of opioids for pain. Other genetic and clinical factors may also influence a dose and efficacy of opioids for pain.

Description

Fentanyl, also spelled fentanil, is an opioid used as a pain medication and together with other medications for anesthesia. Fentanyl is also made illegally and used as a recreational drug, often mixed with heroin or cocaine. It has a rapid onset and effects generally last less than two hours. Medically, fentanyl is used by injection, as a patch on the skin, as a nasal spray, or in the mouth. Common side effects include vomiting, constipation, sedation, confusion, hallucinations, and injuries related to poor coordination. Serious side effects may include decreased breathing (respiratory depression), serotonin syndrome, low blood pressure, addiction, or coma. In 2016, more than 20,000 deaths occurred in the United States due to overdoses of fentanyl and analogues, half of all reported opioid-related deaths. Fentanyl works primarily by activating μ-opioid receptors. It is around 100 times stronger than morphine, and some analogues such as carfentanil are around 10,000 times stronger.

FLUOROURACIL

Variant found:

- **Gene: CYP19A1**
- **Marker: rs4646**
- **Position: chr15:51502844**
- **Genotype: AC**

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Fluorouracil (5-FU), sold under the brand name Adrucil among others, is a medication used to treat cancer. By injection into a vein it is used for colon cancer, esophageal cancer, stomach cancer, pancreatic cancer, breast cancer, and cervical cancer. As a cream it is used for actinic keratosis, basal cell carcinoma, and skin warts. When used by injection most people develop side effects. Common side effects include inflammation of the mouth, loss of

appetite, low blood cell counts, hair loss, and inflammation of the skin. When used as a cream, irritation at the site of application may occur. Use of either form in pregnancy may harm the baby. Fluorouracil is in the antimetabolite and pyrimidine analog families of medications. How it works is not entirely clear but believed to involve blocking the action of thymidylate synthase and thus stopping the production of DNA.

FLUOXETINE

Variant found:

- **Gene: FKBP5**
- **Marker: rs4713916**
- **Position: chr6:35669983**
- **Genotype: GG**

Individuals with the GG genotype may have a reduced response to antidepressants as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to antidepressant treatment.

Description

Fluoxetine, sold under the brand names Prozac and Sarafem among others, is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. It is used for the treatment of major depressive disorder, obsessive–compulsive disorder (OCD), bulimia nervosa, panic disorder, and premenstrual dysphoric disorder. It may decrease the risk of suicide in those over the age of 65. It has also been used to treat premature ejaculation. Fluoxetine is taken by mouth. Common side effects include trouble sleeping, sexual dysfunction, loss of appetite, dry mouth, rash, and abnormal dreams. Serious side effects include serotonin syndrome, mania, seizures, an increased risk of suicidal behavior in people under 25 years old, and an increased risk of bleeding. If stopped suddenly, a withdrawal syndrome may occur with anxiety, dizziness, and changes in sensation. It is unclear if it is safe in pregnancy. If already on the medication, it may be reasonable to continue during breastfeeding. Its mechanism of action is not entirely clear but believed to be related to increasing serotonin activity in the brain.

HYDROCHLOROTHIAZIDE

Variant found:

- **Gene: NEDD4L**
- **Marker: rs4149601**
- **Position: chr18:55816791**
- **Genotype: AA**

White patients with the AA genotype and hypertension who are treated with hydrochlorothiazide may have poorer response as compared with patients with genotype GG. The opposite result has been seen in Asians (at a lower level of evidence). Other genetic and clinical factors may also influence a patient's response to hydrochlorothiazide or other diuretic treatment.

Description

Hydrochlorothiazide (HCTZ or HCT) is a diuretic medication often used to treat high blood pressure and swelling due to fluid build up. Other uses include diabetes insipidus, renal tubular acidosis, and to decrease the risk of kidney stones in those with a high calcium level in the urine. For high blood pressure it is sometimes considered as a first-line treatment, although chlorthalidone is more effective with a similar rate of adverse effects. HCTZ is taken by mouth

and may be combined with other blood pressure medications as a single pill to increase effectiveness. Potential side effects include poor kidney function, electrolyte imbalances including low blood potassium and less commonly low blood sodium, gout, high blood sugar, and feeling lightheaded with standing. While allergies to HCTZ are reported to occur more often in those with allergies to sulfa drugs, this association is not well supported. It may be used during pregnancy, but it is not a first-line medication in this group. It is in the thiazide medication class and acts by decreasing the kidneys' ability to retain water. This initially reduces blood volume, decreasing blood return to the heart and thus cardiac output. It is believed to lower peripheral vascular resistance in the long run.

ISONIAZID

Variant found:

- **Gene: NAT2**
- **Marker: rs1041983**
- **Position: chr8:18257795**
- **Genotype: TT**

Individuals with the TT genotype and tuberculosis (TB) may have an increased risk for hepatotoxicity when treated with anti-TB drugs as compared to patients with the CC genotype. Other genetic and clinical factors may also influence risk for hepatotoxicity.

Variant found:

- **Gene: NAT2**
- **Marker: rs1799930**
- **Position: chr8:18258103**
- **Genotype: AA**

Individuals with the AA genotype and tuberculosis (TB) may have an increased risk of hepatotoxicity when treated with anti-TB drugs as compared to patients with the GG genotype. They also may have decreased clearance of isoniazid as compared to those with the AG or GG genotype. Other genetic and clinical factors may also influence risk for hepatotoxicity and clearance of isoniazid.

Description

Isoniazid, also known as isonicotinylhydrazide (INH), is an antibiotic used for the treatment of tuberculosis. For active tuberculosis it is often used together with rifampicin, pyrazinamide, and either streptomycin or ethambutol. For latent tuberculosis it is often used by itself. It may also be used for atypical types of mycobacteria, such as M. avium, M. kansasii, and M. xenopi. It is usually taken by mouth but may be used by injection into muscle. Common side effect include increased blood levels of liver enzymes and numbness in the hands and feet. Serious side effects may include liver inflammation. It is unclear if use during pregnancy is safe for the baby. Use during breastfeeding is likely safe. Pyridoxine may be given to reduce the risk of side effects. Isoniazid works in part by disrupting the formation of the bacteria's cell wall which results in cell death.

LOVASTATIN

Variant found:

- **Gene: APOA5**
- **Marker: rs662799**
- **Position: chr11:116663707**
- **Genotype: AA**

Individuals with the AA genotype and Hyperlipidemia who are treated with atorvastatin, lovastatin or simvastatin may have a higher reduction in LDL-cholesterol as compared to patients with the AG or GG genotype. Other genetic and clinical factors may also influence a patient's response to statin treatment.

Description

Lovastatin, sold under the brand name Mevacor among others, is a statin medication, to treat high blood cholesterol and reduce the risk of cardiovascular disease. It use is recommended together with lifestyle changes. It is taken by mouth. Common side effects include diarrhea, constipation, headache, muscles pains, rash, and trouble sleeping. Serious side effects may include liver problems, muscle breakdown, and kidney failure. Use during pregnancy may harm the baby and use during breastfeeding is not recommended. It works by decreasing the livers ability to produce cholesterol by blocking the enzyme HMG-CoA reductase.

METHADONE

Variant found:

- **Gene: CYP2B6**
- **Marker: rs3745274**
- **Position: chr19:41512841**
- **Genotype: GT**

Individuals with the GT genotype who are being treated with methadone for heroin addiction may require an increased dose of the drug as compared to patients with the TT genotype. Other genetic and clinical factors may also influence dose of methadone.

Variant found:

- **Gene: ABCB1**
- **Marker: rs1045642**
- **Position: chr7:87138645**
- **Genotype: GG**

Individuals with the GG genotype may experience decreased efficacy of opioids and may require an increased dose as compared to patients with the AA and possibly AG genotypes, although this is contradicted in most studies, which report no association between the allele with dose or efficacy of opioids for pain. Other genetic and clinical factors may also influence a dose and efficacy of opioids for pain.

Description

Methadone, sold under the brand name Dolophine among others, is an opioid used for opioid maintenance therapy in opioid dependence, and for pain. Detoxification using methadone can either be done relatively rapidly in less than a month or gradually over as long as six months. While a single dose has a rapid effect, maximum effect can take five days of use. The pain relieving effects last about six hours after a single dose, similar to morphine's. After long term use, in people with normal liver function, effects last 8 to 36 hours. Methadone is usually taken by mouth and rarely by injection into a muscle or vein. Side effects are similar to those of other opioids. Commonly these include dizziness, sleepiness, vomiting, and sweating. Serious risks include opioid abuse and a decreased effort to breathe. Abnormal heart rhythms may also occur due to a prolonged QT interval. The number of deaths in the United States involving methadone poisoning declined from 4,418 in 2011 to 3,300 in 2015. Risks are greater with higher doses. Methadone is made by chemical synthesis and acts on opioid receptors.

MIRTAZAPINE

Variant found:

- **Gene: FKBP5**
- **Marker: rs4713916**
- **Position: chr6:35669983**
- **Genotype: GG**

Individuals with the GG genotype may have a reduced response to antidepressants as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to antidepressant treatment.

Description

Mirtazapine, sold under the brand name Remeron among others, is an antidepressant primarily used to treat depression. Its full effect may take more than four weeks to occur, with some benefit possibly as early as one to two weeks. Often it is used in depression complicated by anxiety or trouble sleeping. It is taken by mouth. Common side effects include increased weight, sleepiness, and dizziness. Serious side effects may include an increased suicide among children, mania, and low white blood count. Withdrawal symptoms may occur with stopping. It is not recommended together with an MAO inhibitor. It is unclear if use during pregnancy is safe. How it works is not clear but may involve blocking certain adrenergic and serotonin receptors. Chemically, it is a tetracyclic antidepressant (TeCA). It also has strong antihistamine effects.

MORPHINE

Variant found:

- **Gene: ABCB1**
- **Marker: rs1045642**
- **Position: chr7:87138645**
- **Genotype: GG**

Individuals with the GG genotype may experience decreased efficacy of opioids and may require an increased dose as compared to patients with the AA and possibly AG genotypes, although this is contradicted in most studies, which report no association between the allele with dose or efficacy of opioids for pain. Other genetic and clinical factors may also influence a dose and efficacy of opioids for pain.

Description

Morphine is a pain medication of the opiate family which is found naturally in a number of plants and animals. It acts directly on the central nervous system (CNS) to decrease the feeling of pain. It can be taken for both acute pain and chronic pain. It is frequently used for pain from myocardial infarction and during labor. It can be given by mouth, by injection into a muscle, by injection under the skin, intravenously, injection into the space around the spinal cord, or rectally. Maximum effect is reached after about 20 minutes when given intravenously and after 60 minutes when given by mouth, while duration of effect is 3–7 hours. Long-acting formulations also exist. Potentially serious side effects include decreased respiratory effort and low blood pressure. Morphine is addictive and prone to abuse. If the dose is reduced after long-term use, opioid withdrawal symptoms may occur. Common side effects include drowsiness, vomiting, and constipation. Caution is advised when used during pregnancy or breast feeding, as morphine may affect the baby. Morphine was first isolated between 1803 and 1805 by Friedrich Sertürner. This is generally believed to be the first isolation of an active ingredient from a plant. Merck began marketing it commercially in 1827. Morphine was more widely used after the invention of the hypodermic syringe in 1853–1855. Sertürner originally named the substance morphium after the Greek god of dreams, Morpheus, as it has a tendency to cause sleep.

NEVIRAPINE

Variant found:

- **Gene: CYP2B6**
- **Marker: rs3745274**
- **Position: chr19:41512841**
- **Genotype: GT**

Individuals with the GT genotype and HIV infection may have decreased clearance of and increased exposure to nevirapine as compared to patients with the GG genotype. Other genetic and clinical factors may also influence clearance of nevirapine and exposure to drug.

Variant found:

- **Gene: ABCB1**
- **Marker: rs1045642**
- **Position: chr7:87138645**
- **Genotype: GG**

Individuals with the GG genotype and HIV-1 infection who are treated with nevirapine may have an increased risk for nevirapine hepatotoxicity as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's risk for hepatotoxicity with nevirapine treatment.

Description

Nevirapine (NVP), marketed under the trade name Viramune among others, is a medication used to treat and prevent HIV/AIDS, specifically HIV-1. It is generally recommended for use with other antiretroviral medication. It may be used to prevent mother to child spread during birth but is not recommended following other exposures. It is taken by mouth. Common side effects include rash, headache, nausea, feeling tired, and liver problems. The liver problems and skin rash may be severe and should be checked for during the first few months of treatment. It appears to be safe for use during pregnancy. It is a non-nucleoside reverse transcriptase inhibitor (NNRTI) and works by blocking the function of reverse transcriptase.

ONDANSETRON

Variant found:

- **Gene: ABCB1**
- **Marker: rs2032582**
- **Position: chr7:87160618**
- **Genotype: CC**

Individuals with genotype CC may have increased likelihood of nausea and vomiting shortly after being treated with ondansetron as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to ondansetron.

Variant found:

- **Gene: ABCB1**
- **Marker: rs1045642**
- **Position: chr7:87138645**

- Genotype: GG

Individuals with genotype GG may have increased likelihood of nausea and vomiting shortly after being treated with treated with ondansetron as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to ondansetron.

Description

Ondansetron, marketed under the brand name Zofran, is a medication used to prevent nausea and vomiting caused by cancer chemotherapy, radiation therapy, or surgery. It is also useful in gastroenteritis. It has little effect on vomiting caused by motion sickness. It can be given by mouth, or by injection into a muscle or into a vein. Common side effects include diarrhea, constipation, headache, sleepiness, and itchiness. Serious side effects include QT prolongation and severe allergic reaction. It appears to be safe during pregnancy but has not been well studied in this group. It is a serotonin 5-HT3 receptor antagonist. It does not have any effect on dopamine receptors or muscarinic receptors.

OXALIPLATIN

Variant found:

- Gene: XRCC1
- Marker: rs25487
- Position: chr19:44055726
- Genotype: CC

Individuals with cancer and the CC genotype may have increased response (in the form of longer progression-free or overall survival) when treated with platinum-based therapies as compared to patients with the CT or TT genotype. However, a few studies report no association or decreased survival and response for patients with the CC as compared to the TT genotype only. Other genetic and clinical factors may also influence response to platinum-based regimens.

Description

Oxaliplatin, sold under the brand name Eloxatin, is a cancer medication used to treat colorectal cancer. Often it is used together with fluorouracil and folinic acid (leucovorin) in advanced cancer. It is given by injection into a vein. Common side effects include numbness, feeling tired, nausea, diarrhea, and low blood cell counts. Other serious side effects include allergic reactions. Use in pregnancy is known to harm the baby. Oxaliplatin is in the platinum-based antineoplastic family of medications. It is believed to work by blocking the duplication of DNA.

OXYCODONE

Variant found:

- Gene: ABCB1
- Marker: rs1045642
- Position: chr7:87138645
- Genotype: GG

Individuals with the GG genotype may experience decreased efficacy of opioids and may require an increased dose as compared to patients with the AA and possibly AG genotypes, although this is contradicted in most studies, which report no association between the allele with dose or efficacy of opioids for

pain. Other genetic and clinical factors may also influence a dose and efficacy of opioids for pain.

Description

Oxycodone, sold under brand name OxyContin among others, is an opioid medication used for treatment of moderate to severe pain. It is usually taken by mouth, and is available in immediate release and controlled release formulations. Onset of pain relief typically begins within 15 minutes and lasts for up to six hours with the immediate release formulation. In the United Kingdom, it is available by injection. Combination products are also available with paracetamol (acetaminophen) or aspirin. Common side effects include constipation, nausea, sleepiness, dizziness, itching, dry mouth, and sweating. Severe side effects may include addiction, respiratory depression (a decreased effort to breathe), and low blood pressure. Those allergic to codeine may also be allergic to oxycodone. Use of oxycodone in early pregnancy appears relatively safe. Opioid withdrawal may occur if rapidly stopped. Oxycodone acts by activating the μ-opioid receptor. When taken by mouth, it has roughly 1.5 times the effect of the equivalent amount of morphine.

PACLITAXEL

Variant found:

- **Gene: CYP19A1**
- **Marker: rs4646**
- **Position: chr15:51502844**
- **Genotype: AC**

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Paclitaxel (PTX), sold under the brand name Taxol among others, is a chemotherapy medication used to treat a number of types of cancer. This includes ovarian cancer, breast cancer, lung cancer, Kaposi sarcoma, cervical cancer, and pancreatic cancer. It is given by injection into a vein. There is also an albumin-bound formulation. Common side effects include hair loss, bone marrow suppression, numbness, allergic reactions, muscle pains, and diarrhea. Other serious side effects include heart problems, increased risk of infection, and lung inflammation. There are concerns that use during pregnancy may cause birth defects. Paclitaxel is in the taxane family of medications. It works by interference with the normal function of microtubules during cell division.

PAROXETINE

Variant found:

- **Gene: HTR1A**
- **Marker: rs6295**
- **Position: chr5:63258565**
- **Genotype: CG**

Individuals with the CG genotype with panic disorder who are treated with paroxetine may have an reduced response at 4 weeks of treatment as compared to patients with the GG genotype. Other genetic and clinical factors may also influence a patient's response to paroxetine.

Variant found:

- Gene: FKBP5
- Marker: rs4713916
- Position: chr6:35669983
- Genotype: GG

Individuals with the GG genotype may have a reduced response to antidepressants as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to antidepressant treatment.

Description

Paroxetine, sold under the brand names Paxil and Seroxat among others, is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. It is used to treat major depressive disorder, obsessive-compulsive disorder, panic disorder, social anxiety disorder, posttraumatic stress disorder, generalized anxiety disorder and premenstrual dysphoric disorder. It has also been used in the treatment of hot flashes due to menopause and premature ejaculation. It is taken by mouth. Common side effects include drowsiness, dry mouth, loss of appetite, sweating, trouble sleeping, and sexual dysfunction. Serious side effects may include suicide in those under the age of 25, serotonin syndrome, and mania. While rate of side effects appear similar compared to other SSRIs and SNRIs, antidepressant discontinuation syndromes may occur more often. Use in pregnancy is not recommended while use during breastfeeding is relatively safe. It believed to work by blocking the re-uptake of the chemical serotonin by neurons in the brain.

PEGINTERFERON ALFA-2A

Variant found:

- Gene: IFNL3, IFNL4
- Marker: rs12979860
- Position: chr19:39738787
- Genotype: CT

Individuals with the CT genotype may have lower response rates (SVR) to triple therapy (telaprevir, peginterferon alfa-2a/b and ribavirin) in people with Hepatitis C genotype 1 as compared to patients with the CC genotype. The impact of IL28B genotype maybe dampened in patients with prior PegIFN/RBV treatment failure. Other genetic and clinical factors may also influence a patient's response to HCV triple therapy.

Variant found:

- Gene: IFNL3
- Marker: rs11881222
- Position: chr19:39734923
- Genotype: AG

Individuals with the AG genotype and hepatitis C or HIV may have a poorer response to treatment with peginterferon-alpha and ribavirin as compared to patients with the AA genotype. Other genetic and clinical factors may also influence response to peginterferon-alpha and ribavirin treatment.

Description

Pegylated interferon alfa-2a, sold under the brand name Pegasys among others, is medication used to treat hepatitis C and hepatitis B. For hepatitis C it is typically used together with ribavirin and cure rates are between 24 and 92%. For hepatitis B it may be used alone. It is given by injection under the skin. Side effects are common. They may include headache, feeling tired, depression, trouble sleeping, hair loss, nausea, pain at the site of injection, and fever. Severe side effects may include psychosis, autoimmune disorders, blood clots, or infections. Use with ribavirin is not recommended during pregnancy. Pegylated interferon alfa-2a is in the alpha interferon family of medications. It is pegylated to protect the molecule from breakdown.

PEGINTERFERON ALFA-2B

Variant found:

- **Gene: IFNL3, IFNL4**
- **Marker: rs12979860**
- **Position: chr19:39738787**
- **Genotype: CT**

Individuals with the CT genotype may have lower response rates (SVR) to triple therapy (telaprevir, peginterferon alfa-2a/b and ribavirin) in people with Hepatitis C genotype 1 as compared to patients with the CC genotype. The impact of IL28B genotype maybe dampened in patients with prior PegIFN/RBV treatment failure. Other genetic and clinical factors may also influence a patient's response to HCV triple therapy.

Variant found:

- **Gene: IFNL3**
- **Marker: rs11881222**
- **Position: chr19:39734923**
- **Genotype: AG**

Individuals with the AG genotype and hepatitis C or HIV may have a poorer response to treatment with peginterferon-alpha and ribavirin as compared to patients with the AA genotype. Other genetic and clinical factors may also influence response to peginterferon-alpha and ribavirin treatment.

Description

Pegylated interferon alfa-2b, sold under the brand name PegIntron among others, is a medication used to treat hepatitis C and melanoma. For hepatitis C it is typically used with ribavirin and cure rates are between 33 and 82%. For melanoma it is used in addition to surgery. It is given by injection under the skin. Side effects are common. They may include headache, feeling tired, mood changes, trouble sleeping, hair loss, nausea, pain at the site of injection, and fever. Severe side effects may include psychosis, liver problems, blood clots, infections, or an irregular heartbeat. Use with ribavirin is not recommended during pregnancy. Pegylated interferon alfa-2b is in the alpha interferon family of medications. It is pegylated to protects the molecule from breakdown.

PHENPROCOUMON

Variant found:

- **Gene: VKORC1**
- **Marker: rs9923231**
- **Position: chr16:31107689**
- **Genotype: CT**

Individuals with the CT genotype who are treated with warfarin or acenocoumarol may have an increased risk of Hemorrhage as compared to the CC genotypes, however this is contradicted in nearly half the studies. Other clinical and genetic factors may also influence risk of hemorrhage in patients administered warfarin or acenocoumarol.

Variant found:

- **Gene: VKORC1**
- **Marker: rs9923231**
- **Position: chr16:31107689**
- **Genotype: CT**

Individuals with the CT genotype who are treated with acenocoumarol or phenprocoumon may require a lower dose as compared to patients with the CC genotype, although some suggest that the CT genotype may also require a higher dose as compared to patients with the TT genotype. Other genetic and clinical factors may also influence a patient's acenocoumarol or phenprocoumon dose.

Description

Phenprocoumon (marketed under the brand names Marcoumar, Marcumar and Falithrom) is a long-acting oral anticoagulant drug, a derivative of coumarin. It is a vitamin K antagonist that inhibits coagulation by blocking synthesis of coagulation factors II, VII, IX and X. It is used for the prophylaxis and treatment of thromboembolic disorders (thrombosis/pulmonary embolism). It is the standard coumarin used in Germany. Phenprocoumon is a 4-hydroxycoumarin and inhibits vitamin K epoxide reductase.

PLATINUM BASED THERAPIES

Variant found:

- **Gene: XRCC1**
- **Marker: rs25487**
- **Position: chr19:44055726**
- **Genotype: CC**

Individuals with cancer and the CC genotype may have increased response (in the form of longer progression-free or overall survival) when treated with platinum-based therapies as compared to patients with the CT or TT genotype. However, a few studies report no association or decreased survival and response for patients with the CC as compared to the TT genotype only. Other genetic and clinical factors may also influence response to platinum-based regimens.

Description

Platinum is a chemical element with symbol Pt and atomic number 78. It is a dense, malleable, ductile, highly unreactive, precious, silverish-white transition metal. Its name is derived from the Spanish term platino, meaning "little silver". Compounds containing platinum, such as cisplatin, oxaliplatin and carboplatin, are applied in chemotherapy against certain types of cancer.

PRAVASTATIN

Variant found:

- **Gene: KIF6**
- **Marker: rs20455**
- **Position: chr6:39325078**
- **Genotype: AG**

Individuals with the AG genotype may have a higher risk of coronary disease and may be more likely to benefit from pravastatin treatment as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to pravastatin treatment.

Description

Pravastatin, sold under the brand name Pravachol among others, is a statin medication, used preventing cardiovascular disease in those at high risk and treating abnormal lipids. It should be used together with diet changes, exercise, and weight loss. It is taken by mouth. Common side effects include joint pain, diarrhea, nausea, headaches, and muscle pains. Serious side effects may include rhabdomyolysis, liver problems, and diabetes. Use during pregnancy may harm the baby. Like all statins, pravastatin works by inhibiting HMG-CoA reductase, an enzyme found in liver that plays a role in producing cholesterol.

PREDNISOLONE

Variant found:

- **Gene: PNPLA3**
- **Marker: rs738409**
- **Position: chr22:44324727**
- **Genotype: CG**

Individuals with the CG genotype may have increased risk of hepatotoxicity when treated with remission induction therapy (including asparaginase) in children with acute lymphoblastic leukemia (ALL) as compared to patients with genotype CC. Other genetic and clinical factors may also influence the risk of toxicity to remission induction therapy.

Description

Prednisolone is a steroid medication used to treat certain types of allergies, inflammatory conditions, autoimmune disorders, and cancers. Some of these conditions include adrenocortical insufficiency, high blood calcium, rheumatoid arthritis, dermatitis, eye inflammation, asthma, and multiple sclerosis. It is used by mouth, injection into a vein, as a skin cream, and as eye drops. Side effects with short term use include nausea and feeling tired. More severe side effects include psychiatric problems, which may occur in about 5% of people. Common side effects with long term use include bone loss, weakness, yeast infections, and easy bruising. While short term use in the later part of pregnancy is safe, long term use or use in early pregnancy is occasionally associated with harm to the baby. It is a glucocorticoid made from hydrocortisone (cortisol).

PYRAZINAMIDE

Variant found:

- **Gene: NAT2**
- **Marker: rs1799930**

- Position: chr8:18258103
- Genotype: AA

Individuals with the AA genotype and tuberculosis (TB) may have an increased risk of hepatotoxicity when treated with anti-TB drugs as compared to patients with the GG genotype. They also may have decreased clearance of isoniazid as compared to those with the AG or GG genotype. Other genetic and clinical factors may also influence risk for hepatotoxicity and clearance of isoniazid.

Variant found:

- Gene: NAT2
- Marker: rs1041983
- Position: chr8:18257795
- Genotype: TT

Individuals with the TT genotype and tuberculosis (TB) may have an increased risk for hepatotoxicity when treated with anti-TB drugs as compared to patients with the CC genotype. Other genetic and clinical factors may also influence risk for hepatotoxicity.

Description

Pyrazinamide is a medication used to treat tuberculosis. For active tuberculosis, it is often used with rifampicin, isoniazid, and either streptomycin or ethambutol. It is not generally recommended for the treatment of latent tuberculosis. It is taken by mouth. Common side effects include nausea, loss of appetite, muscle pains, and rash. More serious side effects include gout, liver toxicity, and sensitivity to sunlight. It is not recommended in those with significant liver disease or porphyria. It is unclear if use during pregnancy is safe but it is likely okay during breastfeeding. Pyrazinamide is in the antimycobacterial class of medications. How it works is not entirely clear.

RADIOTHERAPY

Variant found:

- Gene: CYP19A1
- Marker: rs4646
- Position: chr15:51502844
- Genotype: AC

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Radiation therapy or radiotherapy, often abbreviated RT, RTx, or XRT, is therapy using ionizing radiation, generally as part of cancer treatment to control or kill malignant cells and normally delivered by a linear accelerator. Radiation therapy may be curative in a number of types of cancer if they are localized to one area of the body. It may also be used as part of adjuvant therapy, to prevent tumor recurrence after surgery to remove a primary malignant tumor (for example, early stages of breast cancer). Radiation therapy is synergistic with chemotherapy, and has been used before, during, and after chemotherapy in susceptible cancers. The subspecialty of oncology concerned with radiotherapy is called radiation oncology. Radiation therapy is commonly applied to the

cancerous tumor because of its ability to control cell growth. Ionizing radiation works by damaging the DNA of cancerous tissue leading to cellular death. To spare normal tissues (such as skin or organs which radiation must pass through to treat the tumor), shaped radiation beams are aimed from several angles of exposure to intersect at the tumor, providing a much larger absorbed dose there than in the surrounding, healthy tissue. Besides the tumour itself, the radiation fields may also include the draining lymph nodes if they are clinically or radiologically involved with tumor, or if there is thought to be a risk of subclinical malignant spread. It is necessary to include a margin of normal tissue around the tumor to allow for uncertainties in daily set-up and internal tumor motion. These uncertainties can be caused by internal movement (for example, respiration and bladder filling) and movement of external skin marks relative to the tumor position. Radiation oncology is the medical specialty concerned with prescribing radiation, and is distinct from radiology, the use of radiation in medical imaging and diagnosis. Radiation may be prescribed by a radiation oncologist with intent to cure ("curative") or for adjuvant therapy. It may also be used as palliative treatment (where cure is not possible and the aim is for local disease control or symptomatic relief) or as therapeutic treatment (where the therapy has survival benefit and it can be curative). It is also common to combine radiation therapy with surgery, chemotherapy, hormone therapy, immunotherapy or some mixture of the four. Most common cancer types can be treated with radiation therapy in some way. The precise treatment intent (curative, adjuvant, neoadjuvant therapeutic, or palliative) will depend on the tumor type, location, and stage, as well as the general health of the patient. Total body irradiation (TBI) is a radiation therapy technique used to prepare the body to receive a bone marrow transplant. Brachytherapy, in which a radioactive source is placed inside or next to the area requiring treatment, is another form of radiation therapy that minimizes exposure to healthy tissue during procedures to treat cancers of the breast, prostate and other organs. Radiation therapy has several applications in non-malignant conditions, such as the treatment of trigeminal neuralgia, acoustic neuromas, severe thyroid eye disease, pterygium, pigmented villonodular synovitis, and prevention of keloid scar growth, vascular restenosis, and heterotopic ossification. The use of radiation therapy in non-malignant conditions is limited partly by worries about the risk of radiation-induced cancers.

RIBAVIRIN

Variant found:

- **Gene: IFNL3, IFNL4**
- **Marker: rs12979860**
- **Position: chr19:39738787**
- **Genotype: CT**

Individuals with the CT genotype may have lower response rates (SVR) to triple therapy (telaprevir, peginterferon alfa-2a/b and ribavirin) in people with Hepatitis C genotype 1 as compared to patients with the CC genotype. The impact of IL28B genotype maybe dampened in patients with prior PegIFN/RBV treatment failure. Other genetic and clinical factors may also influence a patient's response to HCV triple therapy.

Variant found:

- **Gene: IFNL3**
- **Marker: rs11881222**
- **Position: chr19:39734923**
- **Genotype: AG**

Individuals with the AG genotype and hepatitis C or HIV may have a poorer response to treatment with peginterferon-alpha and ribavirin as compared to patients with the AA genotype. Other genetic and clinical factors may also influence response to peginterferon-alpha and ribavirin treatment.

Description

Ribavirin, also known as tribavirin, is an antiviral medication used to treat RSV infection, hepatitis C, and viral hemorrhagic fever. For hepatitis C, it is used in combination with other medications such as simeprevir, sofosbuvir, peginterferon alfa-2b or peginterferon alfa-2a. Among the viral hemorrhagic fevers it is used for Lassa fever, Crimean–Congo hemorrhagic fever, and Hantavirus infection but not Ebola or Marburg. Ribavirin is taken by mouth or inhaled. Common side effects include feeling tired, headache, nausea, fever, muscle pains, and an irritable mood. Serious side effects include red blood cell breakdown, liver

problems, and allergic reactions. Use during pregnancy results in harm to the baby. Effective birth control is recommended for both males and females for at least 7 months during and after use. The mechanism of action of ribavirin is not entirely clear.

RIFAMPIN

Variant found:

- **Gene: NAT2**
- **Marker: rs1041983**
- **Position: chr8:18257795**
- **Genotype: TT**

Individuals with the TT genotype and tuberculosis (TB) may have an increased risk for hepatotoxicity when treated with anti-TB drugs as compared to patients with the CC genotype. Other genetic and clinical factors may also influence risk for hepatotoxicity.

Variant found:

- **Gene: NAT2**
- **Marker: rs1799930**
- **Position: chr8:18258103**
- **Genotype: AA**

Individuals with the AA genotype and tuberculosis (TB) may have an increased risk of hepatotoxicity when treated with anti-TB drugs as compared to patients with the GG genotype. They also may have decreased clearance of isoniazid as compared to those with the AG or GG genotype. Other genetic and clinical factors may also influence risk for hepatotoxicity and clearance of isoniazid.

Description

Rifampicin, also known as rifampin, is an antibiotic used to treat several types of bacterial infections, including tuberculosis, Mycobacterium avium complex, leprosy, and Legionnaires' disease. It is almost always used together with other antibiotics, except when given to prevent Haemophilus influenzae type b and meningococcal disease in people who have been exposed to those bacteria. Before treating a person for a long period of time, measurements of liver enzymes and blood counts are recommended. Rifampicin may be given either by mouth or intravenously. Common side effects include nausea, vomiting, diarrhea, and loss of appetite. It often turns urine, sweat, and tears a red or orange color. Liver problems or allergic reactions may occur. It is part of the recommended treatment of active tuberculosis during pregnancy, though its safety in pregnancy is not known. Rifampicin is of the rifamycin group of antibiotics. It works by stopping the production of RNA by bacteria.

SALBUTAMOL

Variant found:

- **Gene: CRHR2**
- **Marker: rs7793837**
- **Position: chr7:30726777**
- **Genotype: AT**

Individuals with the AT genotype and asthma who are treated with short-acting beta2-antagonists may have a poorer response (decreased acute bronchodilation) as compared to patients with the AA genotype, or may have a better response (increased acute bronchodilation) as compared to patients

with the TT genotype. Other genetic and clinical factors may also influence a patient's response to short-acting beta2-antagonists.

Variant found:

- **Gene: ADRB2**
- **Marker: rs1042713**
- **Position: chr5:148206440**
- **Genotype: AA**

Children with the AA genotype with asthma who are treated with salmeterol or salbutamol may have a decreased response to treatment (as measured by increased risk of asthma excerbations and lower quality of life scores) as compared to children with the GG genotype. This association does not seem to apply to lung function measurements such as peak expiratory flow rate or FEV1. Other genetic and clinical factors may also influence a patient's response to treatment.

Description

Salbutamol, also known as albuterol and marketed as Ventolin among other brand names, is a medication that opens up the medium and large airways in the lungs. It is used to treat asthma, including asthma attacks, exercise-induced bronchoconstriction, and chronic obstructive pulmonary disease (COPD). It may also be used to treat high blood potassium levels. Salbutamol is usually used with an inhaler or nebulizer, but it is also available as a pill and intravenous solution. Onset of action of the inhaled version is typically within 15 minutes and lasts for two to six hours. Common side effects include shakiness, headache, fast heart rate, dizziness, and feeling anxious. Serious side effects may include worsening bronchospasm, irregular heartbeat, and low blood potassium levels. It can be used during pregnancy and breastfeeding, but safety is not entirely clear. It is a short-acting β 2 adrenergic receptor agonist which works by causing relaxation of airway smooth muscle.

SALMETEROL

Variant found:

- **Gene: ADRB2**
- **Marker: rs1042713**
- **Position: chr5:148206440**
- **Genotype: AA**

Children with the AA genotype with asthma who are treated with salmeterol or salbutamol may have a decreased response to treatment (as measured by increased risk of asthma excerbations and lower quality of life scores) as compared to children with the GG genotype. This association does not seem to apply to lung function measurements such as peak expiratory flow rate or FEV1. Other genetic and clinical factors may also influence a patient's response to treatment.

Description

Salmeterol is a long-acting β2 adrenergic receptor agonist (LABA) used in the maintenance and prevention of asthma symptoms and maintenance of chronic obstructive pulmonary disease (COPD) symptoms. Symptoms of bronchospasm include shortness of breath, wheezing, coughing and chest tightness. It is also used to prevent breathing difficulties during exercise (exercise-induced bronchoconstriction). It was patented in 1983 and came into medical use in 1990. It is marketed as Serevent in the US. It is available as a dry powder inhaler that releases a powdered form of the drug. It was previously available as a metered-dose inhaler (MDI) but was discontinued in the US in 2002. It is still available as an MDI in the UK as of 2013.

SILDENAFIL

Variant found:

- **Gene: GNB3**
- **Marker: rs5443**
- **Position: chr12:6954875**
- **Genotype: CT**

Individuals with the CT genotype and erectile dysfunction who are treated with sildenafil may be less likely to have positive erectile response as compared to patients with the TT genotype. Other genetic and clinical factors may also influence a patient's response to sildenafil.

Description

Sildenafil, sold as the brand name Viagra among others, is a medication used to treat erectile dysfunction and pulmonary arterial hypertension. It is unclear if it is effective for treating sexual dysfunction in women. It is taken by mouth or injection into a vein. Onset is typically within 20 minutes and lasts for about 2 hours. Common side effects include headaches, heartburn, and flushed skin. Caution is advised in those with cardiovascular disease. Rare but serious side effects include a prolonged erection that can lead to damage to the penis, vision problems, and hearing loss. Sildenafil should not be taken by people on nitrates such as nitroglycerin (glycerin trinitrate), as this may result in a serious drop in blood pressure. Sildenafil acts by blocking phosphodiesterase 5 (PDE5), an enzyme that promotes breakdown of cGMP, which regulates blood flow in the penis. It requires sexual arousal, however, to work. It also results in dilation of the blood vessels in the lungs.

SIMVASTATIN

Variant found:

- **Gene: ABCB1**
- **Marker: rs2032582**
- **Position: chr7:87160618**
- **Genotype: CC**

Individuals with the CC genotype who are treated with simvastatin may have a reduced response (as measured by lower reductions in total cholesterol) as compared to patients with the AC, AA, TT or AT genotype. Other genetic and clinical factors may also influence a patient's response to simvastatin treatment.

Variant found:

- **Gene: APOA5**
- **Marker: rs662799**
- **Position: chr11:116663707**
- **Genotype: AA**

Individuals with the AA genotype and Hyperlipidemia who are treated with atorvastatin, lovastatin or simvastatin may have a higher reduction in LDL-cholesterol as compared to patients with the AG or GG genotype. Other genetic and clinical factors may also influence a patient's response to statin treatment.

Description

Simvastatin, marketed under the trade name Zocor among others, is a lipid-lowering medication. It is used along with exercise, diet, and weight loss to decrease elevated lipid levels. It is also used to decrease the risk of heart problems in those at high risk. It is taken by mouth. Common side effects include constipation, headaches, and nausea. Serious side effects may include muscle breakdown, liver problems, and increased blood sugar levels. A lower dose may be needed in people with kidney problems. There is evidence of harm to the developing baby when taken during pregnancy and it should not be used by those who are breastfeeding. It is in the statin class of medications and works by decreasing the manufacture of cholesterol by the liver.

TACROLIMUS

Variant found:

- **Gene: CYP3A4**
- **Marker: rs2740574**
- **Position: chr7:99382096**
- **Genotype: TT**

Transplant recipients with the TT (CYP3A4 (*1/*1) genotype may require a decreased dose of tacrolimus as compared to patients with the CT (*1B/*1) or CC (*1/*1) genotype. Other genetic and clinical factors, such as CYP3A5 *3 (rs776746), may also influence a patient's dose requirements.

Description

Tacrolimus, also known as fujimycin or FK506, is an immunosuppressive drug used mainly after allogeneic organ transplant to lower the risk of organ rejection. It achieves this by inhibiting the production of interleukin-2, a molecule that promotes the development and proliferation of T cells, which are vital to the body's learned (or adaptive) immune response. Tacrolimus is also used in the treatment of other T cell-mediated diseases such as eczema (for which it is applied to the skin in a medicated ointment), severe refractory uveitis after bone marrow transplants, exacerbations of minimal change disease, Kimura's disease, and the skin condition vitiligo. Chemically it is a 23-membered macrolide lactone that was first discovered in 1987 from the fermentation broth of a Japanese soil sample that contained the bacterium Streptomyces tsukubaensis. Tacrolimus is also used to treat dry eye syndrome in cats and dogs.

TAMOXIFEN

Variant found:

- **Gene: CYP19A1**
- **Marker: rs4646**
- **Position: chr15:51502844**
- **Genotype: AC**

The AC genotype in women with breast cancer who are treated with tamoxifen (with or without anastrozole, cyclophosphamide, docetaxel, doxorubicin, epirubicin, exemestane, fluorouracil, letrozole, paclitaxel, radiotherapy) may have DECREASED treatment EFFICACY in PRE-MENOPAUSAL women and INCREASED treatment EFFICACY in POST-MENOPAUSAL women as compared to patients with the AA genotypes. Other genetic and clinical factors may also influence response to tamoxifen and other treatment regimens in pre- and post-menopausal women with breast cancer.

Description

Tamoxifen, sold under the brand name Nolvadex among others, is a medication that is used to prevent breast cancer in women and treat breast cancer in women and men. It is also being studied for other types of cancer. It has been used for Albright syndrome. Tamoxifen is typically taken daily by mouth for five years for breast cancer. Serious side effects include a small increased risk of uterine cancer, stroke, vision problems, and pulmonary embolism. Common side effects include irregular periods, weight loss, and hot flashes. It may cause harm to the baby if taken during pregnancy or breastfeeding. It is a selective estrogen-receptor modulator (SERM) and works by decreasing the growth of breast cancer cells. It is of the triphenylethylene group.

TELAPREVIR

Variant found:

- **Gene: IFNL3, IFNL4**
- **Marker: rs12979860**
- **Position: chr19:39738787**
- **Genotype: CT**

Individuals with the CT genotype may have lower response rates (SVR) to triple therapy (telaprevir, peginterferon alfa-2a/b and ribavirin) in people with Hepatitis C genotype 1 as compared to patients with the CC genotype. The impact of IL28B genotype maybe dampened in patients with prior PegIFN/RBV treatment failure. Other genetic and clinical factors may also influence a patient's response to HCV triple therapy.

Description

Telaprevir (VX-950), marketed under the brand names Incivek and Incivo, is a pharmaceutical drug for the treatment of hepatitis C co-developed by Vertex Pharmaceuticals and Johnson & Johnson. It is a member of a class of antiviral drugs known as protease inhibitors. Specifically, telaprevir inhibits the hepatitis C viral enzyme NS3/4A serine protease. Telaprevir is only indicated for use against hepatitis C genotype 1 viral infections and has not been proven to have an effect on or being safe when used for other genotypes of the virus. The standard therapy of pegylated interferon and ribavirin is less effective on genotype 1.

TRAMADOL

Variant found:

- **Gene: ABCB1**
- **Marker: rs1045642**
- **Position: chr7:87138645**
- **Genotype: GG**

Individuals with the GG genotype may experience decreased efficacy of opioids and may require an increased dose as compared to patients with the AA and possibly AG genotypes, although this is contradicted in most studies, which report no association between the allele with dose or efficacy of opioids for pain. Other genetic and clinical factors may also influence a dose and efficacy of opioids for pain.

Description

Tramadol, sold under the brand name Ultram among others, is an opioid pain medication used to treat moderate to moderately severe pain. When taken by mouth in an immediate-release formulation, the onset of pain relief usually begins within an hour. It is also available by injection. It may be sold in combination with paracetamol (acetaminophen) or as longer-acting formulations. Common side effects include constipation, itchiness, and nausea. Serious

side effects may include seizures, increased risk of serotonin syndrome, decreased alertness, and drug addiction. A change in dosage may be recommended in those with kidney or liver problems. It is not recommended in those who are at risk of suicide or in those who are pregnant. While not recommended in women who are breastfeeding, those who take a single dose should not generally stop breastfeeding. Tramadol acts by binding to μ-opioid receptors on neurons. It is also a serotonin–norepinephrine reuptake inhibitor (SNRI). It is converted in the liver to O-desmethyltramadol, an opioid with stronger binding to the μ-opioid receptor.

TRASTUZUMAB

Variant found:

- **Gene: FCGR2A**
- **Marker: rs1801274**
- **Position: chr1:161479745**
- **Genotype: GG**

Individuals with the GG genotype may have decreased response to trastuzumab and shorter progression-free survival in people with Breast cancer as compared to patients with genotype AA. Other genetic or clinical factors may also influence the response to trastuzumab.

Description

Trastuzumab, sold under the brand name Herceptin among others, is a monoclonal antibody used to treat breast cancer. Specifically it is used for breast cancer that is HER2 receptor positive. It may be used by itself or together with other chemotherapy medication. Trastuzumab is given by slow injection into a vein and injection just under the skin. Common side effects include fever, infection, cough, headache, trouble sleeping, and rash. Other severe side effects include heart failure, allergic reactions, and lung disease. Use during pregnancy may harm the baby. Trastuzumab works by binding to the HER2 receptor and slowing down cell duplication.

VENLAFAXINE

Variant found:

- **Gene: FKBP5**
- **Marker: rs4713916**
- **Position: chr6:35669983**
- **Genotype: GG**

Individuals with the GG genotype may have a reduced response to antidepressants as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's response to antidepressant treatment.

Description

Venlafaxine, sold under the brand name Effexor among others, is an antidepressant medication of the serotonin-norepinephrine reuptake inhibitor (SNRI) class. It is used to treat major depressive disorder (MDD), generalized anxiety disorder (GAD), panic disorder, and social phobia. It is taken by mouth. Common side effects include loss of appetite, constipation, dry mouth, dizziness, sweating, and sexual problems. Severe side effects include an increased risk of suicide, mania, and serotonin syndrome. Antidepressant withdrawal syndrome may occur if stopped. There are concerns that use during the later part of pregnancy can harm the baby. How it works is not entirely clear but it is believed to involve alterations in neurotransmitters in the brain.

VINCRISTINE

Variant found:

- **Gene: PNPLA3**
- **Marker: rs738409**
- **Position: chr22:44324727**
- **Genotype: CG**

Individuals with the CG genotype may have increased risk of hepatotoxicity when treated with remission induction therapy (including asparaginase) in children with acute lymphoblastic leukemia (ALL) as compared to patients with genotype CC. Other genetic and clinical factors may also influence the risk of toxicity to remission induction therapy.

Variant found:

- **Gene: intergenic_non-coding**
- **Marker: rs924607**
- **Position: chr5:610093**
- **Genotype: TT**

Individuals with the TT genotype may have increased risk of peripheral nervous system diseases when treated with vincristine may have as compared to patients with the CC or CT genotype. Other genetic and clinical factors may also influence a patient's response to vincristine.

Description

Vincristine, also known as leurocristine and marketed under the brandname Oncovin among others, is a chemotherapy medication used to treat a number of types of cancer. This includes acute lymphocytic leukemia, acute myeloid leukemia, Hodgkin's disease, neuroblastoma, and small cell lung cancer among others. It is given intravenously. Most people experience some side effects from vincristine treatment. Commonly it causes a change in sensation, hair loss, constipation, difficulty walking, and headaches. Serious side effects may include neuropathic pain, lung damage, or low white blood cells which increases the risk of infection. It will likely cause harm to the baby if given during pregnancy. It works by stopping cells from dividing properly.

WARFARIN

Variant found:

- **Gene: VKORC1**
- **Marker: rs7294**
- **Position: chr16:31102321**
- **Genotype: CT**

Individuals with the CT genotype who are treated with warfarin may require a higher dose as compared to patients with the CC genotype. Other genetic and clinical factors may also influence a patient's required dose of warfarin.

Variant found:

- **Gene: VKORC1**
- **Marker: rs9923231**

- Position: chr16:31107689
- Genotype: CT

Individuals with the CT genotype may require a decreased dose of warfarin as compared to patients with the CC genotype or an increased dose as compared to patients with the TT genotype. Other genetic and clinical factors may also influence a patient's warfarin dose requirement.

Variant found:

- Gene: VKORC1
- Marker: rs2359612
- Position: chr16:31103796
- Genotype: AG

Individuals with the AG genotype who are treated with warfarin may require a decreased dose as compared to patients with the GG genotype. Other genetic and clinical factors may also influence dose of warfarin.

Variant found:

- Gene: VKORC1
- Marker: rs8050894
- Position: chr16:31104509
- Genotype: CG

Individuals with the CG genotype who are treated with warfarin may require a lower dose as compared to patients with the CC genotype. Other genetic and clinical factors may also influence a patient's required dose of warfarin.

Variant found:

- Gene: VKORC1
- Marker: rs9923231
- Position: chr16:31107689
- Genotype: CT

Individuals with the CT genotype may have increased risk of over-anticoagulation when treated with warfarin as compared with patients with genotype CC. Other genetic and clinical factors may also influence the toxicity to warfarin.

Variant found:

- Gene: VKORC1
- Marker: rs9923231
- Position: chr16:31107689
- Genotype: CT

Individuals with genotype CT may require shorter time to therapeutic INR when treated with warfarin as compared with patients with genotype CC. Other genetic and clinical factors may also influence the response to warfarin.

Variant found:

- Gene: VKORC1
- Marker: rs2884737

- **Position: chr16:31105554**
- **Genotype: AC**

Individuals with the AC genotype may require higher dose of warfarin as compared to patients with the CC genotype. Other clinical and genetic factors may also influence a patient's warfarin dose.

Description

Warfarin, sold under the brand name Coumadin among others, is a medication that is used as an anticoagulant (blood thinner). It is commonly used to treat blood clots such as deep vein thrombosis and pulmonary embolism and to prevent stroke in people who have atrial fibrillation, valvular heart disease or artificial heart valves. Less commonly it is used following ST-segment elevation myocardial infarction (STEMI) and orthopedic surgery. It is generally taken by mouth but may also be used by injection into a vein. The common side effect is bleeding. Less common side effects may include areas of tissue damage and purple toes syndrome. Use is not recommended during pregnancy. It is recommended that the effects of warfarin typically be monitored by checking prothrombin time (INR) every one to four weeks. Many other medications and dietary factors can interact with warfarin, either increasing or decreasing its effectiveness. The effects of warfarin may be reversed with phytomenadione (vitamin K1), fresh frozen plasma, or prothrombin complex concentrate. Warfarin decreases blood clotting by blocking an enzyme called vitamin K epoxide reductase that reactivates vitamin K1. Without sufficient active vitamin K1, clotting factors II, VII, IX, and X have decreased clotting ability. The anticlotting protein C and protein S are also inhibited but to a lesser degree. A few days are required for full effect to occur and these effects can last for up to five days.

GLOSSARY

ALLELE	An allele is a variant form of a gene that is located at a specific position, or genetic locus, on a specific chromosome. Humans have two alleles at each genetic locus, with one allele inherited from each parent.
CHROMOSOME	Chromosome is a thread-like structure of DNA that carries hereditary information, or genes. Human cells have 22 chromosome pairs plus two sex chromosomes, giving a total of 46 per cell.
GENOME	A genome is an organism's complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism. In 2018 humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus.
GENOTYPE	The genetic makeup of an individual organism. It may also refer to just a particular gene or set of genes carried by an individual. The genotype determines the phenotype, or observable traits of the organism.
ODDS RATIO	The odds ratio is a way of comparing whether the odds of a certain outcome is the same for two different groups. In this report, the odds ratio estimates the probability of a condition occurring in a group of people with a certain genetic variant compared to a group of people without that variant. An odds ratio of 1 means that the two groups are equally likely to develop the condition. An odds ratio higher than 1 means that the people with the genetic variant are more likely to develop the condition, while an odds ratio of less than 1 means that the the people with the variant are less likely to develop the condition.

PHENOTYPE	A description of an individual's physical characteristics, including appearance, development and behaviour. The phenotype is determined by the individual's genotype as well as environmental factors.
POPULATION ALLELE FREQUENCY	The allele frequency represents the incidence of a variant in a population. Alleles are variant forms of a gene that are located at the same position, or genetic locus, on a chromosome.
SNP	Single nucleotide polymorphisms, frequently called SNPs, are the most common type of genetic variation among people. A SNP is a variation in a single nucleotide that occurs at a specific position in the genome.