

Patient Name		Affix barcode label of Patient's sample here
Date of Birth		

Form instructions:

- ✓ Review the information on pages 2-4
- ✓ The patient or legal guardian must sign on page 1

Patient Consent

I have discussed the OncoAlly™ Solid Tumor Analysis with my healthcare provider including the purpose and procedure, risks, benefits and alternatives. I have been given an opportunity to ask questions about the test, and any questions I had were answered to my satisfaction. I acknowledge that I have sufficient information and understanding to give this informed consent.

1. I give permission to Variantyx and their affiliates to perform sample preparation and testing as applicable.
2. I give permission for my genetic materials to be used by Variantyx and their affiliates for test development or improvement, internal validation, orthogonal variant confirmation at an outside referral laboratory and/or for quality assurance and training purposes. If FFPE blocks are provided, the block will be returned. If slides are provided, unused slides will not be returned and may be used for research purposes by Variantyx.
3. I give permission for my anonymized sample and clinical information to be included in variant and allele frequency databases and publications. My name or other personal identifying information will not be used in, or linked to, any databases or publications.
4. In the case of direct insurance billing: I acknowledge that the information provided by me is true and correct. I authorize my healthcare provider and/or insurer to share medical information with Variantyx related to my condition, diagnosis and treatment as relevant to my genetic testing, as well as information about my healthcare plan benefits. I authorize Variantyx to release my medical information concerning my testing to my insurer. I authorize Variantyx to be my designated representative for purposes of appealing any denial of benefits as needed and to request additional medical records for this purpose. I understand that Variantyx will notify me if my out of pocket costs are determined to exceed \$100. I authorize my insurance benefits to be paid directly to Variantyx. I understand that I am responsible for sending Variantyx any and all of the money that I receive directly from my insurer in payment for this test.
5. In the case that independent pre-test and/or post-test genetic counseling is required by my insurance provider and/or physician, I agree, by signing this consent form, to have a third party facilitate the genetic counseling services. By signing this consent form, I authorize Variantyx to release my contact information and any medical information necessary to the third party service, as well as authorize communication and sharing of information between the third party and my referring physician, in order to complete pre-test and/or post-test genetic counseling.
6. I give / do not give permission for Variantyx to contact me / or my healthcare provider about research studies. If no option is selected, no contact will be made.
8. For NY state residents : By checking this box I give permission for Variantyx and their affiliates to retain any remaining sample longer than 60 days for test completion, test development/improvement, internal validation, orthogonal variant confirmation at an outside referral laboratory and/or quality assurance and training purposes.

Patient (or authorized individual) first name	Last name
Patient (or authorized individual) signature	Date



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Test Information

OncoAlly™ Solid Tumor Analysis Test Description

Background

The OncoAlly™ Solid Tumor Analysis is an oncology treatment optimization and therapy association analysis based on comprehensive molecular profiling of tumor and normal tissue. The test includes DNA sequence analysis (single nucleotide variants, deletions/insertions), duplication/deletions, copy number variants (CNVs), onco-pharmacogenomic variants, microsatellite instability status, HPV integration and tumor mutational burden, and RNA analysis, which detects gene fusions and complex rearrangements.

The test identifies and associates treatment, including specific therapies and available clinical trials, in accordance with approved protocols, genomic profiling results and the patient's medical information. The test is not conclusive or prescriptive for the labeled use of any specific therapeutic product. Therefore, this test does not warrant that any particular drug will be effective in the treatment of a disease in any patient. The information provided in the report is applicable and current as of the date the report was issued. While every effort is made to ensure the accuracy of the information contained in this report, the information available in the public domain is continually updated and it is recommended that the ordering clinician review databases for updates. Clinical trials listed in this report may have additional enrollment criteria that may require additional medical screening to determine final eligibility. For information about listed clinical trials, please see clinicaltrials.gov

Methods

Nucleic acids are isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue and normal blood samples and sequenced using next generation sequencing methods. Analyses are performed to detect, analyze and report clinically relevant variants using the Variantyx Claudia for Genomics™ platform. Minimum average on-target read depth coverages are: tumor FFPE by whole genome sequencing, 20X; matched normal blood whole genome sequencing, 20X; tumor FFPE by whole exome sequencing, 200X; matched normal blood whole exome sequencing, 80X; and tumor FFPE RNA sequencing, 60X.

Report Standards

Sequence variation is compared to reference data using genome build GRCh37/hg19. Variants are classified using in-house developed procedures, including the review of applicable functional studies. Benign and likely benign variants are not reported. Pathogenic, likely pathogenic and variants of uncertain clinical significance are reported.

Variant-Drug Association Levels of evidence (LOE) are assigned based on reported pre-clinical or clinical sensitivity to treatment with a specific therapy. The classifications are derived from internally developed protocols based on the recommendations by the FDA, NCCN guidelines, or outcome reports. Predictive drug responses are assigned levels 1, 2A, 2B, 3A, 3B, or 4. Biomarkers predictive of resistance (R) to drugs are assigned R1, or R2. Associations are reported in the absence of known variants conferring resistance (level R1 and the highest level of R2).

Associations with clinical trials are based on a patient's unique genomic profile, and will include title, reference number, therapy, and geographic location. Clinical trials are selected based on a biomarker or a combination of biomarkers that are linked to a drug either directly, by pathway, or synthetic lethality. Additionally, trials are matched based on patient age, cancer type, and history of neoadjuvant or adjuvant therapy including radiotherapy. Investigational therapies are associated if the clinical trial matches with the patient's tumor profile. Trial enrollment is not guaranteed and is subject to the trial's inclusion and exclusion criteria and is depending on the approval by the study director.

The onco-pharmacogenomic variant analysis identifies common variants associated with drug metabolism and pharmacogenetic response of cancer-related drugs. The test includes sequence variants of alleles in nine genes that were recommended by the FDA or CPIC for predicted adverse drug reactions and drug response, or that had significant clinical data that supported the variant-drug association.

Limitations of testing

A lack of association in this analysis does not rule out the possibility that the tested individual carries a variant below the limit of detection. All next generation sequencing (NGS) technologies, including whole genome sequencing analysis, whole exome sequencing and RNA sequencing may generate false positive and false negative results. Results are applicable to the tissue type used for this sequence test and may not reflect variation in other tissue types. Each individual may have slightly different coverage yield distributions within the genome. Genetic aberrations, such as gross genomic rearrangements or variants in portions of genes with highly homologous pseudogenes may not be identified. Variants are not reported if they are not uniquely mappable, are of low coverage or are otherwise determined to be of low quality. Variantyx is not responsible for specimen errors (e.g. labeling, extraction) of samples received that may have occurred prior to our receipt. Variants are not confirmed unless stated and confirmations are not included in published turnaround times. Deletions, duplications and copy number variants between 50 and 300 nucleotides are detected with a lower sensitivity.

Accurate interpretation of results is dependent on complete and accurate patient health information. If an NCI cancer code was not selected by the ordering physician, the closest code will be added by Variantyx according to NCI Thesaurus.

Viral sequences, such as HPV, will be reported as a diagnostic and/or prognostic factor only with a relevant clinical diagnosis. PD-L1 will be reported if opted-in or if previous report results from CLIA licensed laboratory have been provided. If PD-L1 was not opted-in or previous results were not provided some therapy association will not be reported.

Specimens that underwent decalcification procedures (with strong acids) are not suitable for molecular testing and may fail QC. If mild and brief decalcifications with EDTA or weak acids were performed, please inquire with the lab. HPV status will be reported only for: anal, penile, vulvar, cervical, head and neck squamous cell carcinomas (HNSCCs) and rectal malignancies.



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Test Information

For the onco-pharmacogenomic variant analysis, the information provided in the report does not contain medication recommendations, and any dosage adjustments or other changes to medications should be evaluated by the ordering healthcare provider with consideration of current prescriptions, family and patient's history, presenting symptoms and other factors. The detection or absence of results does not replace the need for therapeutic monitoring by healthcare providers.

OncoAlly™ Cancer predisposition

Background

The purpose of this genetic testing is to identify changes in the DNA sequence that have been reported to increase the risk related to cancer. The resulting data is subjected to in-silico analyses optimized for small sequence changes (single nucleotide variants and deletion/insertions), structural variants in chromosomes (deletions, duplications, mobile element insertions, inversions). Variantyx reviews clinical notes and pathology reports, provided with the test submission.

Methods

Whole genome sequencing is performed on DNA isolated from blood samples using next generation sequencing methods. Analyses are performed to detect, analyze and report clinically relevant variants using the Variantyx Genomic Intelligence® platform.

Report standards

Test results will be issued as a separate clinical report for the patient to identify variants in genes consistent with a germline predisposition to cancer. Sequence variation is compared to reference data using genome build GRCh38. The following types of variants will be considered: variants in genes consistent with predisposition to cancer. Pathogenic, likely pathogenic and variants of uncertain clinical significance are reported. Individuals with pathogenic or likely pathogenic variants may wish to consider further independent consultation with their physician or genetic counselor. Variants of uncertain clinical significance are genetic variations that were identified, but based on available information in the medical literature, and research and scientific databases, it is not certain whether the variant is consistent with cancer predisposition. The uncertainty may be resolved over time if additional information becomes available. Periodic reanalysis of the sequence data or further analysis, including testing of additional family members, may be recommended. When no genetic variant consistent with cancer predisposition was identified by this test, it reduces the likelihood of, but does not exclude the possibility of, the disorder being genetic in nature.

Single Nucleotide Variants

Single nucleotide variants and small deletion/insertions (<50 bp) are reported if they are pathogenic, likely pathogenic or variant of uncertain clinical significance in a set of selected genes.

Structural Variants

Intra- and inter-genic deletions and/or duplications, mobile element insertions, inversions are reported if they are pathogenic, likely pathogenic, or variants of uncertain significance in a set of selected genes.

Technical Limitations

Genetic testing is accurate, but may not always identify a genetic variant. This test evaluates selected genes from genome sequence results, but may not be able to detect all DNA changes due to limitations in current technology. Certain regions of the DNA may not be well covered. Certain variant types may not be detectable such as methylation abnormalities, variants in genes with highly homologous pseudogenes, and variants in regions that are difficult to assay based on current technology. Unusual circumstances including bone marrow transplantation, recent blood transfusion, and variants that exist in only a small fraction of cells (mosaicism) may interfere with variant identification. Additionally, interpretation of the results is limited by the current medical understanding of disease and available scientific information. This test does not consider somatic mutations. This test requires high-quality DNA. In some cases, an additional sample may be needed if the volume, quality and/or condition of the initial sample is not adequate. Variants are not confirmed unless stated and confirmations are not part of the test turn-around time.

Additionally, interpretation of the results is limited by the current medical understanding of disease and available scientific information. This test requires high-quality DNA. In some cases, an additional sample may be needed if the volume, quality and/or condition of the initial sample is not sufficient. Samples submitted as genomic DNA will only be processed if the extraction was performed in a CLIA/CAP accredited laboratory.

Genomic Unity® Pharmacogenomics Analysis

Background

The Genomic Unity® Pharmacogenomics Analysis is a whole genome based test designed to identify common variants associated with drug metabolism and pharmacogenetic response. The test includes sequence analysis of known star alleles in 13 genes and copy number variant analysis of selected genes that were recommended by the FDA for predicted adverse drug reactions and drug response.

Methods

Whole genome sequencing is performed on DNA isolated from blood samples using next generation sequencing methods. Analyses are performed to detect, analyze and report clinically relevant variants using the Variantyx Genomic Intelligence® platform.



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Report standards

Test results will be issued as a separate clinical report for the patient to identify variants in genes consistent with current FDA guidance. Sequence variation is compared to reference data using genome build GRCh38. Pharmacogenomic response is outlined by the FDA Table of Pharmacogenetic Associations (2022) and can be found at <https://www.variantyx.com/pharmacogenomics>.

Limitations

The detection or absence of results does not replace the need for therapeutic monitoring by healthcare providers. The report is based on the genotype to phenotype mappings and FDA usage guidelines and includes a set of specific genes, star alleles, and select copy number variants as described in the gene list. This test will not detect all known variants that result in altered gene activity and drug metabolism. The patient's unique genotype is only one factor used in the evaluation in drug metabolism, concentration and response. In addition, this report is limited to certain pharmacogenetic associations only and does not include all of the information necessary for safe and effective use of a drug. For example drug-drug interactions may alter the metabolizer phenotype. This test was designed to provide gene-drug associations and was not designed to diagnose health conditions. The information provided in this report does not contain medication recommendations, and any dosage adjustments or other changes to medications should be evaluated by the ordering healthcare provider with consideration of current prescriptions, family and patient's history, presenting symptoms, and other factors.

Pharmacogenomics results and recommendations are based on current guidance and are not reviewed when guidelines are updated. Patients are not notified if changes impact their results. Research data evolves and amendments to the prescribing information of the drugs listed might change over time as more information becomes available.

General Information

Patient Confidentiality

To maintain confidentiality, test results will only be released to the ordering healthcare provider or ordering laboratory, and upon the patient's request, to additional healthcare provider(s) indicated on this test requisition form. Test results will only be disclosed to others by the patient's written consent and/or if demanded by a court of competent jurisdiction. It is the patient's responsibility to consider the possible impact of test results on insurance rates, the ability to obtain disability, life or long-term care insurance and employment. The Genetic Information Non-discrimination Act (GINA), enacted by the US Federal Government, provides some protection against discrimination by health insurance companies and employers based on genetic test results, but does not cover life, disability or long-term care insurance. Information about GINA is available at <https://www.genome.gov/10002328>. Anonymized information obtained from the test may be included in variant and allele frequency databases used to help healthcare providers and scientists understand human disease, as well as in scientific publications. Names and personal identifying information will not be revealed. Separate from the above, if there are opportunities to participate in research relevant to the patient's condition, and you have consented for recontact, Variantyx may contact you or the patient's healthcare provider for research purposes.

Sample Retention

DNA extracted from submitted samples may be stored for at least 3 months following completion of testing and may be discarded thereafter. Extracted DNA is not returned unless requested prior to testing (additional fees apply). After completion of testing, DNA may be used for test development and improvement, internal validation, quality assurance and training purposes before being discarded. NY state residents: No other test shall be performed on this sample except the test ordered by the clinician, unless waived by the patient or authorized individual. In addition, the patient's biological sample will be destroyed within 60 days or upon the completion of testing, unless waived by the patient or authorized individual. Orthogonal confirmation of results at a reference lab cannot be performed unless the patient or authorized individual provides permission to do so.

Turnaround time

The turnaround time (TAT) of this test is 14 days, which begins at the time of a complete sample receipt (both tumor and normal tissue). Please note that the following scenarios will likely result in extension of the turnaround time (1) when the tumor specimen, DNA or RNA samples fail quality control and are determined to be insufficient for testing, requiring submission of a new sample; (2) If tissue was provided as block or if an H&E stained slide is missing; (3) If the wrong tissue is received. In these scenarios the TAT will be calculated from the day of the new sample receipt.

