GENETIC TEST REPORT

Patient Details:

Name:	Jane Doe
Date of birth:	18 March 1970
Sex:	Female
NHS number:	NH00198
Sample type:	Blood

Test requested by:

Name:	Dr Requesta
Organisation:	Chester Hospital
Telephone:	01223 555555
Copies to:	Dr A. Nother Dr X. Tra

Test carried out by:

Laboratory:	Gentest UK
Telephone:	01223 666555
Date received:	26 February 2018
Date reported:	12 March 2018
Authorised by:	A Tester

REASON FOR TEST

A test was requested to determine if your cancer is related to alterations in the *BRCA1*, *BRCA2*, or *PALB2* genes.

ABOUT THE TEST

This test looked for alterations in specific genes that are known to increase the risk of developing particular kinds of cancers.

YOUR RESULT: An alteration called a 'variant of uncertain significance' was found in the *BRCA1* gene. At this time, we do not know if this particular alteration affects cancer risk.

WHAT THIS RESULT MEANS FOR YOU

Genes are small sections of your DNA that affect, for example, what you look like, or your chances of developing a specific health condition. The test found that you have a gene alteration which is referred to as a "variant of uncertain significance" or VUS.

Gene alterations vary. Some alterations do not affect your risk of cancer and some alterations increase your risk of cancer.

With a variant of uncertain significance, there is not enough information to know whether this particular alteration increases your risk of cancer or not.

Just as a typo in a word may or may not change a word's meaning, a variant of uncertain significance may or may not be associated with an increase in risk. Everyone has many of these "typos" in different genes, but most of the time we don't know about them.

It may be helpful to know that out of all *BRCA1* and *BRCA2* findings that are variants of uncertain significance, one estimate is that 15% to 20% are likely to cause disease, while the other 80% to 85% are not (Voelker 2019). It may also be useful to test for this alteration in other family members, as this can help with the interpretation of your result. More detail about testing family members can be found in the 'Next steps' section.

Genetic research is always moving forward and we may learn more about this alteration in the future. If so, the interpretation of these results may need to be updated.

We do not recommend any further actions beyond those on the next page of this report, unless advised by the person who requested your test.

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Name:	Jane Doe	Name:	Dr Requesta	Laboratory:	Gentest UK
Date of birth:	18 March 1970	Organisation:	Chester Hospital	Telephone:	01223 666555
Sex:	Female	Telephone:	01223 555555	Date received:	26 February 2018
NHS number:	NH00198	Copies to:	Dr A. Nother Dr X. Tra	Date reported:	12 March 2018
Sample type:	Blood			Authorised by:	A Tester

NEXT STEPS

- **If this is the first time you have heard about these results, please bring them to your GP and ask if a referral to the Clinical Genetics Service is appropriate.**
- **You are advised to contact the East Anglian Clinical Genetics Service (01223 216446) again in 2 to 3 years to see if anything has been learned that might affect the interpretation of your results. (The genetics service will not be able to contact you.) Please contact the Clinical Genetics Service if you have any questions.**
- **We do not recommend DNA testing of relatives who have not had cancer,** until there is further evidence of if your variant of uncertain significance increases your risk of cancer or not.
- However, it is possible that testing any other relatives who have had, or develop cancer may clarify whether or not this variant increases the risk of cancer. **Therefore, if your close relatives (parents, siblings or children) have had cancer in the past, or you or your relatives develop cancer in the future, please bring this report to your GP and ask if you can be referred to your local Genetics Service.**

Regardless of the result of this test, everybody is encouraged to be body aware. Both sexes, men and women, should be "chest aware", it's as simple as TLC: Touch, Look and Check. Further information about how to check your chest for signs of breast cancer can be found at: https://is.gd/nhs_uk_breast_awareness.

For females, the symptoms of ovarian cancer do vary (https://is.gd/nhs_uk_ovarian_cancer_symptoms), but some are similar to Irritable Bowel Syndrome, such as frequent bloating or discomfort in your tummy.

For males, prostate cancer symptoms are often related to urination, such as needing to pee more urgently, or more often. Further prostate cancer symptoms can be found at: https://is.gd/nhs_uk_prostate_cancer_symptom.

You are advised to report any changes or concerning symptoms to your GP.

MORE INFORMATION AND SUPPORT

If you have questions about your test result, talk to the person who requested your test. The contact details of the person who requested your test can be found in the header at the top of this page. Your GP can also phone or write to the East Anglian Clinical Genetics Service on 01223 216446 to ask for further advice to help answer your queries.

As genetic research progresses, new information about your test result may come to light. The BRCA Exchange (https://brcaexchange.org/) is one resource that can help individuals keep up to date with what is known about their particular variant. It may not contain any information on your particular variant at the moment, but the developers of BRCA Exchange recommend that people such as yourself check in with them yearly to see if anything has changed (Voelker 2019). To use the BRCA Exchange you'll need the name of your variant (for example, 'c.*123del'), which can be found on the last page of this report.

Further information about variants of uncertain significance can be found here: https://is.gd/nhs_uk_VUS

For more detailed information about genetic testing and *BRCA*, visit:

FOR **YOUR RECORDS**

Technical Information

This page provides technical details from the laboratory about the test.

Patient Details:

Name:	Jane Doe		
Date of birth:	18 March 1970	Sample type:	Blood
Sex:	Female	Sample collected:	10 March 2018
NHS number:	NH00198	Sample received:	12 March 2018

The information on this page provides technical details about the test.

TEST DETAILS FOR ORDERING CLINICIAN

Gene	Zygosity	Inheritance	HGVS Description	Location: GRCh38 (hg38)	*Classification
BRCA1	Heterozygous	Autosomal dominant	c.*872_*873del	17: 43044805-43044806	Variant of uncertain clinical significance

*Variants are classified using the current cancer specific modifications of the ACMG guidelines (http://dx.doi.org/10.1136/jmedgenet-2019-106759 Appendix 1)

- **If the patient has a family history of breast and/or ovarian cancer, and/or has a number of specific queries regarding their result, please make a referral to the Clinical Genetics Service.**
- **Advise patient to contact local genetics service in 2 to 3 years to find out if more information has become available.**
- **We do not recommend that DNA testing is offered to unaffected relatives until there is further evidence for the pathogenicity of this base change.**
- **Clinicians seeing this result in a patient's record for the first time should consider contacting the Clinical Genetics Service to see if the variant has been reclassified.**

FULL INTERPRETATION

DNA from this patient has been screened for pathogenic variants in the *BRCA1*, *BRCA2* and *PALB2* breast/ovarian cancer susceptibility genes by next generation sequencing and for large scale deletions/duplications of the *BRCA1* & *BRCA2* genes by multiplex ligation-dependent probe amplification (MLPA). A heterozygous *BRCA1* sequence variant of uncertain clinical significance, c.*872_*873del, was detected. This variant is absent from gnomAD, has not been reported on the ClinVar variant database, and to our knowledge has not previously been reported in the literature. In silico tools predict this to be a benign sequence change but based on the currently available information and classification guidelines, this variant has been classified as of uncertain clinical significance.

No other potentially pathogenic variants were detected in *BRCA1*, *BRCA2* or *PALB2* nor large scale deletion/duplication detected in *BRCA1* or *BRCA2*.

In the absence of a number of affected relatives available to test or updated information from public databases we are unlikely to be able to comment on the likely pathogenicity of this sequence change.

TEST METHODOLOGY

Fluorescent sequencing analysis using Mutation Surveyor of part of the *BRCA1* gene. Nomenclature according to GenBank accession number NM_007294.3 (*BRCA1*) where +1 is the A of the ATG translation initiation codon.

References

Voelker, R. Taking the uncertainty out of interpreting BRCA variants. JAMA. 2019;321(14):1340-1341. doi:10.1001/jama.2019.0967