GENETIC TEST REPORT

Patient Details:		Test requested by:		Test carried out by:	
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

REASON FOR TEST

Enrolled in a research study aimed at understanding the application of whole genome sequencing to clinical care.

ABOUT THE TEST

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

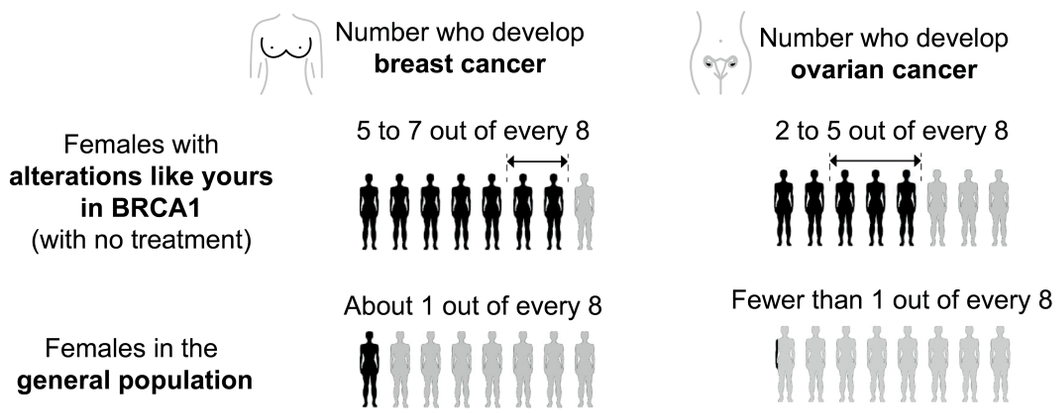
YOUR RESULT: An alteration was found in the *BRCA1* gene.

Females with this alteration have an increased risk of breast and ovarian cancer.
Males with this alteration have an increased risk of breast and possibly prostate cancer.

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 an alteration in the *BRCA1* gene. People with this alteration have an increased risk of particular kinds of cancer.

Females with this alteration are at high risk of developing breast cancer and ovarian cancer in their lifetime. Research suggests that without further treatment 65% to 79% of women with such alterations in *BRCA1* will develop breast cancer in their lifetime, and 36% to 53% will develop ovarian cancer in their lifetime.



Males with this alteration have about a 1% (10 out of every 1000) chance of developing breast cancer in their lifetime, compared to 0.1% (1 out of every 1000) in the general population. They may also have a slightly higher prostate cancer risk than the average man, though this is not conclusive.

The numbers stated here are lifetime average risks. Your personal risk depends on your age, family and medical history, and may be higher or lower than the ranges given above. Your genetic specialist can talk to you about how these factors affect your risk and what treatment options are available to you.

IF YOU HAVE CHILDREN OR BROTHERS AND SISTERS

There is a chance your children, brothers and sisters also have an alteration to the *BRCA1* gene. If you have children, each child, male and female, has a 50% (1 in 2) chance of having this alteration to *BRCA1*. Each of your full brothers and sisters, if you have any, has a 50% (1 in 2) chance of having this alteration to *BRCA1*.

FAMILY TESTING

Genetic testing is generally offered in a family step by step, starting with people who are a close relative (parents, siblings and children) of someone who has the alteration or a related type of cancer.
Male and female family members may wish to consider testing, as both men and women can pass this alteration to their children.

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NEXT STEPS

- **If this is the first time you have heard about these results and you do not already have an appointment with the Clinical Genetics service to discuss these results, please bring these results to the person who requested your test and ask for a referral. You can see who requested your test at the top of this page.** If you have been referred but no one has contacted you about an appointment date within 2 months, call the East Anglian Clinical Genetics Service on 01223 216446.

A genetic specialist will discuss these results and possible treatments with you at your appointment.

You can discuss telling your family members about your result with your genetic specialist. You don't need to tell your family members about your result straight away, if you don't feel ready to. However, if you do feel able, it can be helpful to tell a family member or friend with whom you feel comfortable, so you have some support from a loved one.

- **Family testing is generally made available step by step, starting with parents, siblings and children (over the age of 18). Clinical Genetics can advise on having these conversations with your family. Family members who want to be tested should see their GP to discuss a referral to the Clinical Genetics Service, and bring a copy of this report with them.**

Before your appointment with the Clinical Genetics Service, it may be useful for you to write down any questions you may have.

WHAT CAN BE DONE ABOUT MY CANCER RISK?

The results of a genetic test can be upsetting and difficult to take in. However, there are ways to reduce your risk. Specific recommendations depend on your age, sex, medical history, and what treatments (if any) you have had already. **Your genetic specialist will discuss your treatment options with you in more detail.**

LIFESTYLE

Not smoking, limiting alcohol consumption, maintaining a healthy weight, being physically active and eating healthily can help reduce overall risk of developing cancer.

BEING BODY AWARE

People with this alteration have an increased risk of different types of cancer so it is important 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://www.nhs.uk/common-health-questions/womens-health/how-should-i-check-my-breasts/

For females, the symptoms of ovarian cancer vary (see https://www.nhs.uk/conditions/ovarian-cancer), but some are similar to Irritable Bowel Syndrome, such as frequent bloating or discomfort in your tummy.

For males, prostate cancer symptoms often relate to urination, such as needing to pee more urgently, or more often. Further prostate cancer symptoms can be found at: https://www.nhs.uk/conditions/prostate-cancer.

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

There are other ways to reduce your risk. This may be through medications, screening or surgery; your genetic specialist will discuss your treatment options with you in more detail.

Further information on risk reduction is available at The Royal Marsden's "A beginner's guide to *BRCA1* and *BRCA2*".

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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.

Over 150,000 people in the UK are thought to have alterations to *BRCA1* or *BRCA2* that increase their risk of cancer. There are a number of charities that offer information and support for individuals who face a hereditary risk of breast and ovarian cancer.

These include:

• **Breast Cancer Now** (breastcancernow.org) provides those diagnosed with breast cancer support for the physical and emotional impacts of the disease, as well as undertaking breast cancer research, and working to improve breast cancer services.

• **Ovacome** (ovacome.org.uk) offer a range of support services to anyone affected by ovarian cancer, including women who have either been diagnosed with the disease or think that they might be at risk.

• **Macmillan Cancer Support** (macmillan.org.uk) is an organization that provides physical, financial, and emotional support to individuals who have been affected by cancer, and individuals who face a hereditary risk of cancer.
Support Line: 0808 808 00 00 (everyday 8am - 8pm)

• **BRCA Umbrella** (brcaumbrella.ning.com) is a worldwide support organisation, bringing together those dealing with a *BRCA* or other gene alteration.

For more detailed information about genetic testing and *BRCA*, visit the beginner's guide to *BRCA1* and *BRCA2*.

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.3143delG p.(Gly1048ValfsTer14)	17: 43092388	Pathogenic

*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 does not already have an appointment with the Clinical Genetics Service to discuss their result, please make a referral.**

- **Predictive testing can be offered to this patient's first degree adult relatives; we recommend that genetic counselling is given prior to DNA testing.**

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). Fluorescent sequencing has confirmed the presence of a heterozygous *BRCA1* pathogenic variant identified by next generation sequencing, c.3143delG, which is predicted to result in a truncated *BRCA1* protein, p.(Gly1048ValfsTer14).

This patient's children are at 50% risk of inheriting this *BRCA1* pathogenic variant. Relatives who inherit the familial pathogenic variant will be at increased risk of developing *BRCA1* related cancers. On average, lifetime risks for *BRCA1* carriers are 65%-79% for breast cancer and 36%-53% for ovarian cancer (Kuchenbaecker et al. 2017), but individual risks may be higher or lower than these ranges depending on age, medical history and family history.

TEST METHODOLOGY

Next generation sequencing of all coding sequence and exon/intron boundaries of *BRCA1*, *BRCA2* and *PALB2*. In house sample preparation using Nextera XT library construction protocol and sample processing; Sequencing of long range PCR products on Illumina MiSeq. We cannot completely exclude the possibility that a SNP under the primer binding site could cause allele drop out in this procedure. Fluorescent sequence analysis using Mutation Surveyor to confirm any relevant base changes identified by next generation sequencing. Multiplex ligation dependent probe amplification (MLPA) analysis of *BRCA1* (using kit P002-D1) and *BRCA2* (using kit P090-B1). Nomenclature according to GenBank accession numbers NM_007294.3 (*BRCA1*), NM_000059.3 (*BRCA2*) and NM_024675.3 (*PALB2*) where +1 is the A of the ATG translation initiation codon.

References

Kuchenbaecker, Karoline B., et al. "Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers." JAMA 317.23 (2017): 2402-2416.
https://jamanetwork.com/journals/jama/fullarticle/2632503