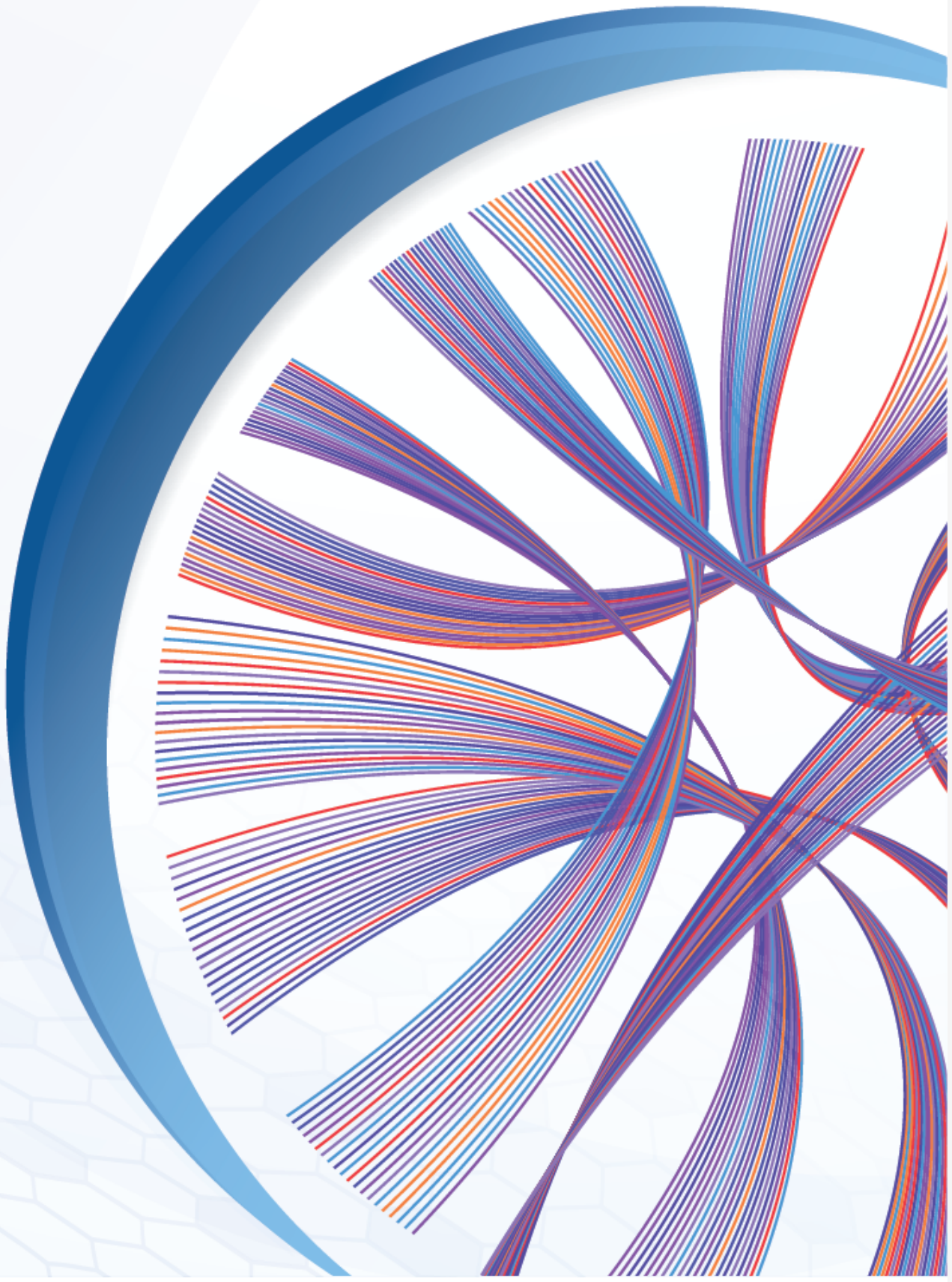
4baseCare
Together, We Beat Cancer

Homologous Recombination Repair (HRR) Germline

TEST REPORT



PATIENT ID	PATIENT NAME	REGISTRATION DATE	REPORTING DATE
IN-423-W4NJ	MAMTA GUPTA	14/04/2023	29/04/2023

SCOPE OF THE TEST

SNVs, InDels, CNAs status

GENES OF INTEREST

HBOC genes including *BRCA1* and *BRCA2*

REPORT DETAILS

Name : Mamta Gupta

Gender : Female

Age/DOB : 50 Years

Sample Source : Whole Blood

Referning Clinician : Dr. Amit Jain

Hospital : Valentis Cancer Hospital, Mussoorie Mawana Road

CLINICAL INDICATIONS / FAMILY HISTORY

High-grade serous carcinoma of ovary

	Proband	Immediate Relatives	Paternal Relatives	Maternal Relatives
Relationship	Self	-	-	-
Cancer Type	High grade serous carcinoma of ovary	-	-	-
Age at diagnosis (in years)	NA	-	-	-

RESULTS

Likely Benign/Benign/No variant Detected

Variant Details:

Clinically relevant genomic alterations associated with therapeutic significance were not detected.

*Genetic test results are reported based on the recommendations of American College of Medical Genetics [1]. Please refer to Annexure for further information

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DISCLAIMER

In absence of pedigree information, detailed curation and clinical significance could not be summarized. Please correlate clinically.

STATUS OF HRR GENES

Gene Name	Detected Mutation	Coverage(%)
ATM	Not Detected	100.00
BARD1	Not Detected	100.00
BRCA1	Not Detected	100.00
BRCA2	Not Detected	100.00
BRIP1	Not Detected	100.00
CDK12	Not Detected	100.00
CHEK1	Not Detected	100.00
CHEK2	Not Detected	100.00

Gene Name	Detected Mutation	Coverage(%)
FANCL	Not Detected	100.00
PALB2	Not Detected	100.00
PPP2R2A	Not Detected	100.00
RAD51B	Not Detected	100.00
RAD51C	Not Detected	100.00
RAD51D	Not Detected	100.00
RAD54L	Not Detected	100.00

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RESULT INTERPRETATION

A negative test result for the HRR screening indicates that the patient has no pathogenic or disease-causing mutation in any of the cancer genes associated with cancer risk that were included in the test panel. The patient might have a mutation in a gene that has not been covered in the panel or in a region excluded from the tested region, owing to test limitations. There are other factors that could play a role in developing cancer, such as environmental and lifestyle, which cause sporadic mutations.

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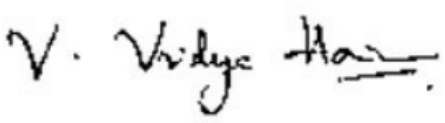

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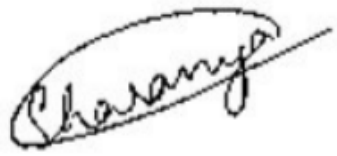

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Team Lead - Clinical Reporting

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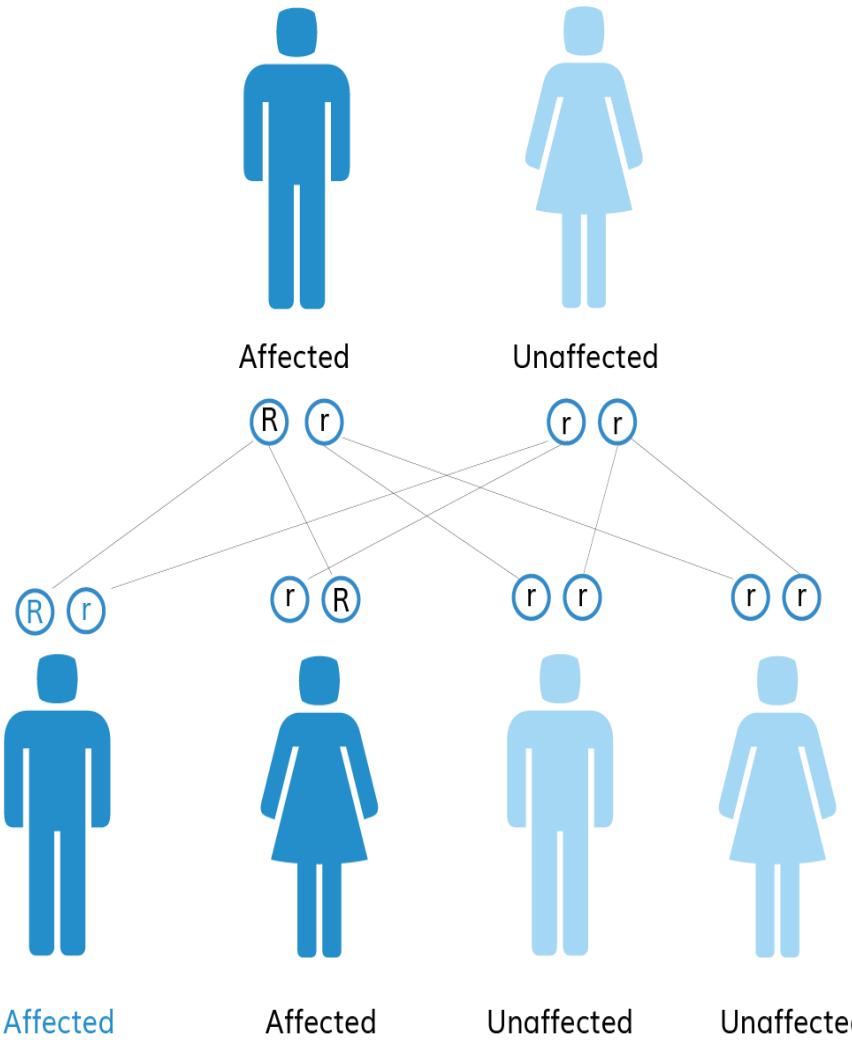
ABOUT THE TESTING

HRR Germline is 15 gene panel which targets Homologous recombination repair (HRR) genes; which are involved in repair of damaged DNA. Mutations in these genes can lead to deficiency in repair of damaged DNA. It has been established that tumors that are deficient in DNA repair mechanism, particularly the Homologous Recombination mechanism are sensitive to PARP inhibitor therapy in certain cancer types such as breast and ovarian cancers, while the clinical trials are ongoing in other cancer types such as pancreatic, prostate, endometrial and other cancers.

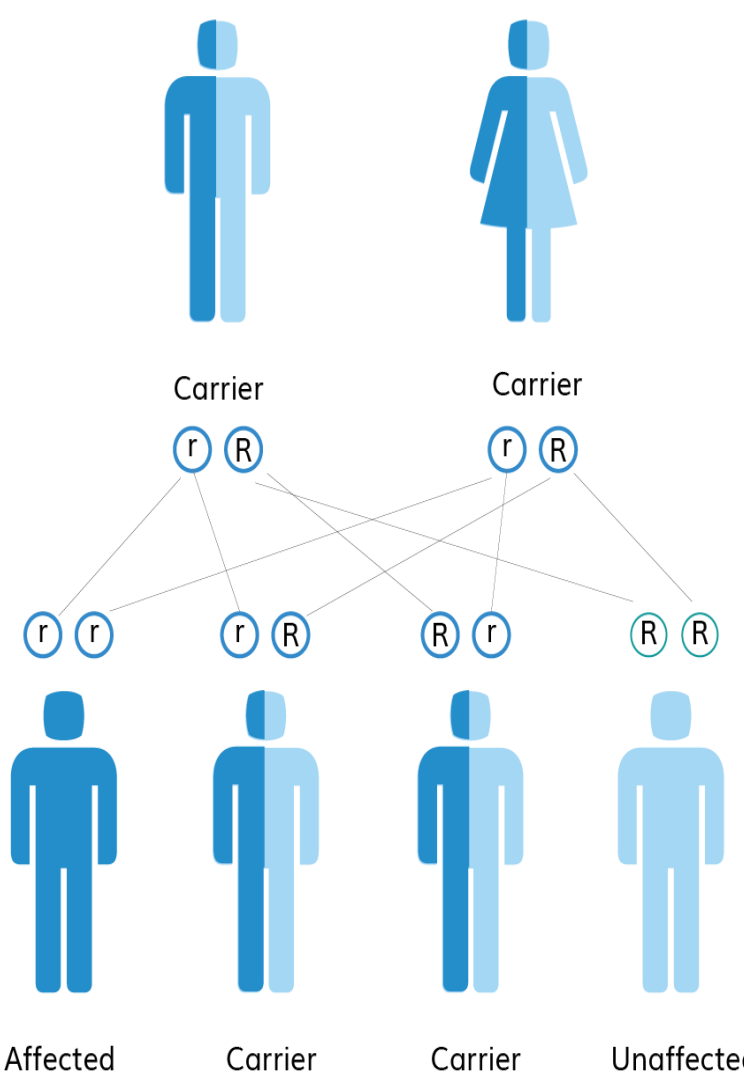
Understanding the genetic testing process and its results require support of a trained genetic counsellor. We suggest the individual to seek genetic counseling prior to consenting for any kind of genetic test to understand the purpose of the test recommended by clinician and its usefulness to the patient and their family.

Variation (fault/mutation) in certain genes can be inherited, which may sometimes cause cancer. The variations found in the genes could be pathogenic, likely pathogenic or variant of uncertain significance and may attribute to low, moderate or high risk of predisposition to cancer.

Autosomal Dominant Inheritance



Autosomal Recessive Inheritance



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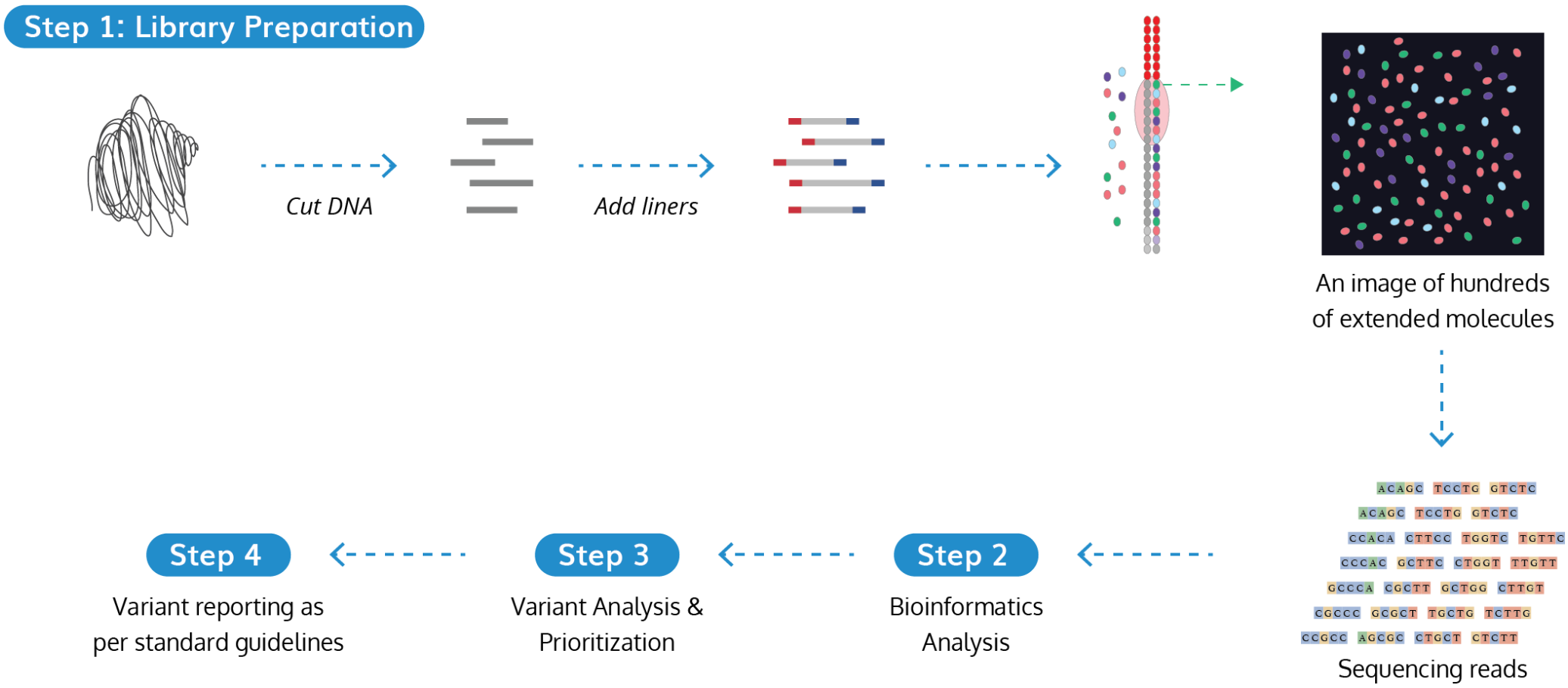
TEST METHODOLOGY

Genomic DNA is isolated from Whole Blood sample for library preparation and quantified using Qubit Fluorometer, 50 ng is taken for library preparation. The NGS libraries were prepared as per standard procedures for Illumina sequencing. The libraries were sequenced with mean coverage depth >100X.

The sequences obtained are aligned to human reference genome (GRCh37/hg19) and variant analysis was performed using set of Bioinformatics Pipeline. Only non-synonymous and splice site variants found in the exome panel consisting of specific set of genes were used for clinical interpretation. Silent variations that do not result in any change in amino acid in the coding region are not reported.

Clinically relevant mutations were annotated using published literature and a set of databases – ClinVar (Landrum et al, 2015.), cbioportal (Cerami et al, 2012; Gao et al, 2013) and dbSNP. Common variants are filtered based on allele frequency in 1000 Genome Phase 3(Auton et al, 2015), ExAC (Karczewski et al. 2016), dbSNP (Sherry et al, 2001), etc. In the absence of a clinically significant reported known variation(s), pathogenicity will be predicted based on in-silico gene prioritization tools: CADD (Rentzsch et al. 2018), SIFT (Ng PC et al, 2003), PolyPhen-2 (Adzhubei et al, 2013) and prioritized for clinical correlation. The identified pathogenic variant will be correlated with observed phenotypic features of the patient and interpreted according to American College of Medical Genetics (ACMG) guidelines.



Annexure:

The classification of the variations is done based on American College of Medical Genetics as described below

Pathogenic : A disease causing variation in a gene which can explain the patient's symptoms has been detected. This usually means that a suspected disorder for which testing had been requested has been confirmed.

Likely Pathogenic : A variant which is very likely to contribute to the development of disease. However, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion of pathogenic

Variant of Uncertain Significance : A variant has been detected, but it is difficult to classify it as either pathogenic (disease causing) or benign (non-disease causing) based on current available scientific evidence. Further testing of the patient or family members as recommended by your clinician may be needed. It is probable that their significance can be assessed only with time, subject to availability of scientific evidence.

Benign/Likely Benign : A variant termed benign has sufficient evidence that it can be concluded that the variant is not the cause of the patient's disorder. A variant termed likely benign has sufficient evidence that it can be concluded that the variant is not the cause of the patient's disorder when combined with other information.

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LIMITATIONS AND DISCLAIMER

- This test has been developed, validated and performed by 4baseCare Oncosolutions Pvt. Ltd., and this test has not been cleared or approved by the FDA..
- A comprehensive risk assessment may include other aspects of the patient's personal/family medical history, as well as lifestyle, environment and other factors. This is not included in the scope of this NGS testing.
- We are using the canonical transcript for clinical reporting which is usually the longest coding transcript with strong/multiple supporting clinical evidence. However, in rare cases, clinically relevant variants annotated in alternate complete coding transcripts could also be reported.
- Changes in personal/family history or additional data regarding specific genes/mutations may affect the cancer risk estimates and management recommendations within this report. Personal/family history should be updated with a healthcare provider on a regular basis
- Certain genes may not be covered completely, and few mutations could be missed. Many factors such as homopolymers, GC-rich regions etc. influence the quality of sequencing and coverage. This may result in an occasional error in sequence reads or lack of detection of a particular genetic alteration.
- As with any laboratory test, there is a small chance that this result may be inaccurate for a preanalytical reasons, such as an error during specimen collection and labeling (incorrect patient identification).
- Large insertions, deletions, duplications, inversions, repeat expansions and complex rearrangements cannot be characterized accurately by NGS as it uses short-read sequencing data. Such structural variants have a much higher false-positive and false-negative rate than seen for SNVs (single nucleotide variant). It is possible that the genomic region where a disease-causing variation exists in the proband was not captured using the current technologies and therefore was not detected.
- It is possible that a particular genetic abnormality may not be recognized as the underlying cause of the genetic disorder due to incomplete scientific knowledge about the function of all genes in the human genome and the impact of variants on those genes.
- Accurate interpretation of this report is dependent on detailed clinical history of the patient. In the event of unavailability of detailed clinical history, the lab cannot guarantee the accuracy of the interpretation.
- This report is strictly not a medical diagnostic report and shall not be construed as the medical certificate or medical laboratory report or diagnostic report.
- The patient’s physician may annually wish to re-analyze the results or recommend re-testing for any variants that may have been newly identified, to associate with the patient’s clinical condition. The patient or family members are recommended to consult their physician and approach us for testing services accordingly.