ONEOME®

OneOme RightMed® oncology report overview

The RightMed comprehensive test is a pharmacogenomic test that analyzes a patient's DNA to determine how he or she may respond to hundreds of medications. When a provider orders a RightMed test, they get the standard RightMed comprehensive test report, plus access to optional reports, including the RightMed oncology report. Learn more about the RightMed oncology report below, and then refer to the attached oncology report.

WHAT IS THE RIGHTMED ONCOLOGY REPORT?

The RightMed oncology report includes a subset of medications used in cancer care. These medications were selected and classified by OneOme and include both chemotherapy drugs and palliative/supportive care medications for things like anxiety, depression, pain, nausea/vomiting, and more. Information about these medications and a patient's predicted response to them is presented in a streamlined, consolidated view.

HOW IS THE ONCOLOGY REPORT DIFFERENT FROM THE RIGHTMED COMPREHENSIVE TEST REPORT (THE STANDARD TEST REPORT)?

Here's how the RightMed oncology report and RightMed comprehensive test report differ:

- MEDICATIONS: The oncology report only includes medications commonly used in cancer care that have been selected and classified by OneOme. The comprehensive test report includes hundreds of medications used in the treatment of a wide range of medical conditions.
- GENES: The oncology report includes only the gene and phenotype summary for the genes that have been shown to impact the metabolism of the selected chemotherapy and supportive/palliative care medications. The comprehensive test report includes the gene and phenotype summary for all genes analyzed by the RightMed test.
- REPORT LAYOUT: The oncology report separates the medications by class, including chemotherapy, targeted therapy, gastrointestinal management, pain management, and more. The RightMed comprehensive test report groups medications by the predicted gene-drug interaction. Download a sample RightMed comprehensive test report at oneome.com/sample-report.
- MAJOR AND MODERATE GENE-DRUG INTERACTION SUMMARY: The oncology report includes a summary of the number of major and moderate gene-drug interactions for chemotherapeutic agents and supportive care medications. This allows the provider to quickly visualize the number of medications that may be impacted for this patient.

HOW DO I GET THE ONCOLOGY REPORT?

Providers can choose to add a complimentary oncology report either when they are ordering the RightMed comprehensive test, or once the patient's test results are completed. To get an oncology report after a patient's results are in, visit portal.oneome.com.

WHAT OTHER REPORTS DOES ONEOME OFFER?

In addition to the comprehensive test report and the oncology report, providers can create custom RightMed Advisor reports and also can get a RightMed psychiatry report—another specialty report available from OneOme. Download a sample RightMed Advisor report at oneome.com/custom-report and a sample psychiatry report at oneome.com/psychiatry-report.

DO YOU OFFER SUPPORT WITH INTERPRETING RESULTS?

Yes. Providers and pharmacists receive access to complimentary, one-on-one consultations with clinical pharmacists from OneOme. Contact support@oneome.com to set up a consultation.

I HAVE A QUESTION; WHO SHOULD I CONTACT?

We'd love to help. Please contact our customer support team at 844-ONEOME-5 (844-663-6635) or support@oneome.com. The team will put you in touch with the right person.

RightMed® oncology report

The RightMed oncology report is a specialty report available as part of the RightMed comprehensive test. It contains a subset of medications selected and classified by OneOme for use in the treatment of oncology patients and their supportive care needs.

Patient and report summary

Patient name: **Stacy Oncology**
Patient date of birth: **1960-08-30**
OneOme report date: **2018-01-31**

Ordering provider: **Sample Doctor**
Ordering facility: **OneOme Health**
Report type: **Specialty**

This report is based on OneOme's database as of the date this report was generated. The original test report issued 2018-01-22 contains secondary findings that should be reviewed. This patient is a carrier for variant(s) associated with pathogenicity in the following gene(s): DPYD, F5, UGT1A1. Genetic counseling may be advised.

Major gene-drug interactions	5 Chemotherapeutic agents	29 Supportive care medications
Moderate gene-drug interactions	6 Chemotherapeutic agents	22 Supportive care medications

Report legend

Based on the genes in our panel, medications are reported according to genotype-predicted interactions described below.

Major gene-drug interaction	Major genotype-drug interaction identified that affects the metabolism of the medication and/or indicates an elevated risk of adverse reaction or loss of efficacy.
Moderate gene-drug interaction	Moderate genotype-drug interaction identified that affects the metabolism of the medication and/or indicates an elevated risk of adverse reaction or loss of efficacy.
Minimal gene-drug interaction	Minimal genotype-drug interaction identified that does not significantly impact medication metabolism or predict an elevated risk of adverse reaction or loss of efficacy.
Limited genetic impact	No clinically relevant genetic variants are known to impact medication.

Icon legend

Some medications are reported with icons to indicate that specific clinical annotations and/or dosing guidelines provided by the FDA and other professional associations are available in the RightMed Advisor.

Increased exposure	Total exposure to active compound(s) may be increased. Monitor for adverse effects.
Decreased exposure	Total exposure to active compound(s) may be decreased. Monitor for lack of therapeutic response.
Difficult to predict	Total exposure to active compound(s) is difficult to predict. Monitor patient response.
Reduced response	Response to medication may be lowered due to genetic changes impacting mechanisms other than exposure (e.g. receptor function).
Additional testing	According to FDA labeling, additional laboratory testing may be indicated.
Professional guideline	Medication has professional guidelines associated with this patient's genetic test results. Avoidance, dose adjustment, or heightened monitoring may be indicated.

Genotype-derived recommendations for chemotherapeutic agents

Chemotherapy

Major gene-drug interaction

- Belinostat [1, 142]
- Irinotecan [1, 35, 64]
- Tamoxifen [1, 2]

Moderate gene-drug interaction

- Capecitabine [1, 15]
- Fluorouracil [1, 2, 15]
- Mercaptopurine [1, 2, 105, 106]
- Thioguanine [1, 2, 105, 106]

Minimal gene-drug interaction

- Bortezomib [1]
- Cabazitaxel [1]
- Docetaxel [1]
- Enzalutamide [1]
- Etoposide [1, 153]
- Everolimus [1, 131]
- Exemestane [1]
- Ifosfamide [1, 19]
- Ixabepilone [1]
- Methotrexate [1, 101, 102, 130, 150]
- Paclitaxel [1]
- Temsirolimus [1]
- Teniposide [65, 107]
- Trabectedin [1]
- Vincristine [1, 131]
- Vinorelbine [1]

Limited genetic impact

- Asparaginase [1]
- Bleomycin [1]
- Carboplatin [1, 6, 18, 26, 121, 136]
- Decitabine [1]
- Fulvestrant [1]
- Lenalidomide [1]
- Leucovorin calcium [1]
- Oxaliplatin [1]
- Pemetrexed [1]
- Sodium phenylbutyrate [1]
- Temozolomide [1]
- Thalidomide [1]

Kinase inhibitors (KIs) and monoclonal antibodies (mAbs)

Major gene-drug interaction

- Nilotinib [1, 3]
- Pazopanib [1]

Moderate gene-drug interaction

- Gefitinib [1]
- Ponatinib [1]

Minimal gene-drug interaction

- Axitinib [1]
- Bosutinib [1]
- Brentuximab vedotin [1]
- Crizotinib [1]
- Dasatinib [1]
- Erlotinib [1, 51]
- Imatinib [1]
- Lapatinib [1, 111]
- Regorafenib [1]
- Ruxolitinib [1]
- Sorafenib [1]
- Sunitinib [1]
- Vemurafenib [1]

Limited genetic impact

- Afatinib [1]
- Alemtuzumab [1]
- Bevacizumab [1]
- Cetuximab [1]
- Ibritumomab [1]
- Obinutuzumab [1]
- Ofatumumab [1]
- Panitumumab [1]
- Pertuzumab [1]
- Rituximab [1]
- Trastuzumab [1]

Genotype-derived recommendations for supportive care medications

Gastrointestinal management (nausea/vomiting, appetite, gastritis, GERD)

Major gene-drug interaction

- Esomeprazole [1, 2]
- Haloperidol [1, 2, 93, 117, 135]
- Lansoprazole [1, 2, 83]
- Omeprazole [1, 2]
- Pantoprazole [1]

Moderate gene-drug interaction

- Dexlansoprazole [1]
- Dolasetron [1]
- Mirtazapine [1, 2, 62, 72, 124, 128]
- Olanzapine [1, 2, 67]
- Ondansetron [1, 10, 54, 134]
- Rabeprazole [1]

Minimal gene-drug interaction

- Aprepitant [1]

Limited genetic impact

Pain management

Major gene-drug interaction

- Codeine [1, 2, 8, 13, 23, 24, 118, 127]
- Hydrocodone [1, 23, 24]
- Oxycodone [1, 23, 24]
- Tramadol [1, 2, 23, 24, 73, 123, 125, 132]

Moderate gene-drug interaction

Minimal gene-drug interaction

- Alfentanil [1, 34, 89, 151]
- Buprenorphine [1]
- Fentanyl [1, 34]
- Methadone [1]

Limited genetic impact

- Hydromorphone [1, 23, 24]

Neuropathy and non-opioid pain management

Major gene-drug interaction

- Amitriptyline [1, 2, 39, 143]
- Clomipramine [1, 2, 39]
- Desipramine [1, 2, 39]
- Doxepin [1, 2, 39]
- Imipramine [1, 2, 39, 141]
- Nortriptyline [1, 2, 39, 90, 137]
- Protriptyline [1]
- Trimipramine [1, 2, 39, 63]

Moderate gene-drug interaction

- Celecoxib [1]
- Diclofenac [1]
- Lidocaine [28, 91]

Minimal gene-drug interaction

Limited genetic impact

- Gabapentin [1]
- Milnacipran [1]
- Pregabalin [1]

Mental health (antidepressant, anxiolytic)

Major gene-drug interaction

- Citalopram 1, 2, 7, 12, 31, 38, 41, 42, 43, 45, 59, 60, 66, 68, 70, 76, 77, 80, 85, 92, 96, 97, 144
- Diazepam 1, 47
- Escitalopram 1, 2, 7, 12, 31, 38, 42, 43, 45, 66, 70, 76, 80, 85, 97, 144
- Fluoxetine 1, 36, 45, 50, 71, 75, 95, 103, 122, 147
- Fluvoxamine 1, 38, 49, 56, 57, 115, 116, 119, 120, 122, 126, 149
- Paroxetine 1, 2, 38, 48, 58, 81, 98, 109, 122, 129, 146
- Vortioxetine 1

Moderate gene-drug interaction

- Duloxetine 1
- Sertraline 1, 2, 30, 32, 38, 71, 82, 84, 88, 104, 108, 133, 140
- Venlafaxine 1, 2, 139

Minimal gene-drug interaction

- Alprazolam 1, 131
- Bupropion 1
- Buspirone 1, 131, 152
- Levomilnacipran 1

Limited genetic impact

- Desvenlafaxine 1, 29

Neuropsychiatry (sleep medicine, anticonvulsant, smoking cessation)

Major gene-drug interaction

Moderate gene-drug interaction

- Fosphenytoin 1, 20, 74, 87
- Nicotine 11, 27
- Phenytoin 1, 5, 14

Minimal gene-drug interaction

- Armodafinil 1
- Carbamazepine 1, 4, 5, 21, 22, 44, 69, 74, 78, 79, 86, 94, 100, 114, 148
- Eszopiclone 1
- Modafinil 1
- Quetiapine 1, 131
- Ramelteon 1
- Trazodone 1
- Triazolam 1, 131
- Vilazodone 1
- Zolpidem 1, 9, 138
- Zonisamide 1

Limited genetic impact

- Temazepam 33
- Varenicline 1

Antimicrobial (antifungal, antibiotic)

Major gene-drug interaction

- Voriconazole [1, 2]

Moderate gene-drug interaction

Minimal gene-drug interaction

- Clarithromycin [1, 131]
- Erythromycin [131]
- Isavuconazole [1]
- Itraconazole [1]
- Ketoconazole [1]
- Telithromycin [1]
- Terbinafine [1]

Limited genetic impact

- Fluconazole [1]
- Levofloxacin [1]
- Meropenem [1]
- Moxifloxacin [1]
- Piperacillin [1]
- Posaconazole [1]
- Sulfadiazine [1]
- Vancomycin [1]

Anticoagulant and cardiovascular management

Major gene-drug interaction

- Carvedilol [1]
- Labetalol [17]
- Metoprolol [1, 2]

Moderate gene-drug interaction

- Clonidine [1]
- Clopidogrel [1, 112, 113]
- Propranolol [1]
- Warfarin [1, 16, 53]

Minimal gene-drug interaction

- Apixaban [1]

Limited genetic impact

- Atenolol [1]
- Dalteparin [1]
- Enoxaparin [1]
- Furosemide [145]
- Heparin [1]
- Hydrochlorothiazide [1]
- Nitroglycerin [1]
- Sotalol [1]

Urology and gynecology

Major gene-drug interaction

- Ethinyl estradiol [1, 2]

Moderate gene-drug interaction

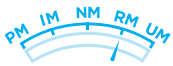
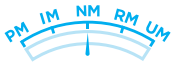
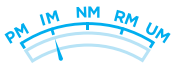
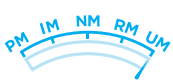
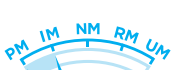
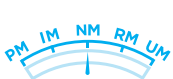
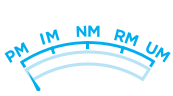
- Fesoterodine [1]
- Tamsulosin [1]
- Tolterodine [1]

Minimal gene-drug interaction

- Darifenacin [25, 61]
- Finasteride [1]
- Oxybutynin [1]
- Sildenafil [1]
- Tadalafil [1]
- Vardenafil [1]

Genotype-derived classification of medications is provided as a service by OneOme and is intended solely for use by a medical professional who has reviewed and understands all sections within this report, including possible limitations of the services provided by OneOme. The relationships between the drugs and pharmacogenes annotated in this report are supported by scientific evidence that meets OneOme's critieria for inclusion. The order in which drugs are listed does not have any clinical or medical implications. For more information on these medications, for a list of additional medications curated but not annotated by OneOme, or to evaluate possible drug-to-drug interactions, please consult the RightMed Advisor, which is accessible through the provider portal at oneome.com.

Gene and phenotype summary

Gene	Genotype		Phenotype summary / Metabolic status
CYP1A2	*1A/*1C		Rapid Increased activity. Drugs converted to active metabolite(s) may cause side effects or toxicity. Active drugs converted to inactive metabolite(s) may lack efficacy.
CYP2B6	*1/*1		Normal Normal level of activity. Drugs metabolized at a normal rate.
CYP2C9	*1/*18		Intermediate Decreased activity. Drugs converted to active metabolite(s) may have reduced efficacy. Active drugs converted to inactive metabolite(s) may cause side effects or toxicity.
CYP2C19	*17/*17		Ultrarapid Increased activity. Drugs converted to active metabolite(s) may cause side effects or toxicity. Active drugs converted to inactive metabolite(s) may lack efficacy.
CYP2D6	*2/*5		Poor to Intermediate Decreased activity. Drugs converted to active metabolite(s) may have reduced efficacy. Active drugs converted to inactive metabolite(s) may cause side effects or toxicity.
CYP3A4	*1/*1		Normal Normal level of activity. Drugs metabolized at a normal rate.
CYP3A5	*3/*3		Poor Normal dosing may be required because original dosing guidelines for drugs have been established on patients with poor metabolizer phenotype.
COMT	rs4680 GG		High COMT activity is predicted to be higher than in patients with the AA or GA genotypes at rs4680.
DPYD	*1/*2A		Increased risk Intermediate metabolizer. Decreased activity in dihydropyrimidine dehydrogenase. Increased risk of toxicities such as myelosuppression, mucositis, neurotoxicity, diarrhea, and hand-foot syndrome related to administration of fluoropyrimidines (5-fluorouracil, capecitabine and tegafur).
F2	rs1799963 GG		Normal risk Normal risk of thrombosis associated with Factor II (prothrombin). Other genetic and clinical factors contribute to the risk for thrombosis.
F5	rs6025 GA		Increased Risk Increased risk of thrombosis associated with Factor V Leiden thrombophilia. Other genetic and clinical factors largely contribute to the risk for thrombosis.
GRIK4	rs1954787 CC		Normal response Genotype predicts a normal response to citalopram in patients with major depressive disorder related to the GRIK4 genotype alone. Other clinical and genetic factors may influence response.

Gene and phenotype summary (cont.)

HTR2A	rs7997012 AA		**Intron 2 genotype AA** Genotype predicts an increased likelihood of response to citalopram. Other clinical and genetic factors may influence response.
NUDT15	rs116855232 CC		**Normal Risk** No increased risk of toxicity of life-threatening toxicities with thiopurine administration related to the NUDT15 genotype. Toxicities with thiopurines can also occur due to impaired TPMT activity, regardless of the NUDT15 status.
OPRM1	rs1799971 GG		**Asp/Asp isoform** Analgesic effects of alfentanil, codeine, and tramadol (and possibly other opioids) may be lower in patients with this genotype. Other genetic and/or clinical factors influence response.
SLC6A4	L/L (La/La)		**Typical to increased expression** Genotype predicts a typical to increased expression of the SLC6A4 transporter compared to patients with other genotypes. The L/L genotype has been associated with increased likelihood and potentially quicker response to the SSRIs fluoxetine, fluvoxamine, and possibly citalopram and escitalopram. The opposite trend in response has been observed in East Asian populations, showing increased likelihood and potentially quicker response in carriers of the S allele.
SLCO1B1	*1/*1		**Normal Risk** Normal function of SLCO1B1. Normal risk of simvastatin-induced myopathy. Likelihood of normal response with pravastatin. Normal risk of methotrexate-induced toxicities when used at high dose.
TPMT	*1/*3C		**Increased Risk** Intermediate TPMT metabolizer. Increased risk of myelotoxicity with azathioprine, mercaptopurine, and thioguanine. Toxicities with thiopurines can also occur due to impaired NUDT15 activity independently of the TPMT status.
UGT1A1	*28/*28		**High Risk (Homozygous *28)** Significantly decreased UGT1A1 activity. High risk for severe neutropenia (irinotecan), toxicity and hyperbilirubinemia (nilotinib), hyperbilirubinemia (pazopanib, atazanavir) and multiple toxicities (belinostat). Consult drug labeling for dosing recommendations. Genotype is also consistent with Gilbert syndrome.
VKORC1	rs9923231 GA		**Intermediate activity** Intermediate activity of the vitamin K epoxide reductase enzyme, associated with the c.-1639GA (rs9923231) variant. The VKORC1 genotype together with the CYP2C9 genotype determines the sensitivity to warfarin therapy.
Warfarin Response (CYP2C9; VKORC1)	*1/*18; rs9923231 GA		**Increased Sensitivity** Increased sensitivity to warfarin; lower doses may be required. Refer to warfarindosing.org and FDA labeling for dosing guidelines.

CYP phenotype abbreviations

PM	Poor metabolizer
IM	Intermediate metabolizer
NM	Normal metabolizer
RM	Rapid metabolizer
UM	Ultrarapid metabolizer

OneOme liability disclaimer

The interpretations and clinical annotations provided by OneOme are intended solely for use by a medical professional and do not constitute medical advice by OneOme. The treating provider remains ultimately responsible for all diagnosis and treatment decisions for the patient. Information included in this report is based upon scientific literature and does not take into account other genetic variants and environmental or social factors that may affect a patient's response. Other factors not included in this report include, but are not limited to, environmental factors (e.g., smoking), health factors (e.g., diet), social and familial factors, various medical conditions, and drug-to-drug interactions. Administration of any medication, including the ones listed in the OneOme reports, requires careful therapeutic monitoring regardless of the phenotype or genotype-derived recommendation. As a matter of practice, OneOme will routinely update its pharmacogenomic database as new information becomes available to the scientific community. Drug binning and annotations found on the patient's RightMed comprehensive test report, RightMed Advisor reports, or RightMed specialty reports are therefore dependent on the date of generation and/or the database version used to generate that report. Providers may access these reports with updated annotations using OneOme's latest released version through the provider portal at portal.oneome.com.

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