

***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: 'test name' (Rxx.x)

**Result summary:** Inconclusive result – consider further action

**Result:** This individual is heterozygous for a germline <GENE> missense/splice/copy number variant of uncertain significance (details below).

**Implications:** This result does not exclude a diagnosis of an inherited cancer predisposition syndrome. As this individual does not have a detectable pathogenic variant in BRCA1 or BRCA2, PARP inhibitor therapy is not currently indicated by this result in isolation2.

**Recommended action:** We recommend testing of the tumour if this individual is still being considered for treatment with PARP inhibitors as ~13% of metastatic prostate cancers have a somatic BRCA1 or BRCA2 pathogenic variant (Sciarra et al 2022 PMID: 36614122).

To aid variant re-classification, further evidence is required. We recommend referral to Clinical Genetics for familial segregation analysis/(RNA studies/etc) if appropriate. Further evidence may become available about this variant in the future: if new clinical decisions based on this variant are required for this family, please request the laboratory to review this variant.

If there is a strong family history of prostate and/or other cancers, further genomic testing and assessment by Clinical Genetics may be appropriate.

Date issued: <AUTHORISEDDATE> Authoriser: Clinical Scientist

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**TECHNICAL INFORMATION**

**Variant details**

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| --- | --- | --- | --- | --- |
| Gene | Zygosity | HGVS description | Location: GRCh37 (hg19) | \*Classification |
| *GENE* | Heterozygous | NM\_xxx:c.xxxT>G | Chr17(GRCh37):g.xxxxxxA>C | Variant of uncertain significance |

1. Genes screened in R430 panel: ATM, BRCA1, BRCA2, CHEK2, MLH1, MSH2, MSH6, PALB2 (all coding exons and exon-intron boundaries). For ATM & CHEK2, only clearly truncating variants (nonsense, frameshift, ±1/2 splice & CNVs) in these genes, plus the ATM c.7271T>G p.(Val2424Gly) pathogenic missense variant, are reported.

2.The PARP inhibitor olaparib is recommended for use within the Cancer Drugs Fund as an option for maintenance treatment of BRCA mutation-positive metastatic castration-resistant prostate cancer [www.nice.org.uk/guidance/gid-ta887].

3.Enrichment method: Agilent SureSelect Custom Design and sequenced on the Illumina platform with a sensitivity of at least 95% for heterozygous SNVs. Low level/mosaic variants below 10% are not detected. The target region of selected transcripts is covered to a minimum read depth of 30x.

4.Screening for large deletions and duplications is performed using comparative depth of coverage of NGS data. The sensitivity of copy number variant detection may be reduced for exons with a high GC content. Deletions/duplications are confirmed by Multiplex Ligation-Dependent Probe Amplification (MRC-Holland).

5.Variant nomenclature and classification - see Appendix 1 overleaf. Only relevant results are shown; full details of methods and results, including benign/likely benign variants and variants of uncertain clinical significance with limited evidence, are stored on file and are available on request.