

***Trust Logo***

**<GLH region name>**

**NHS Genomic Laboratory Hub**

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| ***Head of Department****Name* |  | *Local Genetics Service**Local Trust**Address**Address**Post Code**Web site address* |
| General Enquiries: *telephone contact*Email: *generic email address* |
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**GENOMIC LABORATORY REPORT**

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| Dr xxx | **Patient Name:** | **Jane DOE** |
| Consultant  | Gender: | Female |
| <<Hospital address>> | Date of Birth: | 14 Jan 1968 |
| NHS No: | 123 456 7890 |
| Hospital No: | NK |
| Your ref: | GC12345 |

**Reason for testing**

Diagnostic testing. <<Referral reason>>. Patient phenotype / HPO terms

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| **Result summary** |
| **A hereditary (germline) genetic cause for the patient’s cancer has not been identified** |

**Result**

No pathogenic variants were detected in the genes in this panel.

**Implications**

This testing excludes >99% of pathogenic variants in these genes. This result does not exclude a diagnosis of autosomal dominant hereditary ovarian cancer.

As this individual does not have a detectable pathogenic variant in *BRCA1* or *BRCA2*, PARP inhibitor therapy is not currently indicated by this test in isolation.

**Recommended action**

We recommend testing of the tumour if this individual is still being considered for treatment with PARP inhibitors as ~7% of high grade serous ovarian/fallopiantube/peritoneal cancers have a somatic *BRCA1* or *BRCA2* pathogenic variant (Frugtniet *et al* 2021 PMID: 34657373).

If there is a family history of ovarian, breast and/or other cancers, further assessment by Clinical Genetics may be appropriate.

Date issued: <AUTHORISEDDATE> Authoriser: Clinical Scientist

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**TECHNICAL INFORMATION**

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| **Sequence analysis** | **Dosage analysis** |
| No pathogenic variants detected | No copy number variants detected |

**Test methodology**

1. Genes screened in the panel: *BRIP1*; *BRCA1; BRCA2; MLH1*; *MSH2*; *MSH6*; *PALB2;* *RAD51C*; *RAD51D* (all coding exons & exon-intron boundaries)

2. Enrichment method: Agilent SureSelect Custom Design and sequenced on the Illumina platform with a sensitivity of at least 95%.The target region of those selected transcripts is covered to a minimum read depth of 30x.

3. Screening for large deletions and duplications is performed using comparative depth of coverage of NGS data. Deletions/duplications are confirmed by Multiplex Ligation-Dependent Probe Amplification (MRC-Holland).

4. Variant classification according to the American College of Medical Genetics and Genomics (ACMG)1 and Association for Clinical Genomic Science (ACGS) 2020 guidelines2 and Cancer Variant Interpretation Group-UK gene-specific and consensus specification for Cancer Susceptibility Genes3 1Richards et al. (2015) Genetics in Medicine 17:405-24. (PMID 25741868) 2www.acgs.uk.com/quality/best-practice-guidelines 3Garrett et al (2020) J Med Genet (PMID: 32170000) and <https://www.cangene-canvaruk.org/canvig-uk>

5. NGS technical sensitivity may be reduced for genes with pseudogenes or paralogs, and for copy-number variation >20 nucleotides.

6. Only clinically relevant results are shown; full details of methods and results, including benign/likely benign variants and variants of uncertain clinical significance with very limited evidence for pathogenicity are available on request.

**Sample details**

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| Your lab ref: | 122001180 |  |  |
| Sample ID: | 1234567 | Sample collected: | 05 Jun 2020 |
| Sample type: | DNA from peripheral blood | Sample received: | 05 Jun 2020 |