Comprehensive Cancer Profiling Test Report

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

Private & Confidential

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: WJY	**Specimen I.D.:** MKHSxxxxxxxxx-1A	**Ordering Physician:**
Patient NRIC/FIN/ID:	**Specimen Type/Size:** tissue	**Institution:**
	Specimen Collection Date:	
Gender: Female	**Specimen Received Date:**	
Data of Birth:		
Nationality:		
Diagnosis: Lung Cancer		

Brief Summary of Test Results

Detection Type	Test Results
Targeted Therapy	In this sample, 5 mutations in 4 genes were related to targeted therapies.
Tumor Mutation Burden (TMB)	17.857 Mutations/Megabase
Microsatellite status	MSS

Therapeutics Implications

Targeted Therapy

In this sample, 5 mutations in 4 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	
TP53	NM_000546.5 exon6 c.592G>T p.E198*	45.14%	None	None	Adavosertib + Carboplatin#	None
TP53	NM_000546.5 exon4 c.321_322delCGinsAC p.Y107*	46.29%	None	None	Adavosertib + Carboplatin#	None
ATR	NM_001184.3 intron29 c.5197-2A>G	36.51%	None	None	Prexasertib#, **Talazoparib#**	None
BRIP1	NM_032043.2 intron10 c.1473+1G>A	32.7%	None	None	**Talazoparib#**, **Niraparib#**	None
BRCA2	NM_000059.3 exon11 c.5722_5723delCT p.L1908Rfs*2	Heterozygous	None	None	Avelumab + Talazoparib#, **Olaparib*#**, Adavosertib#, Veliparib + Dinaciclib#, **Talazoparib#**	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)	17.857 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	NM_000249.3 exon12 c.1151T>A p.V384D	Heterozygous	nonsynonymous SNV
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

TP53

Variant	NM_000546.5 exon6 c.592G>T p.E198*			
VAF	45.14%			
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:** TP53 E198* results in a premature truncation of the Tp53 protein at amino acid 198 of 393 [UniProt.org]. Due to the loss of several functional domains [UniProt.org], E198* is predicted to lead to a loss of Tp53 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.

TP53

Variant	NM_000546.5 exon4 c.321_322delCGinsAC p.Y107*			
VAF	46.29%			
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:** TP53 Y107 lies within the DNA-binding domain of the TP53 protein and functionally interacts with WWOX, HIPK1 and ZNF385A [UniProt.org]. Y107X is a nonsense mutation that causes protein truncation. There is no direct research report, but it 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.**			

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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:

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ATR

Variant	NM_001184.3 intron29 c.5197-2A>G			
VAF	36.51%			
Targeted Therapy	Potential Benefit			Potential Resistance
	Level A	Level B	Level C	
	None	None	Prexasertib#, **Talazoparib#**	None
Evidence-based Medicine	**Gene description:** The protein encoded by ATR (ataxia telangiectasia and Rad3 related) is a member of phosphatidylinositol-3-kinase related kinase family and DNA damage sensor, which activates cell cycle checkpoint signaling upon DNA stress. The ATR encoded protein can phosphorylate and activate several proteins involved in the inhibition of DNA replication and mitosis, and can promote DNA repair, recombination, and apoptosis. Mutations of ATR gene are associated with colorectal cancer and endometrial cancer. **Description of signaling pathway:** ATR can interact with ATRIP to recognize single-stranded DNA covered with RPA. **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:** None. **Description of drug resistance:** None. **The clinical trials shown in the table below are recommended.**			

Details of Drug Information

Drugs	Indications
Talazoparib#	FDA approved TALZENNA (Talazoparib) is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer.

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
NCT02873975	A Phase II Study of the CHK1 Inhibitor Prexasertib in Patients with Advanced Solid Tumors Exhibiting Replicative Stress or Homologous Recombination Repair Deficiency	Advanced Cancers	Phase II	Prexasertib (LY2606368 | Prexasertib HCl)	United States

NCT02286687	Phase II Study of the PARP Inhibitor Talazoparib in Advanced Cancer Patients with Somatic Alterations in BRCA1/2, Mutations/Deletions in other BRCA Pathway Genes and Germline Mutation in BRCA1/2 (Not Breast or Ovarian Cancer)	Advanced Cancers	Phase II	**Talazoparib (BMN673)**	United States

Note:

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BRIP1

Variant	NM_032043.2 intron10 c.1473+1G>A			
VAF	32.7%			
Targeted Therapy	Potential Benefit			Potential Resistance
	Level A	Level B	Level C	
	None	None	**Talazoparib#**, **Niraparib#**	None
Evidence-based Medicine	**Gene description:** The protein encoded by BRIP1 (BRCA1 interacting protein C-terminal helicase 1) is a member of the RecQ DEAH helicase family and interacts with the BRCT repeats of breast cancer, type 1 (BRCA1). The bound complex is important in the normal double-strand break repair function of breast cancer, type 1 (BRCA1). This gene is a tumor suppressor gene may be a target of germline cancer-inducing mutations. Mutations of BRIP1 are associated with breast cancer, endometrial cancer, bowel cancer, stomach 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:** None. **Description of drug resistance:** None. **The clinical trials shown in the table below are recommended.**			

Details of Drug Information

Drugs	Indications
Talazoparib#	FDA approved TALZENNA (Talazoparib) is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer.
Niraparib#	FDA approved ZEJULA (Niraparib) is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated: 1. for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy; 2. for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either: a deleterious or suspected deleterious BRCA mutation, or genomic instability and who have progressed more than six months after response to the last platinum-based chemotherapy.

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

NCT02401347	A Phase II Clinical Trial of the PARP Inhibitor Talazoparib in BRCA1 and BRCA2 Wild-Type Patients with (i) Advanced Triple-Negative Breast Cancer and Homologous Recombination Deficiency, and (ii) Advanced HER2-Negative Breast Cancer or Other Solid Tumors with Either a Mutation in Homologous Recombination Pathway Genes	HER2 Negative Solid Tumor; Triple-Negative Breast Cancer; HER2 Negative Breast Cancer	Phase II	**Talazoparib (BMN673)**	United States
NCT03207347	A Phase II Trial of the PARP Inhibitor, Niraparib, in BAP1 and Other DNA Damage Response (DDR) Pathway Deficient Neoplasms (UF-STO-ETI-001)	Solid tumor; Mesothelioma; Uveal Melanoma; Renal Cell Carcinoma; Cholangiocarcinoma	Phase II	**Niraparib (MK4827)**	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.

BRCA2

Variant	NM_000059.3 exon11 c.5722_5723delCT p.L1908Rfs*2			
VAF	Heterozygous			
Targeted Therapy	Potential Benefit			Potential Resistance
	Level A	Level B	Level C	
	None	None	Avelumab + Talazoparib#, **Olaparib*#**, Adavosertib#, Veliparib + Dinaciclib#, **Talazoparib#**	None
Evidence-based Medicine	**Gene description:** The BRCA2 (breast cancer 2, early onset) gene has been mapped in region 12-13 of the long arm of chromosome 13. This gene is oncogenic. Endometrial cancer, bowel cancer and stomach cancer are also related to BRCA2. **Description of signaling pathway:** None. **Variant description:** BRCA2 is a tumor suppressor involved in the DNA damage response and can be mutated in various cancer types. Since truncated protein codified by BRCA2 truncating mutations do not performs a translocation into the nucleus, they are fully non-functional, and likely oncogenic [PMID: 20878484; PMID: 11239455; PMID: 10570174]. **Description of NCCN Guidelines:** None. **Description of prognostic diagnosis:** None. **Related biological and medical information:** In phase I trial, Talazoparib treatment confirmed the safety and initial efficacy of patients with advanced solid tumors and deleterious BRCA1/2 mutations [J Clin Oncol 31, 2013 (suppl; abstr 2580)]. **Description of drug resistance:** None. **The clinical trials shown in the table below are recommended.**			

Details of Drug Information

Drugs	Indications
Talazoparib#	FDA approved TALZENNA (Talazoparib) is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer.

Olaparib*#	FDA approved Lynparza (Olaparib) is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated as monotherapy in patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have previously been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine treatment. FDA approved Lynparza (Olaparib) is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated: 1. for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated (gBRCAm or sBRCAm) advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy; 2. for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy; 3. for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. NMPA approved Olaparib for maintenance treatment of platinum-sensitive regenerative epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer in adult patients after complete or partial remission of platinum-containing chemotherapy.

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
NCT03565991	A Phase II Study to Evaluate Safety and Anti-tumor Activity of Avelumab in Combination with Talazoparib in Patients with BRCA or ATM Mutant Tumors	Locally Advanced or Metastatic Solid Tumors with BRCA or ATM mutant	Phase II	Avelumab + Talazoparib (MSB0010718C + BMN673)	United States; United Kingdom; Japan; etc.
NCT02029001	A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients with Progressive Locally-advanced or Metastatic Solid Tumors	Malignant Solid Neoplasms	Phase II	**Olaparib* (AZD2281 | KU0059436)**	France
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	Advanced Solid Tumors	Phase II	**Olaparib* (AZD2281 | KU0059436)**	United States
NCT02465060	Molecular Analysis for Therapy Choice (MATCH)	Advanced Malignant Solid Neoplasm	Phase II	Adavosertib (AZD1775 | MK1775)	Puerto Rico; United States

NCT02286687	Phase II Study of the PARP Inhibitor Talazoparib in Advanced Cancer Patients with Somatic Alterations in BRCA1/2, Mutations/Deletions in other BRCA Pathway Genes and Germline Mutation in BRCA1/2 (Not Breast or Ovarian Cancer)	Advanced Cancers	Phase II	**Talazoparib (BMN673)**	United States
NCT01434316	Phase 1 Trial of ABT888 and SCH727965 in Patients with Advanced Solid Tumors	Advanced Malignant Solid Neoplasm	Phase I	Veliparib + Dinaciclib (ABT888 + SCH727965)	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	AG	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	AG	Genotype GG is associated with decreased severity of Drug Toxicity when treated with fluorouracil and leucovorin in people with	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
				Colorectal Neoplasms as compared to genotypes AA + AG. [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 Neoplasms as compared to genotypes GG + AG. [PMID:19203783]	2A
Cisplatin,	ERCC1	rs11615	GG	Patients with the GG genotype and Ovarian	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
Cyclophosphamide				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]	
Cisplatin, Cyclophosphamide	XRCC1	rs25487	CC	Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:22188361]	2B
Cyclophosphamide	MTHFR	rs1801133	AG	AG: Patients with the AG 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	CC	CC: Patients with the CC genotype may have 1) increased survival and 2) increased risk of severe neutropenia when treated with cyclophosphamide-containing chemotherapy regimens as compared to patients with the CT or TT 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]	3
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	2A

Chemotherapy		Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
					(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]	
Irinotecan		UGT1A1	rs4148323	GG	GG: Patients with the GG genotype with cancer who are treated with irinotecan-based regimens may have a decreased risk of neutropenia as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's risk of neutropenia. [PMID:19390945]	2A
Irinotecan		C8orf34	rs1517114	CG	CG: Patients with the CG genotype may have increased severity of Diarrhea when treated with irinotecan in people with Non-Small-Cell Lung Carcinoma as compared to patients with the GG 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 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]	3
Fluorouracil	Fluorouracil	MTHFR	rs1801133	AG	AG: Cancer patients with the AG genotype may have increased risk of drug toxicities when treated	3

Chemotherapy		Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
					with fluorouracil- or capecitabine-based therapy as compared to patients with the GG genotype, or a decreased risk of drug toxicities as compared to patients with the AA genotype. 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]	
Fluorouracil	Capecitabine	MTHFR	rs1801133	AG	AG: Cancer patients with the AG genotype may have increased risk of drug toxicities when treated with fluorouracil- or capecitabine-based therapy as compared to patients with the GG genotype, or a decreased risk of drug toxicities as compared to patients with the AA genotype. 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	GT	GT: Patients with the GT genotype may have an increased risk for toxicity with cisplatin treatment, including hearing loss and neutropenia, as compared to patients with the TT genotype. Other genetic and clinical factors may also influence a patient's risk for toxicity. [PMID:21047201] [PMID:19434073]	1B
Platinum	Cisplatin	XRCC1	rs25487	CC	CC: Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:19786980]	2B
Platinum	Cisplatin	GSTP1	rs1695	AA	AA: Allele G is associated with decreased risk of Neutropenia when treated with Platinum	3

Chemotherapy		Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
					compounds in people with Carcinoma, Non-Small-Cell Lung as compared to allele A. [PMID:17409936]	
Platinum	Cisplatin	MTHFR	rs1801133	AG	AG: Patients with the AG 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 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	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Toxicity	Evidence Level
				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	GG	Patients with the GG genotype and colorectal cancer who are receiving FOLFOX/XELOX regimens may have a poorer response rate as compared to patients with the GT or TT 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	AG	Patients with genotype AG and colonic neoplasms may have decreased response to fluorouracil, leucovorin and oxaliplatin (FOLFOX therapy) as compared to patients with genotypes GG. However, other studies showed an increased response to oxaliplatin. [PMID:24980946]	3
Fluorouracil, Leucovorin, Oxaliplatin	XRCC1	rs25487	CC	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 may also influence response to treatment.	3

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				[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	AG	Patients with genotype AG and colonic neoplasms may have decreased response to fluorouracil, leucovorin and oxaliplatin (FOLFOX therapy) as compared to patients with genotypes GG. However, other studies showed an increased response to oxaliplatin. [PMID:24980946]	3
Carboplatin, Docetaxel	MTHFR	rs1801133	AG	Patients with AG 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	CC	Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:24446315]	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
Cisplatin, Docetaxel	MTHFR	rs1801133	AG	Patients with AG 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	AG	Patients with AG 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 may also influence a patient's response to platinum-based chemotherapy. [PMID:25069034]	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
Cisplatin/Carboplatin, Paclitaxel	XRCC1	rs25487	CC	Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:24446315]	2B
Cisplatin/Carboplatin, Paclitaxel	MTHFR	rs1801133	AG	Patients with AG 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	AG	Patients with AG 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
Cisplatin/Carboplatin, Vinorelbine	ERCC1	rs11615	GG	Patients with the GG genotype may have 1) decreased but not absent risk for toxicity, 2)	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				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]	
Cisplatin/Carboplatin, Vinorelbine	XRCC1	rs25487	CC	Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:24446315]	2B
Cisplatin/Carboplatin, Vinorelbine	MTHFR	rs1801133	AG	Patients with AG 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 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]	2A
Cyclophosphamide,	GSTP1	rs1695	AA	Patients with the AA genotype and Breast	2A

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
Epirubicin				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]	
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, 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	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				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	CC	Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. 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 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, 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	2B

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				Neoplasms as compared to genotype AA. [PMID:22026922]	
Cisplatin, Docetaxel, Gemcitabine, Capecitabine	XRCC1	rs25487	CC	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	CC	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
Alkylating Agents	NQO1	rs1800566	AG	AG: Patients with the AG genotype and cancer who are treated with chemotherapy regimens that include platinum compounds, anthracyclines and related substances, and nucleoside inhibitors may have a better outcome (overall survival and progression-free survival) as compared to patients with the AA genotype and a worse outcome as compared to patients with the GG genotype. However, this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's treatment outcome. [PMID:18511948]	2A
Anthracyclines and related substances	NQO1	rs1800566	AG	AG: Patients with the AG genotype and cancer who are treated with chemotherapy regimens that include platinum compounds, anthracyclines and related substances, and nucleoside inhibitors may have a better outcome (overall survival and progression-free survival) as compared to patients with the AA genotype and a worse	2A

Chemotherapy		Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
					outcome as compared to patients with the GG genotype. However, this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's treatment outcome. [PMID:18511948]	
Cyclophosphamide		XRCC1	rs25487	CC	CC: Patients with the CC genotype may have 1) increased survival and 2) increased risk of severe neutropenia when treated with cyclophosphamide-containing chemotherapy regimens as compared to patients with the CT or TT 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:22188361]	3
Pemetrexed		MTHFR	rs1801133	AG	AG: Patients with the AG genotype and lung cancer may have a shorter overall survival time when treated with pemetrexed as compared to patients with the GG genotype. Other genetic and clinical factors may also influence overall survival time. [PMID:24732178]	3
Fluorouracil/	Fluorouracil	NQO1	rs1800566	AG	AG: Patients with the AG genotype and cancer who are treated with chemotherapy regimens that include platinum compounds, anthracyclines and related substances, and nucleoside inhibitors may have a better outcome (overall survival and progression-free survival) as compared to patients with the AA genotype and a worse outcome as compared to patients with the GG genotype. However, this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's treatment outcome. [PMID:18511948]	2A
Platinum/	Carboplatin	MTHFR	rs1801133	AG	AG: Patients with AG 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.	2A

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:21605004] [PMID:19307503]	
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	CC	CC: Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:24446315]CC: Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:25025378] [PMID:22188361] [PMID:22026922] [PMID:16875718]	2B
Platinum/	Cisplatin	XRCC1	rs25487	CC	CC: Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when	2B

Chemotherapy		Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
					treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:24446315]CC: Patients with the CC genotype may have 1) increased survival and response and 2) increased risk of severe neutropenia when treated with platinum-based regimens as compared to patients with the CT or TT genotype. However, one study found decreased survival and response for patients with the CC genotype. Other genetic and clinical factors may also influence response to platinum-based regimens. [PMID:25025378] [PMID:22188361] [PMID:22026922] [PMID:16875718]	
Platinum/	Cisplatin	MTHFR	rs1801133	AG	AG: Patients with the AG 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	CC	CC: 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. [PMID:21057378]	2B
Platinum/	Platinum	NQO1	rs1800566	AG	AG: Patients with the AG genotype and cancer who are treated with chemotherapy regimens that include platinum compounds, anthracyclines and related substances, and nucleoside inhibitors may have a better	2A

Chemotherapy	Gene	Mutation Site	Genotype	Potential Relevance to Chemotherapy Efficacy	Evidence Level
				outcome (overall survival and progression-free survival) as compared to patients with the AA genotype and a worse outcome as compared to patients with the GG genotype. However, this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's treatment outcome. [PMID:18511948]	

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						