آنکوژن یار
OncoGeneAid

"آنکوژن" امکان درمان هدفمند
را برای بیماران فراهم می‌کند.

GENETIC TESTING REPORT FOR

General Information

Patient:	[redacted]	**Gender:**	Male
Age:	16	**Clinic/Hospital:**	[redacted]
Diagnosis:	ALL	**Sample Type:**	Blood

TEST CONTENT:
OncoGene PGx analyzes cancer-related SNVs by microarray, providing the latest therapeutic knowledge.

Expert Recommendations

This patient shows decreased risk of hepatotoxicity to asparaginase (and cyclophosphamide, daunorubicin and vincristine in remission induction treatment) and increased drug response to cyclophosphamide.

In this patient ACT must be considered and cardio vascular monitoring is necessary when treated by daunorubicin and doxorubicin.

Dosage (Mercaptopurine): Use standard dose

Start with normal starting dose (e.g., 75 mg/m2/day or 1.5 mg/kg/day) and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow at least 2 weeks to reach steady-state after each dose adjustment.

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GUIDANCE FOR CHEMOTHERAPY

Therapeutic Effect Prediction	High Drug Sensitivity	Low Risk for Toxicity	Low Drug Sensitivity	High Risk for Toxicity
Drugs recommended byNCCN (for Patient'sCancer)	None	None	None	None
Drugs recommended by NCCN (for Other Cancer)	None	None	None	None
Drugs recommended by Studies (for Patient's Cancer)	Methotrexate	Asparginase, Cyclophosphamide, Mercaptopurine, Vincristine	None	Daunorubicin, Doxorubicin, Methotrexate
Drugs recommended by Studies (for Other Cancer)	Cyclophosphamide	Cyclophosphamide	None	None

Note:

1. Principle of Response Prediction: When more than 70% variation in the results evidence to support low risk for toxicity or high drug sensitivity / high risk for toxicity or low drug sensitivity, the test results could be marked as low risk for toxicity or high drug sensitivity / high risk for toxicity or low drug sensitivity ;

2. The above conclusion are all laboratory test data, for counselling references ONLY and is not intended for diagnostic purpose. All information should be interpret by a qualified healthcare professional.

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Potential Clinical Outcomes

Drug	Potential Clinical Benefit	Potential Lack of Clinical Benefit
Asparginase	Decreased Risk of Hepatotoxicity	
Daunorubicin	Decreased Risk of Hepatotoxicity	Increased Risk of ACT
Doxorubicin		Increased Risk of ACT
Mercaptopurine	Decreased Risk of Toxicity Decreased Risk of Leukopenia Decreased Risk of Neutropenia Decreased Risk of Alopecia	
Methotrexate	Increased Speed of Platelet Recovery Increased Response	Increased Risk of Toxicity Increased Risk of Folate Deficiency
Vincristine	Decreased Risk of Hepatotoxicity	
Cyclophosphamide	Decreased Severity of Toxicity Decreased Risk of Hepatotoxicity	

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Methods and Limitations

OncoGene PGx is designed to analyze SNVs in patient's genome. The assay will be updated periodically to reflect new knowledge about cancer biology. OncoGene PGx provides interpretation on 100+ drugs including 81 FDA-approved targeted therapies, 17 FDA-approved chemotherapies and 6 immunotherapies.

Please Note:

This test is based on microarray technology. It may not provide detection of certain genes or portions of certain genes due to local sequence characteristics or the presence of closely related pseudo genes. The conclusions are based on the current scientific research all over the world and the references for clinical diagnosis, treatments, detection. The results are for reference only. Should there be any queries, please kindly contact your genetic consultant.

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Predictions

Drug	Biomarker	Genotype	Prediction	Level
Asparaginase	PNPLA3 (rs738409)	CC	CC: Patients with the CC genotype may have decreased risk of hepatotoxicity when treated with remission induction therapy (including asparaginase) in children with acute lymphoblastic leukemia (ALL) as compared to patients with genotype GG or CG. Other genetic and clinical factors may also influence the risk of toxicity to remission induction therapy.	2B
Daunorubicin	RARG (rs2229774)	AG	AG: Patients with the AG genotype may have increased risk of developing ACT (Anthracycline-induced cardiotoxicity) when treated with anthracycline in childhood cancer as compared to patients with genotype GG. Other genetic and clinical factors may also influence a patient's risk of Anthracycline-induced cardiotoxicity.	CPNDS
Daunorubicin	PNPLA3 (rs738409)	CC	CC: Patients with the CC genotype may have decreased risk of hepatotoxicity when treated with remission induction therapy (including asparaginase) in children with acute lymphoblastic leukemia (ALL) as compared to patients with genotype GG or CG. Other genetic and clinical factors may also influence the risk of toxicity to remission induction therapy.	2B
Doxorubicin	RARG (rs2229774)	AG	AG: Patients with the AG genotype may have increased risk of developing ACT (Anthracycline-induced cardiotoxicity) when treated with anthracycline in childhood cancer as compared to patients with genotype GG. Other genetic and clinical factors may also influence a patient's risk of Anthracycline-induced cardiotoxicity.	CPNDS
Mercaptopurine	NUDT15 (rs116855232)	CC	CC: Patients with the CC genotype who are treated with thiopurines for inflammatory bowel diseases (IBD) or acute lymphoblastic leukemia (ALL) may have a reduced, but not absent risk of developing leukopenia, neutropenia or alopecia as compared to patients with the CT or TT genotype. Patients may also tolerate higher doses of thiopurines and be less likely to discontinue thiopurine treatment as compared to patients with the CT or TT genotype, possibly due to the reduced risk for adverse effects. Other genetic and clinical factors may also influence a patient's risk for leukopenia, alopecia or treatment discontinuation.	1A
Mercaptopurine	TPMT	TPMT	*1/*1: Patients with the *1/*1 genotype 1) may	1A

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		*1/*1	have increased inactivation of thiopurines due to normal TPMT activity and 2) may have a decreased risk for toxicity when receiving thiopurine drugs and purine analogues as compared to patients with a non-functional allele (e.g. *2, *3A, *3B, *3C, *4). Patients with the *1/*1 genotype may still be at risk for toxicity when taking thiopurine drugs and purine analogues based upon their genotypes. Other genetic and clinical factors may also influence a patient's risk for toxicity.	
Mercaptopurine	TPMT NUDT15	TPMT *1/*1 NUDT15 *1/*1	Use standard dose: Start with normal starting dosea (e.g., 75 mg/m2/day or 1.5 mg/kg/day) and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow at least 2 weeks to reach steady-state after each dose adjustment.	CPIC
Mercaptopurine	NUDT15	NUDT15 *1/*1	*1/*1: Patients with acute lymphoblastic leukemia (ALL) and the NUDT15*1/*1 genotype who are treated with mercaptopurine may tolerate higher doses of mercaptopurine, and suffer fewer toxic effects as compared to patients with NUDT15*2, *3, *4, *5, or *6 alleles. Other genetic and clinical factors may also influence dose of mercaptopurine and incidence of toxicity in patients with ALL.	2B
Methotrexate	ABCB1 (rs1045642)	AG	AG: Patients with the AG genotype and lymphoma or leukemia who are treated with methotrexate may have an increased risk of toxicity as compared to patients with the GG genotype, or a decreased risk of toxicity as compared to patients with the AA genotype, although this is contradicted in some studies. Other genetic and clinical factors may also influence a patient's risk of methotrexate-induced toxicities.	2A
Methotrexate	MTHFR (rs1801133)	AG	AG: Patients with the AG genotype and leukemia or lymphoma who are treated with methotrexate: 1) may have poorer response to treatment 2) may be at increased risk of toxicity 3) may require a lower dose of methotrexate, and 4) may be at greater risk of folate deficiency as compared to patients with the GG genotype, or 1) may have better response to treatment 2) may be at decreased risk of toxicity, and 3) may require a higher dose of methotrexate as compared to patients with the AA genotype. This association has been contradicted or not found in multiple studies. Other genetic and clinical factors may also influence a patient's risk for toxicity and response with methotrexate treatment.	2A

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Methotrexate	MTRR (rs1801394)	AG	AG: Pediatric ALL patients with AG genotypes may have increased likelihood of methotrexate induced toxicity (oral mucositis), increased speed of platelet recovery, increased response and increased catalytic activity of TYMS in lymphoblasts when treated with methotrexate as compared to patients with the AA genotype. Allele G is not associated with decreased IQ in pediatric ALL patients treated with methotrexate. Other genetic and clinical factors may also influence response to methotrexate.	2B
Vincristine	PNPLA3 (rs738409)	CC	CC: Patients with the CC genotype may have decreased risk of hepatotoxicity when treated with remission induction therapy (including asparaginase) in children with acute lymphoblastic leukemia (ALL) as compared to patients with genotype GG or CG. Other genetic and clinical factors may also influence the risk of toxicity to remission induction therapy.	2B
Cyclophosphamide	GSTP1 (rs1695)	AG	AG: Patients with the AG 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 fluorouracilOther genetic and clinical factors may influence a patient's response to cyclophosphamide, epirubicin and fluorouracil.	2A
Cyclophosphamide	PNPLA3 (rs738409)	CC	CC: Patients with the CC genotype may have decreased risk of hepatotoxicity when treated with remission induction therapy (including asparaginase) in children with acute lymphoblastic leukemia (ALL) as compared to patients with genotype GG or CG. Other genetic and clinical factors may also influence the risk of toxicity to remission induction therapy.	2B

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Levels of Evidence

Levels of Evidence	Description
Level 1A	Annotation for a variant-drug combination 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 combination 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 combination 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 pharmacogenes, so functional significance is more likely.
Level 2B	Annotation for a variant-drug combination with moderate evidence of an 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.
CPNDS	Canadian Pharmacogenomics Network for Drug Safety
CPIC	Clinical Pharmacogenetic Implementation Consortium

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