Comprehensive Cancer Profiling Test Report

Patient ID:	XXX
Physician ID:	
Report Date:	2019-12-05

Content

About the Test

NovoPM 2.0 (Personalized Medicine based on cancer-related genomic alterations)

This is a next-generation sequencing (NGS)-based assay that detects genomic alterations (also known as "mutations") in 484 genes that are relevant for the diagnosis and treatment of solid tumors according to clinical guidelines and medical literature. This test interrogates the entire exonic regions of 468 genes and selected intronic regions of 43 genes for mutations that may exist in the forms of single nucleotide variant (SNV), Insertion/Deletion (InDel), copy number variation (CNV) or Fusion. This report presents the mutations detected in the submitted patient sample and information on approved therapies, clinical trials and other scientific findings.

Disclaimer:

- Due to the technical limitations of NGS, not all genomic alterations in the targeted regions can be detected. Therefore, the test results should be interpreted in the context of the patient's clinical and pathological characteristics as well as other laboratory findings. In addition, information/suggestions provided in this report on the relevant treatment options, clinical trials and other scientific findings are based on the clinical guidelines, clinical trial registry and scientific literature which are continuously evolving. It is the user's responsibility to verify these information/suggestions against the most recent advancement in the aforementioned sources. The diagnostic and/or treatment implications of these information/suggestions should be interpreted only by licensed/certified medical professionals.
- This test uses NGS technology combined with bioinformatics algorithms to calculate the MSI status of the sample in the patient sample. In non-colorectal cancer tissue samples (such as other cancer tissue samples, blood samples, etc.), the MSI status is for reference only.
- This test is limited to mutation detection at the gene level. PD-L1 expression via immunohistochemistry has not been evaluated for the guidance on immunotherapy.

Accreditations

This test was conducted in a College of American Pathologists (CAP) accredited facility for next-generation sequencing (CAP Number: 9043632, AU-ID: 1759306). Its performance characteristics was determined in compliance to all applicable standards for the accreditation. This test has not been cleared or approved by the United States Food and Drug Administration (FDA). The FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research.

Report Summary

Patient and Specimen Information

Patient	Specimen	Physician
Name: XXX	**Specimen I.D.:** MKHSxxxxxxxxx-2A	**Ordering Physician:**
Patient NRIC/FIN/ID:	**Specimen Type/Size:** tissue	**Institution:**
	Specimen Collection Date:	
Gender: Female	**Specimen Received Date:**	
Data of Birth:		
Nationality:		
Diagnosis: Breast Cancer		

Brief Summary of Test Results

Detection Type	Test Results
Targeted Therapy	In this sample, 2 mutations in 2 genes were related to targeted therapies.
Tumor Mutation Burden (TMB)	1.481 Mutations/Megabase
Microsatellite status	MSS

Therapeutics Implications

Targeted Therapy

In this sample, 2 mutations in 2 genes were related to targeted therapies. See "Detailed Test Results about Targeted Therapy" for more information.

Gene	Variant	VAF	Targeted Therapies with Potential Benefit			Information on Potential Drug Resistance
			Level A	Level B	Level C	
ERBB2	Amplification	12.1X	None	**Trastuzumab + Pertuzumab + Docetaxel***, **Ado-trastuzumab emtansine**, **Neratinib**	Trastuzumab + Pyrotinib + Docetaxel#, A166#, Trastuzumab + Pertuzumab#	None
TP53	NM_000546.5 exon10 c.1045G>T p.E349*	72.41%	None	None	Adavosertib + Carboplatin#	None

Note:

1. Therapies associated with benefit or lack of benefits are **solely** based on the 484 cancer-related genes sequenced and genomic findings on patient tumor. Other clinicopathological factors will need to be taken into consideration when choosing appropriate therapy for the patient.
2. SNV: single nucleotide variant; InDel: Insertion/Deletion; CNV: copy number variation; VAF: variant allele fraction.
3. If the mutation is SNV, InDel or fusion, the VAF is the percentage of mutation variant reads among the total reads on that locus. If the mutation is CNV, the VAF is the relative copy number of the gene compared to the two normal copies.
4. None: Not Detected.
5. Targeted therapies with potential benefit:

   Level A: Therapies that have been approved by FDA/NMPA, or are included in the clinical guidelines.

   Level B: Therapies that have shown efficacy by published data from large-scale registered clinical trials (Phase II/Phase III/Phase IV).

   Level C: Therapies that that have been approved by FDA or NMPA for another tumor type, or have shown evidence of efficacy by published data from Phase I clinical trials or clinical case studies, or small-scale investigator-initiated clinical trials, or are being tested in large-scale registered clinical trials for which the patient may be eligible to enroll.
6. Information on potential drug resistance: patients with the detected mutations may have reduced sensitivity or resistance the listed drugs that have been approved by FDA/NMPA, or are recommended by the clinical guidelines for this patient's tumor type, which may reduce drug sensitivity or produce drug resistance.
7. The therapies labeled by * have been approved by NMPA.
8. The therapies in **bold font** have been approved by FDA/NMPA and others have not yet been approved by FDA/NMPA.
9. The therapies labeled by # are being tested in large-scale registered clinical trials for which the patient may be eligible to enroll.
10. Further details can be found in the “Detected Mutations and Related Targeted Therapy”.

Immunotherapy

Type of Genomic Alterations	Test Result
Microsatellite status	MSS
Tumor Mutation Burden (TMB)	1.481 Mutations/Megabase

Note:

1. Microsatellite status (or a measure of microsatellite instability or "MSI") reflects the condition of genetic hypermutability (predisposition to mutation) that results from impaired DNA mismatch repair (MMR). Microsatellite status is an effective marker for Lynch syndrome diagnosis and prognosis prediction in the treatment of certain cancer types. Microsatellite status is also an approved biomarker for predicting the efficacy of anti-PD-L1/PD-1 immunotherapeutic agents such as Keytruda® (Pembrolizumab), Opdivo® (Nivolumab) and Yervoy® (Ipilimumab) in solid tumors. This test uses NGS technology combined with bioinformatics algorithms validated on colorectal cancer patient samples to detect the MSI status: MSI-high (MSI-H) or microsatellite stable (MSS). In non-colorectal cancer tissue samples (such as other cancer tissue samples, blood samples, etc.), the MSI status is for reference only.
2. Tumor mutation burden (TMB) represents the total number of mutations per coding area of a tumor genome calculated through the genomic sequencing of tumor tissue samples. The value of TMB has been found to correlate with the efficacy of certain anti-PD-L1/PD-1 immunotherapies in some tumor types. TMB studies of MSK IMPACT suggests a threshold of 13.8 Mutations/Megabase as indicative of a high TMB.

Test Results about Mismatch Repair (MMR)			
Gene	**Variant**	**VAF**	**Mutation Type**
MLH1	None	/	/
MSH2	None	/	/
MSH6	None	/	/
PMS2	None	/	/

Clinical significance of mismatch repair deficient (dMMR):

1. MLH1, MSH2, MSH6 and PMS2 germline mutations often lead to increased risk of Lynch syndrome, colorectal cancer, gastric cancer, endometrial cancer and some other cancers. Meanwhile, several retrospective studies have shown that somatic mutations in the MMR gene can also cause dMMR/MSI-H, which is associated with sporadic colorectal cancer and endometrial cancer [PMID: 24333619; 25194673; PMID: 25194673].
2. A clinical study showed that the objective response rate (ORR) of Pembrolizumab for dMMR/MSI-H was 36% in colorectal cancer patients and 46% in non-colorectal cancer patients.

   Based on this study, FDA has approved the use of Pembrolizumab in the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient:

   - solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
   - colorectal cancer that has progressed following treatment with a Fluoropyrimidine, Oxaliplatin, and Irinotecan
3. The clinical study of CheckMate 142 showed that the ORR of Nivolumab treatment for colorectal cancer patients with dMMR/MSI-H was 28%, including 1 complete response and 14 partial response; the ORR of Nivolumab and Ipilimumab treatment for colorectal cancer patients with dMMR/MSI-H was 46%, including 3 complete response and 35 partial response [PMID: 28734759].

   Based on this study, the FDA has approved Nivolumab monoclonal antibody for treatment of adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a Fluoropyrimidine, Oxaliplatin, and Irinotecan, as a single agent or in combination with Ipilimumab.
4. The result of the variation of mismatch repair genes is determined to be dMMR if there is a function-affected mutation, and pMMR if none.
5. This test is limited to gene level mutation detection. It does not include IHC expression test and is for reference only.

Reported by: **Reviewed by:**

Date: 2019-12-05 **Date: 2019-12-05**

Detailed Test Results about Targeted Therapy

Detected Mutations and Related Targeted Therapy

ERBB2

Variant	Amplification			
VAF	12.1X			
Targeted Therapy	**Potential Benefit**			**Potential Resistance**
	Level A	**Level B**	**Level C**	
	None	**Trastuzumab + Pertuzumab + Docetaxel***, **Ado-trastuzumab emtansine**, **Neratinib**	Trastuzumab + Pyrotinib + Docetaxel#, A166#, Trastuzumab + Pertuzumab#	None
Evidence-based Medicine	**Gene description:** The ERBB2/HER2 (v-erb-b2 erythroblastic leukemia viral oncogene homolog 2) gene encodes a member of the epidermal growth factor (EGF) receptor family of receptor tyrosine kinases. It binds tightly to other ligand-bound EGF receptor family members to form a heterodimer, stabilizing ligand binding and enhancing kinase-mediated activation of downstream signalling pathways. Amplification and/or overexpression of this gene have been reported in breast cancer, non-small cell lung cancer, etc. **Description of signaling pathway:** Its related signaling pathways such as PI3K/AKT/mTOR and Ras/Raf/MEK/ERK are involved in the regulation of cell proliferation, survival and differentiation. HER2 amplification results in numerous downstream molecular cascades, leading to enhanced proliferative signals. **Variant description:** This variation is a gene amplification that may result in increased protein expression. **Description of NCCN Guidelines:** None. **Description of prognostic diagnosis:** None. **Related biological and medical information:** The randomized trial was a multicenter, double-blind, placebo-controlled, phase III trial of 808 patients with HER2-positive metastatic breast cancer (breast tumor specimens were required to show HER2 overexpression defined as 3+ IHC or FISH amplification ratio determined at a central laboratory). Patients were randomized 1:1 to receive placebo plus Trastuzumab and Docetaxel or Pertuzumab plus trastuzumab and docetaxel. The randomized trial demonstrated a statistically significant improvement in IRF-assessed PFS in the Pertuzumab-treated group compared with the placebo-treated group [hazard ratio (HR) = 0.62 (95% CI: 0.51, 0.75), p < 0.0001] and an increase in median PFS of 6.1 months (median PFS of 18.5 months in the Pertuzumab-treated group vs. 12.4 months in the placebo-treated group) [FDA Reference ID:4198338]. In a phase III, randomized, multicenter, open-label trial that enrolled 991 patients, patients in the trial had to have breast tumor specimens that showed HER2 overexpression or amplification. Patients were randomly assigned (1:1) to receive Ado-trastuzumab emtansine, or Lapatinib plus Capecitabine. Patients who received Ado-trastuzumab emtansine lived statistically significantly longer without their disease getting worse (PFS) compared with those who received Lapatinib plus Capecitabine [HR of progression 0.65 (95 percent CI: 0.55, 0.77), p < 0.0001]. The median PFS was 9.6 months for patients who received Ado-trastuzumab emtansine and 6.4 months for patients who received Lapatinib plus Capecitabine. At the time of the second interim OS analysis, patients who received Ado-trastuzumab emtansine had a statistically significant improvement in OS compared with people who received Lapatinib and Capecitibine [HR of death 0.68 (95 percent CI: 0.55, 0.85), p = 0.0006]. The median			

OS was 30.9 months for patients who received Ado-trastuzumab emtansine and 25.1 months for patients who received Lapatinib plus Capecitabine [FDA reference ID: 4323855]. Based on results of ExteNET trial, which is a multicenter, randomized, double-blind, placebo-controlled trial, women (n = 2840) were randomized to receive either neratinib (n = 1420) or placebo (n = 1420) for one year. The major efficacy outcome measure was invasive disease-free survival (iDFS) defined as the time between the randomization date to the first occurrence of invasive recurrence (local/regional, ipsilateral or contralateral breast cancer), distant recurrence, or death from any cause. iDFS was 94.2% in patients treated with neratinib compared with 91.9% in those receiving placebo (HR 0.66; 95% CI: 0.49, 0.90, p = 0.008) [FDA Reference ID: 4284195].

Description of drug resistance: None.

The clinical trials shown in the table below are recommended.

Details of Drug Information

Drugs	Indications
Trastuzumab + Pertuzumab + Docetaxel*	FDA approved PERJETA (Pertuzumab) is a HER2/neu receptor antagonist indicated for use in combination with Trastuzumab and Docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. NMPA approved Pertuzumab in combination with Trastuzumab and chemotherapy for adjuvant treatment of patients with HER2-positive early breast cancer with a high risk of recurrence.
Ado-trastuzumab emtansine	FDA approved KADCYLA (Ado-trastuzumab emtansine) is a HER2-targeted antibody and microtubule inhibitor conjugate indicated, as a single agent, for: 1. the treatment of patients with HER2-positive, metastatic breast cancer who previously received Trastuzumab and a Taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy; 2. the adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant Taxane and Trastuzumab-based treatment.
Neratinib	FDA approved NERLYNX (Neratinib) is a kinase inhibitor indicated for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer, to follow adjuvant Trastuzumab-based therapy.

Information on Related Clinical Trials

Trial ID on ClinicalTrials.gov or chinadrugtrials.org.cn	Clinical Trial Name	Tumor Type	Phase	Drug Candidate(s)	Locations of Recruiting Sites
CTR20180941	Preoperative Treatment of HER2-Positive Breast Cancer with Pyrrolidine plus Herceptin/Docetaxel Versus Placebo plus Herceptin/Docetaxel	HER2 Positive Breast Cancer	Phase III	Trastuzumab + Pyrotinib + Docetaxel (Anti-HER2 + SHR1258 + RP56976)	Shanghai; Beijing; Zhejiang; etc.
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	Advanced Solid Tumors	Phase II	Trastuzumab + Pertuzumab (Anti-HER2 + 2C4 Antibody)	United States

NCT03602079	A Phase I/II, FIH Study of A166 in Locally Advanced/Metastatic Solid Tumors Expressing Human Epidermal Growth Factor Receptor 2 (HER2) or Are HER2 Amplified That Did Not Respond or Stopped Responding to Approved Therapies	HER2-positive Breast Cancer; HER2 Positive Gastric Cancer; Lung Cancer; Colo-rectal Cancer; Solid Tumor; etc.	Phase I/II	A166	United States

Note:

The above information is constantly evolving. Therefore, the health care providers are responsible for obtaining the most recent and appropriate information through proper resources.

TP53

Variant	NM_000546.5 exon10 c.1045G>T p.E349*			
VAF	72.41%			
Targeted Therapy	**Potential Benefit**			**Potential Resistance**
	Level A	**Level B**	**Level C**	
	None	None	Adavosertib + Carboplatin#	None
Evidence-based Medicine	**Gene description:** The TP53 (tumor protein p53) gene encodes a tumor suppressor protein containing transcriptional activation, DNA binding, and oligomerization domains. The encoded protein responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Mutations in this gene are associated with a variety of human cancers, including hereditary cancers such as Li-Fraumeni syndrome, soft tissue and osteosarcoma, breast cancer, brain cancer, adrenal cortical cancer, etc. **Description of signaling pathway:** None. **Variant description:** This variation is an inactive mutation that may result in a loss of protein function. **Description of NCCN Guidelines:** None. **Description of prognostic diagnosis:** None. **Related biological and medical information:** Adavosertib is a WEE1 kinase inhibitor targeting G2 checkpoint control, preferentially sensitizing TP53-deficient tumor cells to DNA damage. A phase I study evaluated safety, tolerability, pharmacokinetics, and pharmacodynamics of oral Adavosertib as monotherapy or in combination with chemotherapy in patients with refractory solid tumors. Of 176 patients evaluable for efficacy, 94 (53%) had stable disease as best response, and 17 (10%) achieved a partial response. The response rate in TP53-mutated patients (n = 19) was 21% compared with 12% in TP53 wild-type patients (n = 33). So Adavosertib was safe and tolerable as a single agent and in combination with chemotherapy at doses associated with target engagement [PMID: 27601554]. **Description of drug resistance:** None. **The clinical trial shown in the table below is recommended.**			

Information on Related Clinical Trials

Trial ID on ClinicalTrials.gov or chinadrugtrials.org.cn	Clinical Trial Name	Tumor Type	Phase	Drug Candidate(s)	Locations of Recruiting Sites
NCT01827384	Molecular Profiling-Based Assignment of Cancer Therapy for Patients with Advanced Solid Tumors	Advanced Malignant Solid Neoplasm	Phase II	Adavosertib + Carboplatin (AZD1775 | MK1775 + CBDCA)	United States

Note:

The above information is constantly evolving. Therefore, the health care providers are responsible for obtaining the most recent and appropriate information through proper resources.

Detailed Test Results about Chemotherapy

Detected Mutations and the Relevance to Chemotherapy Toxicity

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
Fluorouracil, Leucovorin, Irinotecan	UGT1A1	rs8175347	(TA)6/(TA)6	Patients with the (TA)6/(TA)6 genotype (i.e. UGT1A1*1/*1) and cancer who are treated with irinotecan-based regimens may have a decreased risk of neutropenia, diarrhea, or asthenia, as compared to patients with the (TA)7/(TA)7 (*28/*28) genotype. Evidence for an association between this genotype and neutropenia is stronger than that for diarrhea or asthenia, and some studies only show significant associations with neutropenia and diarrhea at medium and high doses of the drug (>125 mg/m2). No significant associations have been seen for nausea, mucositis, infection, overall gastrointestinal toxicities (diarrhea, nausea, vomiting, and mucositis combined), overall hematologic toxicities (neutropenia, thrombocytopenia, anemia and leukopenia combined) or tumor response. One study found a decreased risk of vomiting for this genotype, and another found a decreased risk of treatment-related death, both compared to the (TA)7/(TA)7 genotype. Other genetic and clinical factors may also influence a patient's risk of neutropenia, diarrhea, asthenia, vomiting, or treatment-related death. [PMID:17549067] [PMID:18797458] [PMID:18300238]	2A
Fluorouracil, Leucovorin, Oxaliplatin	ERCC1	rs11615	GG	Patients with the GG genotype and colon cancer may have a decreased risk of neutropenia when treated with FOLFOX (fluorouracil, leucovorin, oxaliplatin) as compared to patients with the AA genotype. Other genetic and clinical factors may also influence risk of neutropenia. [PMID:23314736]	3
Fluorouracil, Leucovorin, Oxaliplatin	MTHFR	rs1801133	GG	Genotype AG is associated with increased risk of Drug Toxicity when treated with capecitabine, fluorouracil, leucovorin and oxaliplatin in people with Colorectal Neoplasms. [PMID:23314736]	3
Fluorouracil, Leucovorin	MTHFR	rs1801133	GG	Cancer patients with the GG genotype may have a decreased risk of drug toxicities when treated with fluorouracil- or capecitabine-based therapy as	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
				compared to patients with the AA or AG genotype, however this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's risk of toxicities when taking these drugs. [PMID:19384296]	
Capecitabine, Irinotecan	UGT1A1	rs8175347	(TA)6/(TA)6	Patients with the (TA)6/(TA)6 genotype (i.e. UGT1A1*1/*1) and cancer who are treated with irinotecan-based regimens may have a decreased risk of neutropenia, diarrhea, or asthenia, as compared to patients with the (TA)7/(TA)7 (*28/*28) genotype. Evidence for an association between this genotype and neutropenia is stronger than that for diarrhea or asthenia, and some studies only show significant associations with neutropenia and diarrhea at medium and high doses of the drug (>125 mg/m2). No significant associations have been seen for nausea, mucositis, infection, overall gastrointestinal toxicities (diarrhea, nausea, vomiting, and mucositis combined), overall hematologic toxicities (neutropenia, thrombocytopenia, anemia and leukopenia combined) or tumor response. One study found a decreased risk of vomiting for this genotype, and another found a decreased risk of treatment-related death, both compared to the (TA)7/(TA)7 genotype. Other genetic and clinical factors may also influence a patient's risk of neutropenia, diarrhea, asthenia, vomiting, or treatment-related death. [PMID:18594531]	2A
Cyclophosphamide, Epirubicin	GSTP1	rs1695	AA	Patients with the AA genotype and Breast Neoplasms who are treated with cyclophosphamide and epirubicin may have 1) increased drug response 2) decreased severity of toxicity as compared to patients with GG genotype. Some patients were additionally treated with fluorouracil. Other genetic and clinical factors may influence a patient's response to cyclophosphamide, epirubicin and fluorouracil. [PMID:21362365]	2A
Carboplatin, Paclitaxel	GSTP1	rs1695	AA	Genotype AA is associated with increased risk of hematological toxicity when treated with Platinum compounds and taxanes in people with Ovarian	2A

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
				Neoplasms as compared to genotypes GG + AG. [PMID:19203783]	
Cisplatin, Cyclophosphamide	ERCC1	rs3212986	AC	Patients with the AC genotype may have increased risk for nephrotoxicity with platinum-based regimens as compared to patients with the CC genotypes. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:19786980]	2B
Cisplatin, Cyclophosphamide	ERCC1	rs11615	GG	Patients with the GG genotype and Ovarian Neoplasms who are treated with cisplatin and cyclophosphamide may have a decreased, but not absent, risk of nephrotoxicity as compared to patients with the AG genotype. This association has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's risk for adverse events with cisplatin and cyclophosphamide treatment. [PMID:19786980]	3
Cisplatin, Cyclophosphamide	XRCC1	rs25487	CT	Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:22188361]	2B
Cyclophosphamide	MTHFR	rs1801133	GG	GG: Patients with the GG genotype may have decreased likelihood of Drug Toxicity when treated with cisplatin, cyclophosphamide, dactinomycin, doxorubicin, methotrexate and vincristine in people with Osteosarcoma as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's risk of toxicity to cyclophosphamide. [PMID:19159907] [PMID:20638924]	3
Cyclophosphamide	XRCC1	rs25487	CT	CT: Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
				cyclophosphamide-containing chemotherapy regimens as compared to patients with the CC genotype. However, all studies evaluated also included platinum drugs which may interact with this variant. Other genetic and clinical factors may also influence response to treatment. [PMID:19786980]	
Irinotecan	UGT1A1	rs8175347	(TA)6/(TA)6	(TA)6/(TA)6: Patients with the (TA)6/(TA)6 genotype (i.e. UGT1A1*1/*1) and cancer who are treated with irinotecan-based regimens may have a decreased risk of neutropenia, diarrhea, or asthenia, as compared to patients with the (TA)7/(TA)7 (*28/*28) genotype. Evidence for an association between this genotype and neutropenia is stronger than that for diarrhea or asthenia, and some studies only show significant associations with neutropenia and diarrhea at medium and high doses of the drug (>125 mg/m2). No significant associations have been seen for nausea, mucositis, infection, overall gastrointestinal toxicities (diarrhea, nausea, vomiting, and mucositis combined), overall hematologic toxicities (neutropenia, thrombocytopenia, anemia and leukopenia combined) or tumor response. One study found a decreased risk of vomiting for this genotype, and another found a decreased risk of treatment-related death, both compared to the (TA)7/(TA)7 genotype. Other genetic and clinical factors may also influence a patient's risk of neutropenia, diarrhea, asthenia, vomiting, or treatment-related death. [PMID:24519753] [PMID:23529007] [PMID:26862009]	2A
Irinotecan	C8orf34	rs1517114	GG	GG: Patients with the GG genotype may have decreased severity of Diarrhea when treated with irinotecan in people with Non-Small-Cell Lung Carcinoma as compared to patients with the CC or CG genotype. Other genetic and clinical factors may also influence a patient's risk for toxicity. [PMID:22664479]	2B
Fluorouracil	Fluorouracil	GSTP1	rs1695	AA	AA: Patients with the AA genotype and cancer who are treated with fluorouracil may have a higher risk of hematological toxicity as compared	3

Chemotherapy		Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
					to patients with the GG genotype. Other genetic and clinical factors may also influence a patient's risk for hematological toxicity when exposed to fluorouracil. [PMID:18540691]	
Fluorouracil	Fluorouracil	MTHFR	rs1801133	GG	GG: Cancer patients with the GG genotype may have a decreased risk of drug toxicities when treated with fluorouracil- or capecitabine-based therapy as compared to patients with the AA or AG genotype, however this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's risk of toxicities when taking these drugs. [PMID:23314736] [PMID:19384296] [PMID:20638924]	3
Fluorouracil	Capecitabine	MTHFR	rs1801133	GG	GG: Cancer patients with the GG genotype may have a decreased risk of drug toxicities when treated with fluorouracil- or capecitabine-based therapy as compared to patients with the AA or AG genotype, however this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's risk of toxicities when taking these drugs. [PMID:20819423]	3
Platinum	Carboplatin	GSTP1	rs1695	AA	AA: Allele G is associated with decreased risk of Neutropenia when treated with Platinum compounds in people with Carcinoma, Non-Small-Cell Lung as compared to allele A. [PMID:17409936]	3
Platinum	Cisplatin	XPC	rs2228001	TT	TT: Patients with the TT genotype may have a decreased but not non-existent risk for toxicity with cisplatin treatment as compared to patients with the GG or GT genotype. Other genetic and clinical factors may also influence a patient's risk for toxicity. [PMID:21047201] [PMID:19434073]	1B
Platinum	Cisplatin	XRCC1	rs25487	CT	CT: Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other	2B

Chemotherapy		Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
					genetic and clinical factors may also influence response to platinum-based regimens. [PMID:19786980]	
Platinum	Cisplatin	GSTP1	rs1695	AA	AA: Allele G is associated with decreased risk of Neutropenia when treated with Platinum compounds in people with Carcinoma, Non-Small-Cell Lung as compared to allele A. [PMID:17409936]	3
Platinum	Cisplatin	MTHFR	rs1801133	GG	GG: Patients with the GG genotype may have: Genotype AA is associated with increased likelihood of Drug Toxicity when treated with cisplatin, cyclophosphamide, dactinomycin, doxorubicin, methotrexate and vincristine in people with Osteosarcoma as compared to genotypes GG + AG. [PMID:19159907]	3
Platinum	Oxaliplatin	GSTP1	rs1695	AA	AA: Patients with the AA genotype and cancer who are treated with oxaliplatin or platinum compounds may have an increased risk for hematological toxicity, neurotoxicity, neutropenia, and discontinuation of treatment as compared to patients with the AG or GG genotype. Conflicting data exist for the neurotoxicity risk showing that patients with the AA might have a decreased, but not absent, risk. Other genetic and clinical factors may also influence a patient's risk for adverse events with oxaliplatin or platinum compounds treatment. AG: Patients with the AG genotype and cancer who are treated with oxaliplatin or platinum compounds may have a decreased, but not absent, risk for hematological toxicity, neurotoxicity, neutropenia, and discontinuation of treatment as compared to patients with the AA genotype. Conflicting data exist for the neurotoxicity risk showing that patients with the AG might have an increased risk. Other genetic and clinical factors may also influence a patient's risk for adverse events with oxaliplatin or platinum compounds treatment. GG: Patients with the GG genotype and cancer who are treated with oxaliplatin or platinum compounds may have a decreased, but not absent, risk for hematological toxicity, neurotoxicity, neutropenia, and	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
				discontinuation of treatment as compared to patients with the AA genotype. Conflicting data exist for the neurotoxicity risk showing that patients with the GG might have an increased risk. Other genetic and clinical factors may also influence a patient's risk for adverse events with oxaliplatin or platinum compounds treatment. [PMID:20530282] [PMID:16707601]	

Detected Mutations and the Relevance to Chemotherapy Efficacy

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
Fluorouracil, Leucovorin, Oxaliplatin	GSTP1	rs1695	AA	Genotype GG is associated with increased progression free survival when treated with fluorouracil, leucovorin and oxaliplatin in people with Colorectal Neoplasms as compared to genotypes AA + AG. [PMID:20078613]	2A
Fluorouracil, Leucovorin, Oxaliplatin	ABCG2	rs2231142	GT	Patients with the GT genotype and and colorectal cancer who are receiving FOLFOX/XELOX regimens may have a better response rate as compared to patients with the GG genotype. Other genetic and clinical factors may also influence response to chemotherapy regimens. [PMID:24338217]	3
Fluorouracil, Leucovorin, Oxaliplatin	ERCC1	rs11615	GG	Patients with the GG genotype and colorectal cancer may have increased overall and progression-free survival time when treated with FOLFOX (fluorouracil, leucovorin, oxaliplatin) as compared to patients with the AA or AG genotype. Other genetic and clinical factors may also influence overall and progression-free survival time. [PMID:21057378] [PMID:15213713]	3
Fluorouracil, Leucovorin, Oxaliplatin	MTHFR	rs1801133	GG	Patients with genotype GG and colonic neoplasms may have increased response to fluorouracil, leucovorin and oxaliplatin (FOLFOX therapy) as compared to patients with genotypes AA and AG. However, other studies showed decreased response to oxaliplatin. [PMID:24980946]	3
Fluorouracil, Leucovorin, Oxaliplatin	XRCC1	rs25487	CT	Genotype CC is associated with increased overall survival progression-free survivaland when treated with fluorouracil, leucovorin and oxaliplatin in people with Colorectal Neoplasms as compared to genotypes CT + TT. Other genetic and clinical factors may also influence response to platinum-based regimens. Other genetic and clinical factors	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				may also influence response to treatment. [PMID:21057378] [PMID:23314736]	
Fluorouracil, Oxaliplatin	GSTP1	rs1695	AA	Patients with the AA genotype and colorectal cancer who are treated with fluorouracil and oxaliplatin may have poorer treatment outcome (reduced responsiveness, lower overall survival time, increased risk of death) as compared to patients with the GG genotype. Other genetic and clinical factors may also influence a patient's response to fluorouracil and oxaliplatin treatment. [PMID:21449681]	2A
Fluorouracil, Oxaliplatin	ERCC1	rs11615	GG	Genotype AA is associated with increased risk of dying when treated with Platinum compounds in people with Colorectal Neoplasms as compared to genotype GG. [PMID:15213713]	3
Capecitabine, Oxaliplatin	MTHFR	rs1801133	GG	Patients with genotype GG and colonic neoplasms may have increased response to fluorouracil, leucovorin and oxaliplatin (FOLFOX therapy) as compared to patients with genotypes AA and AG. However, other studies showed decreased response to oxaliplatin. [PMID:24980946]	3
Carboplatin, Docetaxel	MTHFR	rs1801133	GG	Patients with GG genotype may have 1) decreased likelihood of response 2) decreased progression free survival to carboplatin in people with Non-Small-Cell Lung Carcinoma as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to carboplatin. [PMID:21605004]	3
Cisplatin, Docetaxel	XRCC1	rs25487	CT	Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				may also influence response to platinum-based regimens. [PMID:24446315]	
Cisplatin, Docetaxel	MTHFR	rs1801133	GG	Patients with GG genotype may have 1) decreased likelihood of response 2) decreased progression free survival to carboplatin in people with Non-Small-Cell Lung Carcinoma as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to carboplatin. [PMID:21605004]	3
Cisplatin/Carboplatin, Gemcitabine	ERCC1	rs11615	GG	Patients with the GG genotype may have 1) decreased but not absent risk for toxicity, 2) increased survival and 3) a better response when treated with platinum-based chemotherapy as compared to patients with the AA or AG genotype. However, some studies find no association with drug toxicity, and one study found a poorer response as compared to patients with the AA or AG genotype. Other genetic and clinical factors may also influence a patient's response to platinum-based chemotherapy. [PMID:25069034]	2B
Cisplatin/Carboplatin, Gemcitabine	MTHFR	rs1801133	GG	Patients with GG genotype may have 1) decreased likelihood of response 2) decreased progression free survival to carboplatin in people with Non-Small-Cell Lung Carcinoma as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to carboplatin. [PMID:21605004]	3
Cisplatin/Carboplatin, Paclitaxel	ERCC1	rs11615	GG	Patients with the GG genotype may have 1) decreased but not absent risk for toxicity, 2) increased survival and 3) a better response when treated with platinum-based chemotherapy as compared to patients with the AA or AG genotype. However, some studies find no association with drug toxicity, and one study found a poorer response as compared to patients with the AA or AG genotype. Other genetic and clinical factors	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				may also influence a patient's response to platinum-based chemotherapy. [PMID:25069034]	
Cisplatin/Carboplatin, Paclitaxel	XRCC1	rs25487	CT	Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:24446315]	2B
Cisplatin/Carboplatin, Paclitaxel	MTHFR	rs1801133	GG	Patients with GG genotype may have 1) decreased likelihood of response 2) decreased progression free survival to carboplatin in people with Non-Small-Cell Lung Carcinoma as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to carboplatin. [PMID:21605004]	3
Cisplatin/Carboplatin, Pemetrexed	ERCC1	rs11615	GG	Patients with the GG genotype may have 1) decreased but not absent risk for toxicity, 2) increased survival and 3) a better response when treated with platinum-based chemotherapy as compared to patients with the AA or AG genotype. However, some studies find no association with drug toxicity, and one study found a poorer response as compared to patients with the AA or AG genotype. Other genetic and clinical factors may also influence a patient's response to platinum-based chemotherapy. [PMID:25069034]	2B
Cisplatin/Carboplatin, Pemetrexed	MTHFR	rs1801133	GG	Patients with GG genotype may have 1) decreased likelihood of response 2) decreased progression free survival to carboplatin in people with Non-Small-Cell Lung Carcinoma as compared to patients with genotype AA.	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				Other genetic and clinical factors may also influence a patient's response to carboplatin. [PMID:24732178]	
Cisplatin/Carboplatin, Vinorelbine	ERCC1	rs11615	GG	Patients with the GG genotype may have 1) decreased but not absent risk for toxicity, 2) increased survival and 3) a better response when treated with platinum-based chemotherapy as compared to patients with the AA or AG genotype. However, some studies find no association with drug toxicity, and one study found a poorer response as compared to patients with the AA or AG genotype. Other genetic and clinical factors may also influence a patient's response to platinum-based chemotherapy. [PMID:25069034]	2B
Cisplatin/Carboplatin, Vinorelbine	XRCC1	rs25487	CT	Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:24446315]	2B
Cisplatin/Carboplatin, Vinorelbine	MTHFR	rs1801133	GG	Patients with GG genotype may have 1) decreased likelihood of response 2) decreased progression free survival to carboplatin in people with Non-Small-Cell Lung Carcinoma as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to carboplatin. [PMID:21605004]	3
Cyclophosphamide, Epirubicin, Fluorouracil	GSTP1	rs1695	AA	Patients with the AA genotype and Breast Neoplasms who are treated with cyclophosphamide and epirubicin may have 1) increased drug response 2) decreased severity of toxicity as compared to patients	2A

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				with GG genotype. Some patients were additionally treated with fluorouracil. Other genetic and clinical factors may influence a patient's response to cyclophosphamide, epirubicin and fluorouracil. [PMID:20568049]	
Cyclophosphamide, Epirubicin	GSTP1	rs1695	AA	Patients with the AA genotype and Breast Neoplasms who are treated with cyclophosphamide and epirubicin may have 1) increased drug response 2) decreased severity of toxicity as compared to patients with GG genotype. Some patients were additionally treated with fluorouracil. Other genetic and clinical factors may influence a patient's response to cyclophosphamide, epirubicin and fluorouracil. [PMID:21362365]	2A
Carboplatin, Cyclophosphamide	ERCC1	rs11615	GG	AA: Genotype AA is associated with decreased response to Platinum compounds in women with Ovarian Neoplasms as compared to genotype GG.Genotype AA is associated with increased risk of recurrence of disease when treated with Platinum compounds in women Ovarian Neoplasms as compared to genotype GG.Genotype AA is associated with increased risk of Death when treated with Platinum compounds in women Ovarian Neoplasms as compared to genotype GG. [PMID:22329723]	2B
Carboplatin, Paclitaxel	ERCC1	rs11615	GG	Genotype AA is associated with decreased response to Platinum compounds in women with Ovarian Neoplasms as compared to genotype GG.Genotype AA is associated with increased risk of recurrence of disease when treated with Platinum compounds in women Ovarian Neoplasms as compared to genotype GG.Genotype AA is associated with increased risk of Death when treated with Platinum compounds in women Ovarian Neoplasms as compared to genotype GG. [PMID:22329723]	2B
Cisplatin,	ERCC1	rs11615	GG	AA: Genotype AA is associated with	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
Cyclophosphamide				decreased response to Platinum compounds in women with Ovarian Neoplasms as compared to genotype GG.Genotype AA is associated with increased risk of recurrence of disease when treated with Platinum compounds in women Ovarian Neoplasms as compared to genotype GG.Genotype AA is associated with increased risk of Death when treated with Platinum compounds in women Ovarian Neoplasms as compared to genotype GG. [PMID:22329723]	
Cisplatin, Cyclophosphamide	XRCC1	rs25487	CT	Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:19786980]	2B
Cisplatin, Cyclophosphamide	GSTP1	rs1695	AA	Patients with the AA genotype and Ovarian Neoplasms who are treated with cisplatin and cyclophosphamide may have an increased likelihood of progression free survival as compared to patients with the AG and GG genotype. However, this association was contradicted in other studies. Other genetic and clinical factors may also influence a patient's response to cisplatin and cyclophosphamide treatment. [PMID:19786980]	3
Cisplatin, Paclitaxel	ERCC1	rs11615	GG	AA: Genotype AA is associated with decreased response to Platinum compounds in women with Ovarian Neoplasms as compared to genotype GG.Genotype AA is associated with increased risk of recurrence of disease when treated with Platinum compounds in women Ovarian Neoplasms as	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				compared to genotype GG.Genotype AA is associated with increased risk of Death when treated with Platinum compounds in women Ovarian Neoplasms as compared to genotype GG. [PMID:22329723]	
Cisplatin, Fluorouracil	ERCC1	rs3212986	AC	Genotypes AA + AC are associated with increased overall survival when treated with cisplatin and fluorouracil in people with Esophageal Neoplasms as compared to genotype CC. [PMID:23962907]	3
Cisplatin, Docetaxel, Gemcitabine, Capecitabine	ERCC1	rs11615	GG	Genotypes AG + GG are associated with decreased overall survival when treated with capecitabine, cisplatin, docetaxel, epirubicin and gemcitabine in people with Pancreatic Neoplasms as compared to genotype AA. [PMID:22026922]	2B
Cisplatin, Docetaxel, Gemcitabine, Capecitabine	XRCC1	rs25487	CT	Genotypes CT + TT are associated with decreased overall survival when treated with capecitabine, cisplatin, docetaxel, epirubicin and gemcitabine in people with Pancreatic Neoplasms as compared to genotype CC. [PMID:22026922]	2B
Cisplatin, Epirubicin, Gemcitabine, Capecitabine	ERCC1	rs11615	GG	Genotypes AG + GG are associated with decreased overall survival when treated with capecitabine, cisplatin, docetaxel, epirubicin and gemcitabine in people with Pancreatic Neoplasms as compared to genotype AA. [PMID:22026922]	2B
Cisplatin, Epirubicin, Gemcitabine, Capecitabine	XRCC1	rs25487	CT	Genotypes CT + TT are associated with decreased overall survival when treated with capecitabine, cisplatin, docetaxel, epirubicin and gemcitabine in people with Pancreatic Neoplasms as compared to genotype CC. [PMID:22026922]	2B
Cyclophosphamide	XRCC1	rs25487	CT	CT: Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with cyclophosphamide-containing chemotherapy regimens as compared to patients with the CC genotype. However, all studies evaluated also included platinum drugs which may interact with this variant. Other genetic and	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				clinical factors may also influence response to treatment. [PMID:22188361]	
Pemetrexed	MTHFR	rs1801133	GG	GG: Patients with GG genotype may have 1) decreased likelihood of response 2) decreased progression free survival to carboplatin in people with Non-Small-Cell Lung Carcinoma as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to carboplatin. [PMID:24732178]	3
Platinum/ Carboplatin	MTHFR	rs1801133	GG	GG: Patients with GG genotype may have 1) decreased likelihood of response 2) decreased progression free survival to carboplatin in people with Non-Small-Cell Lung Carcinoma as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to carboplatin. [PMID:21605004] [PMID:19307503]	2A
Platinum/ Carboplatin	ERCC1	rs11615	GG	GG: Patients with the GG genotype may have 1) decreased but not absent risk for toxicity, 2) increased survival and 3) a better response when treated with platinum-based chemotherapy as compared to patients with the AA or AG genotype. However, some studies find no association with drug toxicity, and one study found a poorer response as compared to patients with the AA or AG genotype. Other genetic and clinical factors may also influence a patient's response to platinum-based chemotherapy. [PMID:25069034]	2B
Platinum/ Carboplatin	XRCC1	rs25487	CT	CT: Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				platinum-based regimens. [PMID:24446315]CT: Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:25025378] [PMID:22188361] [PMID:22026922] [PMID:16875718]	
Platinum/	Cisplatin	XRCC1	rs25487	CT	CT: Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:24446315]CT: Patients with the CT genotype may have 1) decreased survival and 2) decreased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CC genotype. However, one study found increased survival as compared to patients with the CC genotype. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:25025378] [PMID:22188361] [PMID:22026922]	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				[PMID:16875718]	
Platinum/	Cisplatin	MTHFR	rs1801133	GG	GG: Patients with the GG genotype may have: 1) decreased likelihood of response to chemotherapy, 2) decreased likelihood of Drug Toxicity when treated with cisplatin in cancer patients as compared to patients with genotype AA. Other genetic and clinical factors may also influence a patient's response to cisplatin. [PMID:21605004]	3
Platinum/	Oxaliplatin	XRCC1	rs25487	CT	CT: Genotype CC is associated with increased overall survival progression-free survivaland when treated with fluorouracil, leucovorin and oxaliplatin in people with Colorectal Neoplasms as compared to genotypes CT + TT. Other genetic and clinical factors may also influence response to platinum-based regimens. Conflicting results exist for the relationship between the CT genotype and response to platinum-based treatment. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:21057378]	2B

Note:

* Description of the Levels of Evidence (PharmGKB)

Level 1A: Annotation for a variant-drug correlation in a CPIC or medical society-endorsed PGx guideline or implemented at a PGRN site or in another major health system.

Level 1B: Annotation for a variant-drug correlation where the preponderance of evidence shows an association. The association must be replicated in more than one cohort with significant p-values, and preferably will have a strong effect size.

Level 2A: Annotation for a variant-drug correlation that qualifies for level 2B where the variant is within a VIP (Very Important Pharmacogene) as defined by PharmGKB. The variants in level 2A are in known pharmacogenetics related genes, therefore the functional significance is more likely.

Level 2B: Annotation for a variant-drug combination with moderate evidence of association. The association must be replicated but there may be some studies that do not show statistical significance, and/or the effect size may be small.

Level 3: Annotation for a variant-drug combination based on a single significant (not yet replicated) study or annotation for a variant-drug combination evaluated in multiple studies but lacking clear evidence of an association.

Level 4: Annotation based on a case report, non-significant study or in vitro, molecular or functional assay evidence only.

* The toxicity and efficacy of chemotherapy drugs are often affected by multiple genetic polymorphisms. Due to the limitations of the current knowledge in pharmacogenomics, the conclusions based on genotypes alone may sometimes contradict to each other. In addition, other genetic or environmental factors could also influence the toxicity and efficacy of chemotherapy drugs.

Appendix

Gene List

SNV | InDel | CNV						
ABCB1	ABCC2	ABCC4	ABCG2	ABL1	ABL2	ABRAXAS1
ACVR1B	ADGRA2	AKT1	AKT2	AKT3	ALK	ALOX12B
AMER1	APC	APCDD1	AR	ARAF	ARFRP1	ARID1A
ARID1B	ARID2	ASXL1	ATM	ATR	ATRX	AURKA
AURKB	AXIN1	AXIN2	AXL	BACH1	BAP1	BARD1
BCL2	BCL2A1	BCL2L1	BCL2L2	BCL6	BCOR	BCORL1
BCR	BLM	BMPR1A	BRAF	BRCA1	BRCA2	BRD4
BRIP1	BTG1	BTG2	BTK	C8orf34	CALR	CARD11
CASP8	CBFB	CBL	CCND1	CCND2	CCND3	CCNE1
CD22	CD274	CD70	CD74	CD79A	CD79B	CDC73
CDH1	CDH2	CDH20	CDH5	CDK12	CDK4	CDK6
CDK8	CDKN1A	CDKN1B	CDKN2A	CDKN2B	CDKN2C	CEBPA
CFTR	CHD2	CHD4	CHEK1	CHEK2	CHUK	CIC
CRBN	CREBBP	CRKL	CRLF2	CSF1R	CSF3R	CTCF
CTNNA1	CTNNB1	CUL3	CUL4A	CUL4B	CXCR4	CYLD
CYP17A1	CYP1B1	CYP2C19	CYP2C8	CYP2D6	CYP3A4	CYP3A5
DAXX	DDR1	DDR2	DICER1	DIS3	DNMT3A	DOT1L
DPYD	EED	EGFR	EMSY	EP300	EPCAM	EPHA3
EPHA5	EPHA6	EPHA7	EPHB1	EPHB4	EPHB6	ERBB2
ERBB3	ERBB4	ERCC1	ERCC2	ERCC3	ERCC4	ERG
ERRFI1	ESR1	ESR2	ETV1	ETV4	ETV5	ETV6
EWSR1	EZH2	EZR	FAM46C	FANCA	FANCC	FANCD2
FANCE	FANCF	FANCG	FANCI	FANCL	FANCM	FAS
FAT1	FAT3	FBXW7	FCGR3A	FGF10	FGF12	FGF14
FGF19	FGF23	FGF3	FGF4	FGF6	FGF7	FGFR1
FGFR2	FGFR3	FGFR4	FH	FLCN	FLT1	FLT3
FLT4	FOXL2	FOXP1	FRS2	FUBP1	GABRA6	GALNT12
GATA1	GATA2	GATA3	GATA4	GATA6	GEN1	GID4
GLI1	GNA11	GNA13	GNAQ	GNAS	GREM1	GRIN2A
GRM3	GSK3B	GSTP1	H3F3A	HDAC1	HDAC2	HFE
HGF	HLA-A	HLA-B	HLA-C	HNF1A	HOXB13	HRAS
HSD3B1	HSP90AA1	ID3	IDH1	IDH2	IDO1	IDO2
IGF1	IGF1R	IGF2	IGF2R	IKBKE	IKZF1	IL7R
INHBA	INPP4B	INSR	IRF2	IRF4	IRS2	ITPA
JAK1	JAK2	JAK3	JUN	KAT6A	KDM5A	KDM5C
KDM6A	KDR	KEAP1	KEL	KIT	KLHL6	KMT2A
KMT2C	KMT2D	KRAS	LMO1	LRP1B	LRP2	LRP6
LTK	LYN	LZTR1	MAF	MAGI2	MAN1B1	MAP2K1

SNV | InDel | CNV						
MAP2K2	MAP2K4	MAP3K1	MAP3K13	MAPK1	MAX	MC1R
MCL1	MDM2	MDM4	MED12	MEF2B	MEN1	MERTK
MET	MITF	MKNK1	MKNK2	MLH1	MLH3	MPL
MRE11	MSH2	MSH3	MSH6	MST1R	MTAP	MTHFR
MTOR	MUTYH	MYB	MYC	MYCL	MYCN	MYD88
NBN	NCOR1	NF1	NF2	NFE2L2	NFKBIA	NKX2-1
NOTCH1	NOTCH2	NOTCH3	NOTCH4	NPM1	NQO1	NRAS
NRP2	NSD1	NSD2	NSD3	NT5C2	NTHL1	NTRK1
NTRK2	NTRK3	NUDT1	NUP93	NUTM1	P2RY8	PAK3
PAK5	PALB2	PARP1	PARP2	PARP3	PARP4	PAX5
PBRM1	PDCD1	PDCD1LG2	PDGFRA	PDGFRB	PDK1	PHLPP2
PIK3C2B	PIK3C2G	PIK3C3	PIK3CA	PIK3CB	PIK3CG	PIK3R1
PIK3R2	PIM1	PLCG2	PMS2	PNRC1	POLD1	POLE
PPARG	PPM1D	PPP2R1A	PPP2R2A	PRDM1	PREX2	PRKAR1A
PRKCI	PRKDC	PRKN	PRSS1	PRSS8	PTCH1	PTCH2
PTEN	PTPN11	PTPRD	PTPRO	QKI	RAC1	RAD21
RAD50	RAD51	RAD51B	RAD51C	RAD51D	RAD52	RAD54L
RAF1	RANBP2	RARA	RB1	RBM10	REL	RET
RICTOR	RNF43	ROS1	RPA1	RPTOR	RSPO2	RUNX1
RUNX1T1	SDC4	SDHA	SDHAF2	SDHB	SDHC	SDHD
SETD2	SF3B1	SGK1	SH2B3	SLC19A1	SLC22A2	SLC34A2
SLCO1B3	SLIT2	SMAD2	SMAD3	SMAD4	SMARCA4	SMARCB1
SMARCD1	SMO	SNCAIP	SOCS1	SOD2	SOX10	SOX2
SOX9	SPEN	SPINK1	SPOP	SPTA1	SRC	STAG2
STAT3	STAT4	STK11	SUFU	SULT1A1	SYK	TAF1
TBX3	TDO2	TEK	TERC	TERT	TET2	TGFBR2
TIPARP	TMEM127	TMPRSS2	TNF	TNFAIP3	TNFRSF14	TNKS
TNKS2	TOP1	TOP2A	TP53	TP53BP1	TPMT	TRRAP
TSC1	TSC2	TSHR	TYMS	TYRO3	U2AF1	UGT1A1
UMPS	VEGFA	VHL	WISP3	WRN	WT1	XPC
XPO1	XRCC1	XRCC2	XRCC3	ZBTB2	ZNF217	ZNF703
ZNRF3						

Fusion						
ALK	BCL2	BCR	BRAF	BRCA1	BRCA2	BRD4
CD74	EGFR	ERBB2	ETV1	ETV4	ETV5	ETV6
EWSR1	EZR	FGFR1	FGFR2	FGFR3	IDH1	IDH2
KIT	KMT2A	MET	MSH2	MYB	MYC	NOTCH2
NTRK1	NTRK2	NTRK3	NUTM1	PDGFRA	RAF1	RARA
RET	ROS1	RSPO2	SDC4	SLC34A2	TERC	TERT
TMPRSS2						